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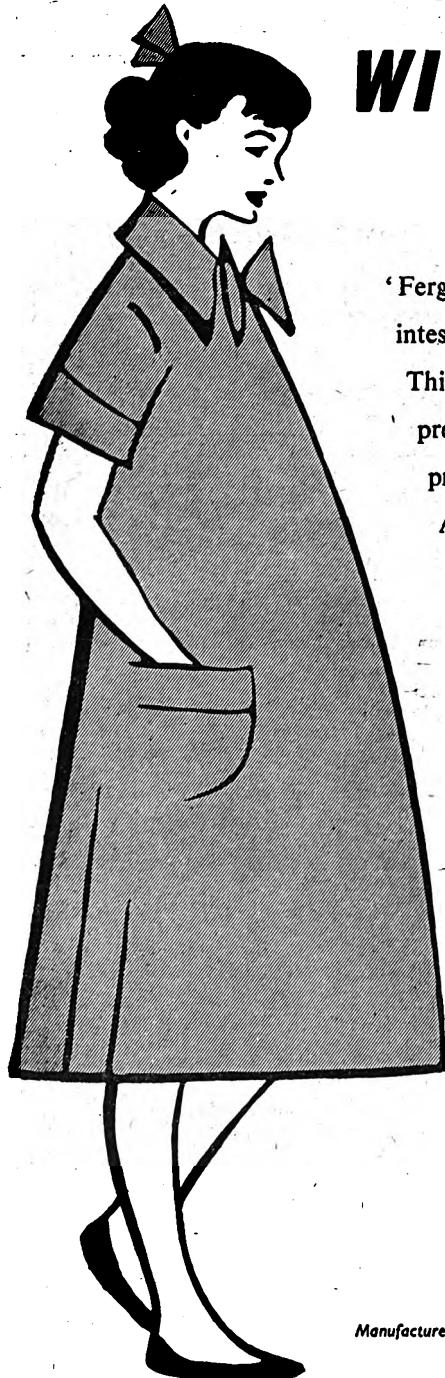
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Sir RUSSELL BRAIN

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With illustrations on plate

I HAVE chosen to talk about a particular kind of intervertebral disc lesion for several reasons. Degeneration of the intervertebral discs is responsible for a very large amount of pain, suffering, and disability, which ranges from episodes which, however painful, are comparatively short-lived, though they may be recurrent, to permanent incapacity of the most severe and disabling kind. Moreover, intervertebral disc degeneration is, on the whole, a disorder of the second half of life, occurring particularly in the fifth and sixth decades; hence, as we have an ageing population, it is steadily increasing in frequency and in social importance.

My interest in the subject has been primarily concerned with the effects of the disc degeneration upon the nervous system; but the neurological manifestations, of course, are end-results, which often declare themselves only after the disc lesion has been present for many years; so if we are to prevent these most disabling consequences of disc degeneration we must know far more than we do about the aetiology of both. For even when the disc degeneration has already occurred and brought the patient to the doctor on account of pain in the spine or its effect upon the nerve-roots or the spinal cord, we still know far too little about what is really happening, and often we have not sufficient knowledge upon which to base a rational therapy. Our problem, then, is to correlate the patient's symptoms and signs with the radiological appearance of the affected portion of the spine and both with the pathological changes which are responsible for the symptoms. For example, the patient's symptoms may be acute and severe, yet it may be difficult to detect any X-ray abnormality. At the other extreme are patients with gross radiological changes but no symptoms at all. In between fall patients who seem at first sight the easiest to understand—namely, those who have chronic symptoms associated with chronic changes as shown by the X rays; but it is equally likely that another patient with X-ray films which show apparently similar chronic changes will come to the doctor because of symptoms which are acute. These discrepancies, which could easily be multiplied, show how difficult it is in many cases to form an opinion as to the precise nature of the pathological change which is responsible for the current symptoms; and without that knowledge treatment must be, as we must admit it often is, largely empirical. Hence the differing views about the value of, and indications for, physiotherapy of various kinds, immobilisation, traction, manipulation, and operation.

Nomenclature in Relation to Pathology

I do not propose to deal with those lesions of the intervertebral discs which are produced by their invasion by neoplasms or by infection: I shall confine myself to the changes which have come to be grouped under the term "spondylosis," which, of course, implies that the lesions are degenerative and not inflammatory. This term, however, is itself deceptively simple, if it is taken to mean that we are dealing with a single pathological

process; and current terminology reflects the confusion in our ideas about the pathogenesis of what is called spondylosis. Sometimes the term "herniation" of the intervertebral discs is used and sometimes the term "protrusion"; and it is widely believed that the two are synonymous. Frykholm (1951b) points out that

"... the large amount of data available concerning the thoraco-lumbar discs cannot... be used indiscriminately to explain the pathologic condition affecting the cervical discs. The two groups differ too much both anatomically and with regard to the forces to which they are subjected. This is also apparent from the fact that in the cervical region soft nuclear herniations, similar to those in the lumbosacral region, are relatively infrequent compared to the hard and calcified types."

Nevertheless I believe that the pathological classification of cervical disc protrusions which Frykholm has himself proposed is equally applicable to intervertebral disc protrusions occurring lower in the spine, provided suitable qualifications as to their pathogenesis are introduced.

In 1948 I suggested (Brain 1948) a distinction between two main types of intervertebral disc protrusion—(1) nuclear herniations and (2) annular protrusions—and this has been confirmed by Frykholm.

Nuclear herniation probably starts with swelling of the nucleus. The annulus, which is encroached upon by the expanding nucleus, undergoes fibrillary degeneration. Its inner fibres emerge with the nucleus while its outer fibres disintegrate, as the result of which nuclear material may be extruded into one or other intervertebral foramen, or more dorsally. Bull (1948) has calculated that the total volume of the nucleus pulposus in the cervical region corresponds to that of a red currant. Theoretically, therefore, this would be the maximal size of a complete nuclear herniation. Frykholm points out, however, that the mass always contains fragments of the annulus, and in addition it has a tendency to grow in size through a process of metaplasia and the addition of new tissue. The nuclear material is replaced by fibrous and cartilaginous elements and may show evidence of inflammatory reaction. Calcification or ossification may supervene. The mass finally presents the appearance of a well-defined tumour.

The production of an *annular protrusion* is different. Owing to various factors, of which age is probably the most important, the intervertebral disc becomes dehydrated and loses its elasticity. As a result it collapses and the annulus bulges in all directions. Local bulgings may also occur at some point if the fibres of the annulus are less resistant. The protruded material becomes vascularised and its fibrous elements are increased in the same manner as in the nuclear herniation. Similarly the added tissue increases the size of the original protrusion, and again calcification or ossification may occur.

So far we have been describing the alterations which occur in the intervertebral discs themselves, but the impairment of their normal functions leads to reactive changes in the bodies of the adjacent vertebrae. These are stimulated to new bone formation—i.e., the production of the osteophytes which tend to fuse with the disc protrusions. Frykholm distinguishes two types of osteophytes: the one which is produced in the manner just described he calls marginal lipping, which may be either localised or affect the entire circumference of the vertebral margins. Ventral spurs, on the other hand, are anatomically related to the anterior longitudinal ligaments, and, according to Schmorl (1929), they are the result of increased strain on this ligament, the fibres of which are firmly attached to the vertebral margins. Furthermore, the collapse of a disc also results in subluxation of the corresponding intervertebral joints with secondary osteophyte formation on the articular processes, which leads to further narrowing of the intervertebral foramina.

* The Heberden Oration for 1953, delivered before the Heberden Society in London on Dec. 4. Published also in the March issue of the *Annals of the Rheumatic Diseases*.

If, as I believe, this account is fundamentally correct it follows that "intervertebral disc protrusion" is a name applied to two conditions which are pathologically distinct: one type of protrusion is the product of a nuclear herniation while the other is not a herniation but an annular protrusion. A nuclear herniation which has occurred acutely and which is observed before it has had time to harden may be relatively soft: later, calcification and ossification, together with the reactive bony changes in the adjacent vertebrae, may make it extremely difficult to distinguish from an annular protrusion which is the result of disc degeneration. But the matter is more complicated than that, because the beginnings of a nuclear protrusion, which goes no further than tearing some of the fibres of the annulus, may interfere with the function of the intervertebral disc in the same way as primary degeneration and excite the same reactions from adjacent vertebrae, so that the changes which tend to produce nuclear protrusion are probably one cause of disc degeneration. Finally, be it noted, intervertebral disc degeneration may occur without leading to protrusion.

Thus when we use the term spondylosis we are describing something which is not pathologically homogeneous: we are dealing in fact with a spine which manifests the end-results of either or both of two distinct pathological processes, nuclear herniation and annular protrusion. To some extent radiography is responsible for suggesting that spondylosis is a single disorder, since in the late stages it is not, as far as I know, possible to distinguish the one type from the other by means of X rays. If we are to study the natural history of what is called spondylosis, however, we cannot confine ourselves to the end-results, but we must also take into account the acute nuclear herniation with which one type of spondylosis begins.

Problems of Aetiology

We see, therefore, how complex the causation of spondylosis may be. How large a part does trauma play? In our series of cases of cervical spondylosis (Brain, Northfield, and Wilkinson 1952) two-thirds of our patients gave no history of trauma, and only 6 out of 45 gave a history of trauma which could possibly have contributed to the causation of the disorder. Nevertheless the frequency with which disc degeneration is limited to a single disc—as was the case in 18 out of 38 of our patients with cervical spondylosis, and is very common in the lumbar spine—suggests that local causes are at least as important as a diffuse degenerative process, and a minor trauma which may have started the process years previously may easily have been forgotten. The rôle of trauma in producing acute disc protrusion in the lumbar region is well recognised, and it may often exacerbate a pre-existing one.

The wear and tear of normal spinal movements may be a contributory factor, especially when disc degeneration has already begun; and congenital abnormalities, especially Klippel-Feil fusion, throw an added strain on adjacent articulations. Undoubtedly the most important causal factor is the biochemical change in the intervertebral discs which occurs with ageing and is associated with a loss of water (Collins 1949, Sylvén et al. 1951): and prevention of spondylosis must largely depend upon an elucidation of this process. The importance of disc degeneration is well illustrated by those patients who exhibit spondylosis from top to bottom of the spine and by the frequency with which symptoms

of cervical and lumbar spondylosis occur in the same individual.

The Pathology of the Nerve-roots in Cervical Spondylosis

We owe much of our knowledge of the structure of the coverings of the cervical spinal nerve-roots, and their relationship with the cervical vertebrae, to the careful studies of Frykholm (1951c). The cervical intervertebral foramina are bounded above and below by the pedicles of the two adjacent vertebrae. The radicular nerves are situated in the foramina, and the dorsal root ganglia lie just outside in the gutter of the transverse process. The posterior wall of the foramen is formed by the superior articular process of the vertebra below, which in turn is covered posteriorly by the inferior articular process of the vertebra above. The ventral delimitation of the foramen is effected partly by the two adjacent vertebral bodies and partly by the dorsolateral rim of the intervertebral disc. This is termed the uncinate process, and there has been some discussion as to whether between the uncinate process of the lower vertebra and the corresponding facet of the vertebra above there is a true joint, as Luschka supposed. This has been called the uncovertebral joint and the neurocentral joint; but some, including Frykholm (1951b) believe that what has been regarded as a joint cavity is merely part of the annulus of the intervertebral disc.

The rather complicated structure of the investment of the radicular nerves can be best understood by reference to a diagram (fig. 1). Opposite each foramen the dural sac has a small infundibular extension, the dural root-pouch, or axillary pouch of some authors. By means of the funnel-like shape of the pouches, each nerve-root is

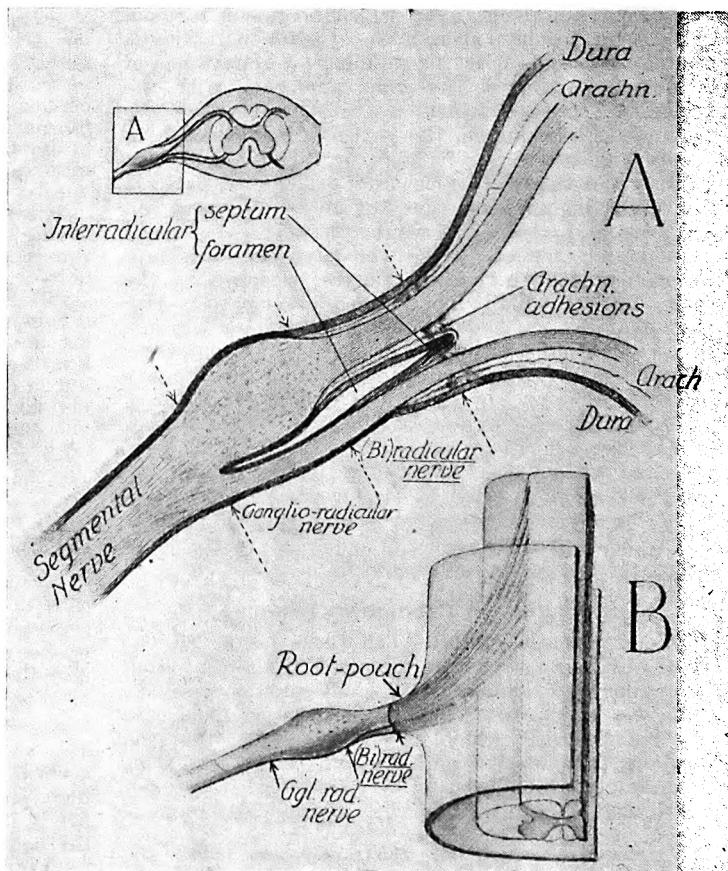


Fig. 1.—Drawing showing principal features of the anatomy of cervical nerve-roots and their dural and arachnoidal investments (Frykholm 1951c). For details see text.

conveyed in a smoothly curved course to the point at which it leaves the dural sac. At the bottom of the root-pouches there are two openings, the dural root-ostia, one ventral and one dorsal, which are separated by a small dural septum, the inter-radicular septum. Each root-ostium leads into an individual root-sleeve, of which there are consequently two, one dorsal and one ventral. The root-sleeves, which are lateral extensions of the dural sacs, are separated by a small cleft known as the inter-radicular foramen. Consequently, outside the dural sac, the dorsal and ventral roots pass through individual sheaths which are entirely separated. A tubular extension of the arachnoid membrane encloses each root in its proper root-sleeve. Between the dural sac and the dorsal root ganglion the two roots lie close together and form an anatomical entity referred to as the radicular nerve.



Fig. 2—Dissection of cervical nerve-roots in their passage through the intervertebral foramina, showing variations in shape of the dural root-pouches.

In seeking to interpret the effect of the bony changes of cervical spondylosis upon the radicular nerves it is of cardinal importance to remember that the radicular nerve normally occupies only one-fifth to one-fourth of the diameter of the foramen; hence, if the nerve lay always in the middle, considerable narrowing of the foramen could occur without producing any effect upon it. Frykholm (1951c), however, points out that the morphology of the lower cervical radicular nerves and their root-pouches is extremely variable, as illustrated by fig. 2. In early childhood the dural sac and the radicular nerves are only loosely attached to the bone. As age advances they gradually become relatively well fixed in their definite positions. In most cases the radicular nerves then take a slightly downward course and pass through the centre of their respective foramina. Variations in this arrangement may occur in normal individuals, probably as the result of disproportionate growth of the dural sac and the cord relative to the vertebral column. Displacement of the radicular nerves within the foramina may, however, occur also as the result of cervical disc degeneration quite independently of the pressure of disc protrusion, since the cord and the dural sac retain their original length while the spine is shortened owing to osteoporosis and disc degeneration. The lower cervical radicular nerves thus tend to be displaced towards the lower part of their foramina and hence become more upwardly directed. The displacement downwards also tends to distort the root-pouches, which results in sharp angulation of the nerve-roots; and at this point of angulation the roots are subjected to undue strain and increased friction with the dural lining. Frykholm points out that in consequence the segmental level of such a lesion does not necessarily correspond to a level of a disc degeneration.

Now let us consider the more direct effect of cervical intervertebral disc protrusion and the associated vertebral changes upon the nerve-roots and radicular nerves. In this connection I shall not concern myself with acute nuclear herniation, but with the end-results of disc protrusion, however produced, and disc degeneration, in cervical spondylosis. Such disc protrusions have been variously classified according to their position in the circumference of the disc, but one or more of these different types of protrusion may be encountered in the same disc, and they merge into one another. From the point of view of the radicular nerves and nerve-roots, however, the only two with which we need concern ourselves are the dorsolateral protrusion, which does not invade the intervertebral foramen but may compress the intrameningeal nerve-roots against the vertebral laminae, and the intraforaminal protrusion, which emerges from the uncinate part of the disc and compresses the radicular nerve against the articular processes (fig. 3). The mechanism of root compression, however, depends not only upon the size and location of the protrusion but also upon the angulation of the radicular nerve and its situation in the foramen. Thus, for example, a protrusion restricted to the lower part of the foramen may leave the roots quite intact if the radicular nerve is downwardly directed and situated cranially in the foramen, whereas if the nerve is caudally situated and outwardly or upwardly directed there is a much greater chance that it will be implicated. Furthermore, a protrusion which is strictly localised to the lower half of the foramen may produce a selective compression of the ventral root and leave the dorsal root intact, because the ventral root often runs along the caudal border of the dorsal root. Finally, cervical disc degeneration without protrusion may lead to marginal liping as a result of the increased stress which falls directly

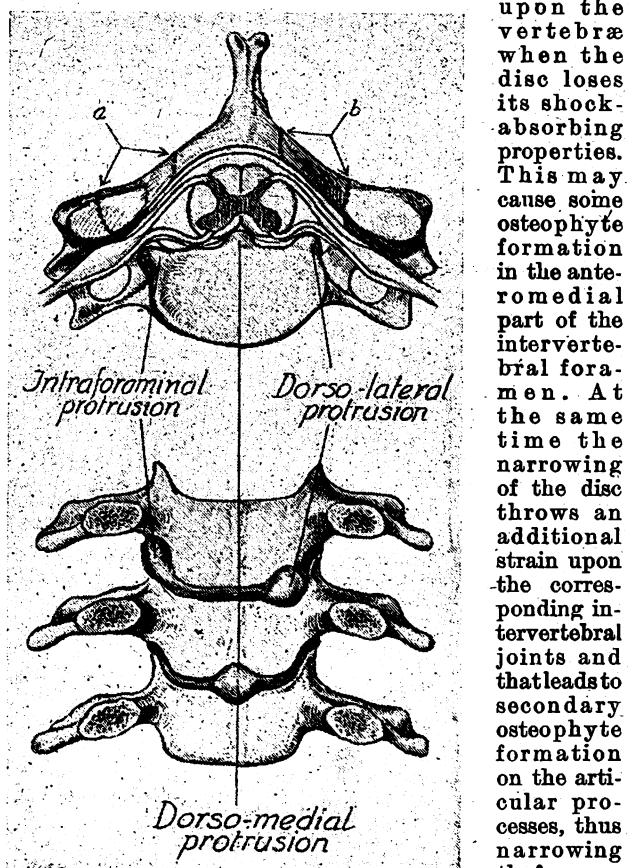


Fig. 3—Drawing (Frykholm 1951b) showing principal types of disc protrusion: (i) dorsomedial; (ii) dorsolateral; and (iii) intraforaminal.

upon the vertebræ when the disc loses its shock-absorbing properties. This may cause some osteophyte formation in the anteromedial part of the intervertebral foramen. At the same time the narrowing of the disc throws an additional strain upon the corresponding intervertebral joints and that leads to secondary osteophyte formation on the articular processes, thus narrowing the foramen postero-laterally.

The pathological effects of these bony changes in the neighbourhood of the intervertebral foramen have been studied by Frykholm (1951a). In their fully developed form they consist of what he calls "root-sleeve fibrosis." This is characterised by (1) thickening and opacity of the dural root-sleeve and adjacent parts of the dural sac (i.e., the root-pouch); (2) narrowing, or complete abolition, of the dural funnel which forms the root-pouch; (3) sharpening of the upper and lower duro-radicular junction, which sometimes causes a distinct constriction or notching of the radicular nerve; (4) thickening of the dura at the root-ostia and occasionally, also, thickening of the inter-radicular septum resulting in a constricting ring of fibrous tissue around each nerve-root; (5) thickening and fibrosis of the arachnoid membrane in the neighbourhood of the root-ostia, and (6) disintegration and hyalinisation of the dural tissue involved. The chronic constriction of the nerve-roots and radicular nerve, and associated ischaemia, lead in time to the degeneration of the nerve-fibres. Frykholm points out that in many cases root-sleeve fibrosis is observed in the absence of any constriction of the corresponding foramen, though in such cases there is usually X-ray evidence of disc degeneration either at the same segmental level or at one or two levels above that of the radicular lesion. Occasionally also root-sleeve fibrosis may be present in spite of the fact that the cervical spine shows no X-ray abnormality.

Thus, cervical intervertebral disc degeneration initiates a complex and variable series of changes which may affect the nerve-roots and radicular nerve in a number of different ways which need to be assessed individually in each case. These changes may be summarised as follows:

(1) Disc degeneration affects the mobility of the cervical spine. The simplest example of this is the effect of degeneration of a single disc. Usually this greatly limits flexion and extension at the intervertebral joints between the two vertebrae separated by the affected disc. Since the main movement must now occur above and below, abnormal stresses may fall not only upon adjacent intervertebral joints but also upon adjacent radicular nerves. Exceptionally, disc degeneration leads to abnormal mobility, in which case, as a rule, the body of the upper vertebra slips forward upon that of the lower on flexion and slips back again on extension, a movement which must obviously tend to produce damage to the radicular nerves in the corresponding foramina.

(2) Narrowing of intervertebral discs shortens the cervical spine and disturbs the relation between the radicular nerves and their corresponding foramina, the lower ones, particularly, tending to rest upon the lower margins of the foramina and to be kinked over them.

(3) Disc degeneration by itself can produce lipping of the adjacent vertebral bodies and so narrow the inner margins of the intervertebral foramina, whilst increased strain upon the intervertebral articulations produces osteophytic narrowing posteriorly.

(4) All this may occur without intervertebral disc protrusion. In addition, however, a dorsolateral protrusion may compress the nerve-roots within the spinal canal, while an intra-foraminal protrusion may compress them or the radicular nerve within the foramen.

(5) All the above-mentioned processes tend to lead to root-sleeve fibrosis, the characteristic reaction of the investment of the nerve-roots and radicular nerve to chronic irritation and compression. These pathological changes, therefore, though most likely to occur in the nerve-roots which pass through the intervertebral foramina at the level of the degenerated disc, may be present also at other levels at which there is no evidence of disc degeneration.

(6) Finally, the affected nerve-roots and radicular nerves, tethered to the foramina by root-sleeve fibrosis, and lacking their normal mobility, are far more susceptible to trauma than normal nervous tissue. Consequently not only may severe and lasting radicular

symptoms be set up by head injury in such cases, but it is probable that comparatively slight trauma may be responsible for the acute onset of symptoms in patients with cervical spondylosis and of symptoms which may be multiradicular in distribution although the bony pathological changes may be limited to one intervertebral disc and its adjacent vertebrae.

The Significance and Insignificance of Radiographic Changes

We are now in a position to assess the value and limitations of radiography in the diagnosis of the radicular lesions accompanying cervical spondylosis, and also, perhaps, to clear up some of the apparent anomalies. In the radiological investigation of a patient suspected of cervical spondylosis it is usually necessary to take three lateral views (in the erect, flexed, and extended positions) as well as an anteroposterior view and right and left oblique views to show the intervertebral foramina. Without the flexed and extended lateral views it may be impossible to detect spondylolisthesis (fig. 4). In addition, plain radiographs may show a narrowed intervertebral disc space indicating disc degeneration; posterior osteophytes, in the manifestation of which specially soft films may be helpful; and osteophytic invasion of the intervertebral foramina (fig. 5). It is important to bear in mind the following points in the interpretation of the X-ray appearances:

(1) A narrowed intervertebral disc space indicates disc degeneration which may or may not be associated with disc protrusion.

(2) The absence of posterior osteophytes, which are radiographically visible, does not necessarily mean the absence of a disc protrusion.

(3) A normal intervertebral foramen does not necessarily mean healthy nerve-roots or radicular nerves, for

(4) The nerve-roots may be compressed in the spinal canal by a dorsolateral disc protrusion which does not involve the foramen, or they may be the subject of root-sleeve fibrosis within a normal foramen for one of the reasons mentioned above.

(5) A narrowed intervertebral foramen does not necessarily mean that the corresponding nerve-roots or radicular nerves are compressed, since normally the nerve takes up only a small proportion of the space in the foramen and if it is centrally situated may for a long time avoid damage or even tolerate a considerable degree of compression without giving rise to symptoms.

(6) Myelography may be valuable for the purpose of showing a disc protrusion, which is not visible on the plain radiograph, or a root-sleeve fibrosis which may be demonstrable by obliteration of the root-pouch in the

LEGENDS TO ILLUSTRATIONS ON PLATE

SIR RUSSELL BRAIN

Fig. 4—Cervical spine showing, as a result of spondylosis (i) narrowing of C5-6 and C6-7 disc spaces with anterior and posterior osteophytes; (ii) spondylolisthesis. C4 slipping forward on C5 in flexion.

Fig. 5—Oblique view showing narrowing of intervertebral foramina C5-6 and C6-7 by osteophytes.

Fig. 6—Myelogram showing compression of the spinal cord by disc protrusions, C3-4 and C5-6. Note the slightness of the narrowing of the discs anteriorly and absence of anterior osteophytes.

Figs. 8 and 9—Lumbar spondylosis causing narrowing of the 5th lumbar disc space and foramen: anteroposterior and lateral views. (Kindly lent by Dr. M. H. Jupe.)

DR. DORNHORST AND OTHERS

Fig. 6—Localisation of cardia. Simultaneous pressure records show that in both *a* and *b*, the upper recording-site is in the oesophagus and the lower in the stomach. The middle site is on the gastric side of the cardia in *a*, and has just passed into the oesophagus in *b*.

Fig. 8—Film corresponding to arrow in fig. 7 and the film immediately preceding that.

myelogram although the intervertebral foramen may appear normal on the plain radiographs.

Some Radicular Syndromes of Cervical Spondylosis

I believe that the various clinical pictures described in the past as "brachial neuritis" or "brachial neuralgia" are in most cases the result of the pathological changes described by Frykholm as root-sleeve fibrosis. I shall not now retread the well-worn path of the clinical symptomatology of "brachial neuritis" but shall confine myself to a consideration of some of the less familiar clinical pictures and, in particular, those upon which light is thrown by the newer knowledge of the pathology of the condition.

Acroparäesthesiae

Acroparäesthesiae may be defined as unpleasant tingling sensations affecting some or all of the digits of one or both upper limbs, developing during the night and usually passing off within an hour or so of awakening and particularly liable to occur in middle-aged women. Thus defined, acroparäesthesiae are merely a symptom, and it is inherently unlikely that a symptom of irritation of sensory nerve-fibres is characteristic of a lesion occurring at only one point in their course. I believe that acroparäesthesiae may occur as a symptom of either (1) cervical spondylosis, (2) a costoclavicular syndrome involving particularly perhaps vasomotor elements, or (3) compression of the median nerve in the carpal tunnel. Acroparäesthesiae, however, are so common a symptom of cervical spondylosis that all patients who complain of them should have their necks radiographed.

Pain Referred to Myotome and Sclerotome

A dermatome is the area of skin supplied by a single spinal nerve. The importance of the dermatome in neurological diagnosis has perhaps tended to obscure the fact that a spinal nerve distributes sensory nerve-fibres to muscles, bones, joints, and ligaments which have an anatomical distribution ranging widely beyond the cutaneous area innervated by the same segment. The muscles supplied by a single radicular nerve have been termed a myotome, and the bones and joints similarly supplied have been termed a sclerotome. Pain due to irritation of a spinal posterior root or radicular nerve, therefore, may irradiate widely, and this may sometimes give rise to difficulties in diagnosis. For example, both the 6th and 7th cervical radicular nerves supply sensory

fibres to the posterior cervical muscles, pectoralis major, latissimus dorsi, and serratus magnus as well as to other muscles of the trunk and upper limbs and the corresponding dermatomes. Irritation of either of these nerves may therefore cause pain referred to the neck and back and front of the chest as well as to the upper limbs, and, it has been pointed out, may suggest pain of cardiac origin.

Muscular Wasting

Muscular wasting is not usually severe as a result of the radicular lesions of cervical spondylosis, but it may be a prominent symptom and even occur in the absence of objective sensory abnormalities. It may then lead to an erroneous diagnosis of motor-neurone disease. Frykholm points out that such muscular wasting is probably due to a selective damage to the anterior spinal roots by compression arising from the lower part of the foramina. It may affect the muscles supplied from several segments or from one only.

"The Frozen Shoulder"

Pain of radicular distribution due to cervical spondylosis and referred to the shoulder is not infrequently followed by the condition known as "frozen shoulder" in which gross limitation of active and passive movements of the shoulder occurs and any attempt to move the joint causes pain. The possibility that a "frozen shoulder" is a symptom of cervical spondylosis should always be borne in mind.

Acute or Subacute Multiradicular Symptoms

As a rule the radicular symptoms of cervical spondylosis are limited to one, or perhaps two, segments. The older clinical accounts of brachial neuritis, however, usually describe pain radiating down the whole length of the arm to all the digits and associated with some degree of generalised muscular wasting, weakness, diminution of the tendon reflexes, and perhaps very diffuse cutaneous sensory loss. This clinical picture may undoubtedly occur as the result of cervical spondylosis, and even when the X-ray changes are limited to one or two intervertebral joints. As I have suggested above, the probable explanation is that in such cases root-sleeve fibrosis is much more widespread than X-ray changes would suggest, and some change—perhaps a slight trauma or even possibly exposure to cold—has intensified the lesion in most of the roots from which the brachial plexus is derived. An alternative possibility is that an acute lesion of a single root may sometimes cause pain which, owing to the considerable overlap of dermatomes, radiates to a large area of the upper limb and at the same time reflexly interferes with muscular function.

LEGENDS TO ILLUSTRATIONS ON PLATE

DR. LUTWYCHE

- Fig. 1 (case 1)—Bilateral apical calcification with infiltration and probable cavitation in the right upper lobe.
- Fig. 2 (same case)—Eighteen months later: opacity radiating from right hilum.
- Fig. 3 (case 2)—Cavitating lesion in the left upper lobe.
- Fig. 4 (same case)—Seven weeks later: cavity apparently closed.
- Fig. 5 (case 3)—Opacity in right upper lobe.
- Fig. 6 (same case)—Twenty-one months later: partial collapse of the right upper lobe and calcified paratracheal and hilar glands.
- Fig. 7 (case 4)—Rounded lesion in the left upper lobe with some increase in the left hilar shadow.
- Fig. 8 (same case)—Twelve months later: increase in the size of the lesion which has now cavitated.
- Fig. 9 (case 5)—Small opacity in the second right interspace and thickening of the interlobar septum with some opacity medially.
- Fig. 10 (same case)—Eighteen months later: elevation of the right diaphragm with an opacity radiating out from the right hilum.
- Fig. 11 (case 6)—Opacity in right upper lobe with increased translucency of the lower lobe.
- Fig. 12 (case 7)—Opacity in the left mid-zone.

The Pathogenesis of Myelopathy in Spondylosis

Cervical spondylosis damages the spinal cord less often than the nerve-roots, but sufficiently often to make spondylotic myelopathy one of the commonest, if not the commonest, disease of the spinal cord during and after middle life. This is illustrated by the fact that 41 patients with cervical spondylosis have been admitted as inpatients to the neurological department of the London Hospital during the last two years, mostly because of myelopathy. The pathogenesis of the myelopathy, like that of the root-sleeve fibrosis, is complex, and certainly a number of factors are concerned. The most obvious is direct compression of the cord by one or more protruding intervertebral discs. When the disc protrusion is large, the cord may be compressed between it and the laminæ posteriorly (fig. 6), the pressure being sufficient even to cause thinning of the laminæ. Greenfield (1953), however, believes that in most cases the areas of demyelination are too limited to be explained as the result of simple compression. He thinks that compression may operate indirectly by interfering with the blood-flow through the anterior spinal artery. The blood-supply to

the spinal cord may be further impaired by narrowing of the intervertebral foramina through which the radicular arteries penetrate. Compression of the anterior spinal veins has also been regarded as a contributory factor. Stretching of the ligamenta denticulata also, in Greenfield's opinion, plays an important part, since by anchoring the spinal cord these ligaments tend to increase the effects of compression on the anterior spinal vessels. Moreover they exert tension on the lateral aspects of the spinal cord. The neck, however, is not static, but in constant movement throughout waking life, and a considerable amount of movement still occurs in a spine which is the site of severe spondylosis. As already mentioned, movement may be pathological when one body slips forward upon the one immediately below it on flexion of the neck (fig. 4). Root-sleeve fibrosis, which is invariably present to a greater or less extent in these cases, tends to anchor the roots in the foramina, and by thus limiting the mobility of the cervical cord must add to the traumatic effect of repeated movement of the neck when the cord is already compressed by a disc protrusion. All these factors combine to produce a condition which is best described as cervical myelopathy. Moreover, in the presence of cervical spondylosis, even though the spinal cord has so far apparently escaped injury, severe damage may be produced by forcible extension of the neck as the result of a blow upon the front part of the head, or even, as Symonds (1953) has shown, in the course of the administration of an anaesthetic or an operation upon the tonsils.

Symptomatology of Cervical Myelopathy due to Spondylosis

I do not propose now to discuss in detail the symptomatology of cervical myelopathy resulting from spondylosis (see Brain 1948, Brain et al. 1952), but only to draw attention to the relation between the pathology and the symptomatology, and, in particular, to try to show how the pathology explains the extremely varied clinical picture.

To simplify matters, let us consider only the factor of disc protrusion. Since disc protrusions may be single or multiple, and may occur at any, or all, levels of intervertebral discs, it is clear that any segment of the cervical cord may be compressed from the 3rd to the 8th—that is, either above or in the course of the cervical enlargement. Furthermore, a disc protrusion into the vertebral canal may be situated either in the midline or to one or other side, or be more or less continuous; and, except in extreme cases, the resulting demyelination does not involve the whole transverse extent of the cord. It is therefore easy to understand how varied is the resulting clinical picture and how many other disorders it may simulate.

Since the onset of symptoms is usually insidious, and may be either intermittently or steadily progressive, the disorder will tend to resemble those lesions of the spinal cord which occur in middle life and have these general characteristics. Muscular wasting, fasciculation, and weakness in the upper limbs, combined with spastic weakness of the lower limbs in the absence of sensory loss, may closely simulate motor-neurone disease. Weakness, numbness, and clumsiness of the upper limbs, associated with ataxic paraparesis, and perhaps some sensory loss in the lower limbs, is a clinical picture resembling disseminated sclerosis. When the damage falls chiefly upon the pyramidal tracts and the posterior columns, with which may be associated some wasting of the hands and sensory loss of glove distribution in the upper limbs, there is a considerable resemblance to subacute combined degeneration. Extramedullary tumour, intramedullary tumour, and syringomyelia may all easily be simulated. When the symptoms are those of pure bilateral pyramidal degeneration a diagnosis of

primary lateral sclerosis may be made. In some cases cervical myelopathy may for a long time cause only paraparesis without detectable abnormalities in the upper limbs, and then the cause may be thought to originate in the dorsal region of the spinal cord. Occasionally, as Symonds (1953) points out, cervical spondylosis may be the cause of quadriplegia of sudden onset, which may be permanent or, as in one recent patient of my own, brief and intermittent. Finally, to add to the hazards of diagnosis, not only may cervical spondylosis coexist with a quite independent lesion of the nervous system which is itself responsible for the symptoms, but it may sometimes be associated with some other abnormalities of the spine or of the spinal cord—particularly of congenital origin, such as congenital fusion of vertebrae, cervical spina bifida, and the Arnold-Chiari malformation—while syringomyelia and tabes may cause a cervical arthropathy which is not only difficult to distinguish from spondylosis but may actually be complicated by it.

Thoracic Intervertebral Disc Protrusion

I am inclined to include thoracic intervertebral disc protrusions more among the unknown than among the known facts of spondylosis. They are certainly far less common than disc protrusions at the cervical and lumbar regions, presumably for mechanical reasons. The neurologist and neurosurgeon are familiar with them as rather uncommon causes of extramedullary compression of the spinal cord. I have sometimes suspected one as the cause of an otherwise unexplained root pain, but, apart from those causing compression of the spinal cord, I have never been able to demonstrate one by myelography. This is a field which I am sure would repay research. Apart from the presence of thoracic disc protrusions sufficient to cause symptoms, I have also encountered a good many patients suffering from progressive paraparesis in association with severe thoracic spondylosis. The opportunity

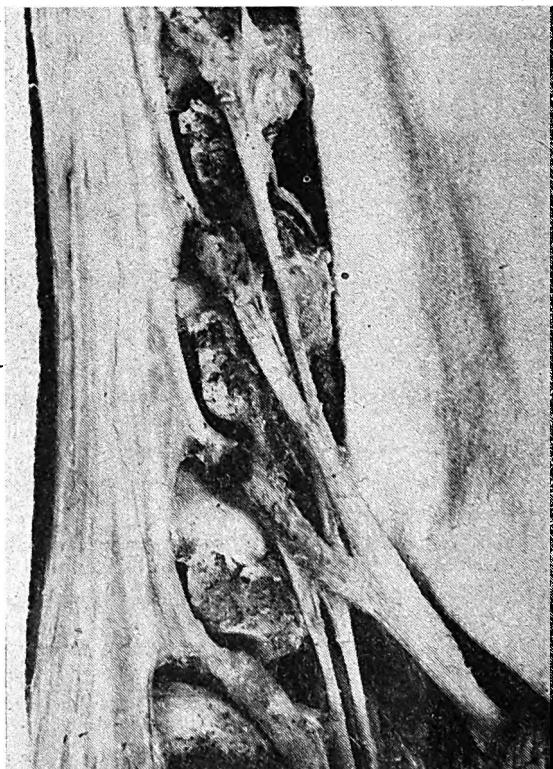


Fig. 7.—Dissection of lumbar nerve-roots (L2-5). The lowest (5th) can be traced up from the lumbosacral foramen, where it lies on the lumbosacral disc, to where, intradurally, it passes behind the 4th lumbar disc.

for the pathological investigation of such cases rarely occurs. I have suspected that the narrowing of the intervertebral foramina by interfering with the vascular contribution which the radicular arteries make to the vasocorona of the spinal cord may contribute to an ischaemic myelopathy. Here, also, pathological research might prove rewarding.

Lumbar Disc Protrusion and Foraminal Narrowing

I have left lumbar spondylosis until last because it has been the subject of research for a much longer period than cervical spondylosis, and, until recently at least, much more has been known about it. This, however, does not mean that there are not still many important unknown factors.

It is, I think, desirable to bear in mind that the same distinction between nuclear and annular protrusions, which I discussed in connection with cervical discs, applies also to those in the lumbar region. There are certain points of difference, however, between the two. In the lumbar region acute nuclear protrusions are a much commoner cause of symptoms than at the cervical level, but it is probable that in the lumbar region pre-existing disc degeneration is a more important predisposing cause of such nuclear protrusion than it is in the neck. At the lumbar level, as at the cervical, a nuclear protrusion, if undisturbed, may provoke an osteophytic reaction from the vertebral bodies so that in the end it may be difficult to distinguish from an annular protrusion. In particular, plain radiographs may provide no clue as to whether a narrowed lumbar intervertebral disc space is the result of simple disc degeneration, annular protrusion, or nuclear protrusion.

Whereas in the neck compression of spinal nerve-roots by disc protrusion in the vertebral canal is rare compared with compression in the foramina, the reverse is generally thought to be the case at the lumbar level. Nevertheless, in the lumbar spine, exactly as in the cervical, intervertebral disc degeneration can produce damage to the spinal nerve within the foramen and in precisely the same way : first, the narrowing of the intervertebral disc narrows the corresponding foramina by bringing their edges nearer together ; and, secondly, it throws an additional strain upon the articulation, so leading to osteophyte formation which in turn narrows the foramina still further. This cause of sciatic pain was hinted at by Sicard (1921) and elaborated by Putti (1927), but the subsequent discovery of intervertebral disc protrusion has led to its neglect. I believe that the symptoms of lumbar intraforaminal root compression are usually distinguishable from those of intrathecal root compression by disc protrusion. This is only to be expected on anatomical grounds, for intrathecal compression is exerted upon the posterior root of an intact ganglion whereas intraforaminal compression is exerted upon the ganglion or the spinal nerve. It should be noted that the 5th lumbar root, for example, may be compressed either by a protrusion of the 4th lumbar disc or by narrowing of the 5th lumbar foramen (fig. 7). Radiologically the 4th disc space will probably be narrowed in the first instance and the 5th in the second, with the addition, in the latter, of osteophytic invasion of the L5-S1 intervertebral foramen (fig. 8). Of course, both may be present in the same patient.

Lumbar foraminal pressure-radiculitis increases in frequency with age, and is most commonly encountered in the seventh and eighth decades. It is, however, especially common in diabetics, in whom it may occur at an earlier age. It may be uniradicular or multi-radicular and unilateral or bilateral. Pain is usually less severe than in sciatica resulting from disc protrusion and is less likely to be exacerbated by coughing or sneezing. It is often, however, influenced by posture and may be worse when the patient is sitting. There

may be no pain, but only dysaesthesiae in the distribution of the dermatomes supplied by the affected root or roots. Cutaneous sensibility is often blunted over these areas. When several roots are involved there may be conspicuous muscular weakness and wasting associated with fasciculation, and diminution or loss of the knee-jerks.

* * *

Look back for a moment and recall that it is just twenty years since sciatica was first attributed to an intervertebral disc protrusion. Before that it was called sciatic neuritis and put down to various hypothetical toxins. Even at that time the same view was taken of brachial neuritis, and nothing at all was known of the protean clinical picture of spinal-cord compression by disc protrusion except for a small number of cases gathered by neurosurgeons and in which the lesion was called a chondroma. How much we have learnt since then ! But how much still remains to be discovered.

I am grateful to W. R. J. Harrison for kindly providing the dissections and photographs for figs. 2 and 7.

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THE DIFFERENTIAL DIAGNOSIS OF CARCINOMA OF THE BRONCHUS AND PULMONARY TUBERCULOSIS

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With illustrations on plate

CARCINOMA of the bronchus has, in the past, figured more often in the American than in the English medical literature. It is this fact, together with the increasing incidence of the disease, partly apparent and partly real, and the frequency with which the condition is met in routine chest-clinic practice, that has prompted this description of 7 cases. They are reported not because of any points of unusual interest but because each may be representative of many hundreds of similar cases throughout the country.

Many writers have pointed out how the early radiological changes may often resemble those produced by other conditions, making early diagnosis difficult. Burrell (1938) described the inflammatory reaction which may occur around a collapsed area of lung when a bronchus is blocked by a carcinoma. McGibbon et al. (1939) reported the results of bronchoscopic examination in 38 patients diagnosed as suffering from unresolved pneumonia ; in 8 of these, bronchial carcinoma was present and the X-ray appearances were due to a secondary inflammatory reaction.

Overholt (1943) noted that, of a series of 165 patients with bronchial carcinoma, no less than 104 were at first incorrectly diagnosed ; this he ascribed partly to the fact that in many cases the radiographic changes were caused by secondary effects rather than by the neoplasm itself.

Brock (1952) drew attention to the frequency with which bronchial carcinoma may present as a lung abscess; in his series of 477 cases of lung abscess, 83 (17.5%) were found to have a bronchial carcinoma as the primary cause of the condition. He stressed that this diagnosis should always be considered in every case of lung abscess, particularly in a person over the age of 45. In his series no less than 33.5% of abscesses in people over this age were due to a bronchial neoplasm.

The close similarity which may exist between the radiological appearance of a bronchial carcinoma and that of pulmonary tuberculosis is well known. In Overholt's series, 40 patients were incorrectly diagnosed as suffering from pulmonary tuberculosis and were treated in a sanatorium. Pillsbury and Wassersug (1945) described 12 similar mistakes that they had seen during the previous ten years, and Moersch and Tinney (1943) found 13 examples in their series of 448 cases.

The 7 cases described here include 5 where the correct diagnosis was not reached until it was too late to benefit the patient. In the other 2 cases the correct diagnosis was reached early in the illness, and the patients are now alive and well six and three years later respectively.

The Patients

Case 1.—A man, aged 61, a gas-meter fitter, was referred to the chest clinic in November, 1947, because he had had a recent attack of bronchitis and had lost a considerable amount of weight. The chest radiograph (fig. 1) showed bilateral apical calcification with extensive infiltration and probable cavitation in the upper part of the right lung. (The right hilar enlargement was not noted at that time.) The condition was considered to be tuberculous, although examination of ten specimens of sputum failed to reveal tubercle bacilli, and he was put to bed at home pending admission to sanatorium. His condition steadily improved with bed rest; the radiograph showed some clearing within seven weeks and he gained over 1 stone in weight in seven months. The improvement was such that his name was removed from the sanatorium list.

Eight weeks after returning to work in May, 1949, his sputum became bloodstained and he began to lose weight; at the same time he complained of hoarseness of voice and a swelling appeared at the angle of the right jaw. The left vocal cord was paralysed; and the radiograph now showed bilateral hilar enlargement. Bronchoscopy revealed considerable distortion of the carina and right main bronchus by glandular enlargement. His condition continued to deteriorate; he lost a stone in weight during the next five months, and the mass in the right posterior triangle of the neck became larger. The radiograph three weeks before death (fig. 2) showed an opacity radiating from the right hilum, consistent with a diagnosis of bronchial carcinoma. No necropsy was performed.

In spite of the fact that a carcinoma was not proved by post-mortem examination nor by histological examination of the cervical mass, it is considered that the history of this case, combined with the clinical progress, radiographs, bronchoscopic findings, and the failure to find tubercle bacilli in the sputum, leave little doubt that the whole of this patient's illness during the last three years of his life was caused by a bronchial neoplasm rather than pulmonary tuberculosis.

Case 2.—A man, aged 72, a clerk, was referred to the clinic in July, 1950, because of a febrile illness two months previously and a history of frequent attacks of bronchitis. The radiograph showed a cavitating lesion in the upper lobe of the left lung (fig. 3). This was considered to be tuberculous, though no tubercle bacilli were found in six specimens of sputum. He was put to bed at home and as a result his condition improved; he gained 5 lb. in weight during the next few months, and a radiograph after seven weeks (fig. 4) showed that the cavity was no longer visible.

Eight months after this, however, he became hoarse, his sputum was bloodstained, and he had substernal pain when lying down at night. The left vocal cord was found to be paralysed and the radiograph showed increased opacity in the left upper lobe. Bronchoscopy was not performed because it was considered that the patient would now derive no benefit from it. When seen four months later he was suffering from severe anaemia and was very dyspnoeic; he had lost 1 $\frac{1}{2}$ stone in weight during this period. The radiograph confirmed the

clinical findings of collapse of the left lung. He died four weeks later.

In spite of the fact that in this case also the diagnosis of carcinoma was not confirmed by necropsy, it is again considered that the history, clinical progress, and radiographs, combined with the failure to demonstrate tubercle bacilli in the sputum, leave little doubt that this man, too, had a bronchial carcinoma.

Case 3.—A salesman, aged 56, was referred to a hospital outpatient department in December, 1949, on account of loss of weight and anorexia. Gastric investigations failed to find any cause for his symptoms, but a chest radiograph (fig. 5) showed some opacity in the right upper lobe, increased translucency of the lower lobe, and definite calcification of the paratracheal and hilar glands. Three specimens of sputum failed to show tubercle bacilli. In view of the calcified lesions and a negative sputum, the radiographic appearances were attributed to quiescent tuberculosis and the patient was referred back to his private doctor.

Twenty-two months later, he attended the chest clinic because of bloodstained sputum and pain in the right side of the chest; the pain had been present at intervals for eighteen months. The radiograph (fig. 6) now showed partial collapse of the right upper lobe. Bronchoscopy showed a considerable stenosis of the right upper-lobe bronchus, and biopsy proved this to be the result of a squamous-celled carcinoma. The condition was thought to be operable and the patient underwent a right pneumonectomy; but there were metastases in the mediastinal glands. The patient died from oedema of the remaining lung on the second post-operative day.

Case 4.—A window-cleaner, aged 63, was referred to the clinic in November, 1949, because of a recent attack of bronchitis and a complaint of wheeziness when lying down at night. He had had a somewhat similar pyrexial illness a year previously. The radiograph (fig. 7) at this time showed a small rounded lesion in the left upper lobe with slight enlargement of the left hilar shadow. The erythrocyte-sedimentation rate was 3 mm. in one hour (Westergren) and three specimens of sputum showed no tubercle bacilli. Bronchoscopy did not reveal any evidence of primary growth.

Twelve months later he complained of increased cough and wheeziness. The radiograph (fig. 8) now showed the lesion to be larger and a cavity was present; in addition there was more definite enlargement of the left hilum. Sputum examination still failed to show tubercle bacilli. Two months later he was admitted to hospital elsewhere for the investigation of abdominal pain, and finally underwent laparotomy, when numerous deposits of secondary growth were found in the liver and other organs. He died shortly afterwards. At necropsy a carcinomatous growth was found encircling the left upper-lobe bronchus.

Case 5.—A man, aged 51, had a routine radiograph of his chest taken when his daughter was found to be suffering from pulmonary tuberculosis. This showed a small opacity in the second right interspace, and also thickening of the interlobar septum with some opacity medially (fig. 9). There were no symptoms and these appearances were interpreted as those of an early tuberculous lesion; this opinion was substantiated two months later when the radiograph showed some clearing.

Eighteen months later he said that he had had a recent pyrexial illness with cough and that he had lost weight steadily during the past year. The radiograph (fig. 10) now showed elevation of the right diaphragm with an opacity radiating out from the right hilum. Screen examination confirmed paralysis of the right diaphragm. Bronchoscopy revealed a carcinoma of the middle-lobe orifice which biopsy proved to be of an undifferentiated squamous-celled type. Operation was considered to be contra-indicated owing to involvement of the right phrenic nerve. The patient died five months later, and there was no necropsy.

Case 6.—A fish merchant, aged 48, was referred to the clinic in May, 1947, because of cough, lassitude, pain in the right side of the chest, and loss of weight. The radiograph (fig. 11) showed an opacity in the right upper lobe with increased translucency of the lower lobe, and this was at first considered to be tuberculous, but sputum examination failed to show tubercle bacilli. He was put to bed at home while awaiting admission to hospital for further investigation, and during a period of four weeks he gained in weight.

On admission to hospital, bronchography showed a partial block of the right upper-lobe bronchus. Bronchoscopy

revealed no abnormality, but a biopsy was taken from the depth of the right upper-lobe orifice and showed a squamous-celled carcinoma to be present. A right pneumonectomy was performed and he is well and working six and a half years later.

Case 7.—A man, aged 56, a florist, first attended the clinic in October, 1947, as a contact of his wife, who had pulmonary tuberculosis; at that time his chest radiograph was normal. In October, 1950, he came again because his sputum had been bloodstained for the previous few weeks. A radiograph (fig. 12) now showed a rounded opacity in the left mid-zone, with increased translucency in the lower zone. Bronchoscopy showed no abnormality, but in view of the symptoms and radiological appearance admission to a thoracic unit for further investigation was advised. Bronchoscopy was repeated four weeks later, when a small area of the left stem bronchus was considered to be suspicious; biopsy of this proved a columnar-celled carcinoma to be present. A left pneumonectomy was performed and he is now well and working three years later.

Discussion

A study of these 7 cases, all middle-aged or elderly men, shows several points of interest. Firstly, it is very important to hesitate before accepting a diagnosis of pulmonary tuberculosis in people of this age, unless tubercle bacilli have been found in the sputum; in 5 of these 7 cases repeated examination of the sputum failed to reveal tubercle bacilli. Among others, Scatchard (1944) has stressed this point; he noted how often the radiological picture of bronchial carcinoma resembled that of pulmonary tuberculosis and urged that, if a lesion were unilateral and the sputum were negative, a diagnosis of tuberculosis should be made with great caution. He also emphasised the not infrequent occurrence of cavitation in association with a bronchial carcinoma, and he pointed out the danger that this feature alone, especially if the cavity was in an upper lobe, might lead to a mistaken diagnosis of tuberculosis. Overholt (1950), writing on the detection of cancer by means of surveys, made the same point; he remarked that, whereas abnormal shadows in the upper lobes were too often considered to be tuberculous, those in the lower lobes were often attributed to bronchiectasis or virus pneumonia.

Secondly, not every bronchial carcinoma is visible through the bronchoscope, so that the report of a normal bronchial tree does not necessarily exclude the presence of a carcinoma. In 3 of the 7 cases described above, bronchoscopy showed nothing abnormal when the examination was first made: in 1 case the true diagnosis was made four weeks later when the examination was repeated, while in another the diagnosis was made on a biopsy taken from the depths of the bronchial orifice. These 2 patients are the only survivors of the 7. Reiss et al. (1952), in a series of 70 patients with bronchial carcinoma, noted that a positive bronchoscopy (either viewing the growth direct or demonstrating neoplastic cells in the bronchial secretions) was obtained in only 63% of patients undergoing bronchoscopy. Churchill (1948) observed that bronchoscopy was of little use in aiding the diagnosis in 30-40% of cases of primary carcinoma of the lung.

It is well known that patients with a bronchial carcinoma often present with a history of recent bronchitis or other respiratory infection; and 4 of the 7 patients described here gave such a history. Jewett (1952) noted that as many as one-third of his series of 150 patients had had recurrent respiratory infections, and he pointed out how misleading was the temporary improvement which so often followed treatment with antibiotics. Another factor which may also obscure the true diagnosis is the improvement in general condition and the alleviation of symptoms when the patient is confined to bed; this improvement was considerable in 3 of the 7 cases, and in 2 of them it was accompanied by definite improvement in the radiological appearances.

Conclusions

The diagnosis of bronchial carcinoma at an early stage is seldom easy, but if the prognosis is to be improved this diagnosis should constantly be borne in mind, particularly when a middle-aged man has suspicious symptoms or an unexplained shadow in the chest. To quote Reiss et al. (1952) again, "cancer of the lung should be given primary consideration whenever one is confronted with an unexplained pulmonary lesion"; or Overholt (1950), "all patients with abnormal shadows which cannot be adequately explained on another basis should have the benefit of surgical exploration."

Physicians at chest clinics should work in close collaboration with the radiologists and surgeons; and they should discuss together all cases in which the radiological appearances are suggestive of tuberculosis but the sputum is negative, and all cases of pulmonary abscess or virus pneumonia.

Facilities for immediate bronchoscopy should be available to every chest-clinic physician; and beds should be provided in a thoracic surgical unit for the urgent admission of suspected cases.

I wish to thank Dr. C. H. C. Toussaint for his help and interest in the preparation of this paper and for permission to publish it, and Mr. A. Booker for the radiographs. I am grateful to Mr. R. Laird for the bronchoscopy reports.

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OBSERVATIONS ON THE NORMAL OESOPHAGUS AND CARDIA

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With illustrations on plate

THE growing interest in oesophageal disorders and their surgical treatment has revealed the need for a better understanding of the behaviour of the normal oesophagus and cardia. The following observations are based mainly on radiography and intra-oesophageal pressure measurements—two methods often employed before but not, as far as we are aware, simultaneously. We have also, in order to settle certain points, directly observed at operation the behaviour of the cardiac region.

METHODS

Pressures were measured with capacitance manometers through fine 'Polythene' tubes. Up to three tubes were used; their tips were joined and the few centimetres below the lateral recording-hole of each tube filled with mercury. The upper parts of the tubes were filled with water. In this way the spaced recording-sites could easily be located on a radiograph as the upper ends of

the mercury columns. Thin barium emulsion (specific gravity 1.2) was used as contrast medium during drinking, and 70% diiodone for injection into the oesophagus through a tube. An electrical link indicated on the pressure record when the X-ray tube was energised and so provided precise timing of the radiograph. In some experiments radiographs at the rate of two a second were obtained with a Helm camera.

The subjects of the more complicated procedures were 6 normal volunteers. Much information on normal swallowing patterns was also available from records made for investigation of respiratory disorder by the method of Dornhorst and Leathart (1952).

RESULTS

Oesophageal Propulsive Wave

This wave is of characteristic form, taking about 4 seconds to complete, with peak pressure between 20 and 50 mm. Hg. It travels about 4 cm. per second with little change of form (fig. 1). There is no relaxation preceding the contraction; indeed there is usually a gentle rise of pressure, accompanying the passive expansion of the oesophagus as the contents are forced down ahead of the wave.

The propulsive wave is normally initiated by a pharyngeal swallow, but if swallows are repeated at intervals of a few seconds the propulsive wave often fails to follow; this suggests that the oesophageal muscle has a refractory period.

A propulsive wave starting in the upper oesophagus may also be initiated by the injection of air or liquid into the lower oesophagus through a fine tube.

When liquid is swallowed in a continuous series of gulps, there is no propulsive wave until the last gulp (fig. 2).

In the immediate vicinity of the cardia, the contraction becomes less forceful and lingers for up to 20 seconds (fig. 3). It is uncertain whether gastric muscle is involved in this.

Competence of the Cardia

During inspiration the intra-oesophageal pressure drops and the abdominal pressure rises. A pressure difference tending to force gastric contents into the oesophagus is set up, amounting with a moderately deep inspiration to

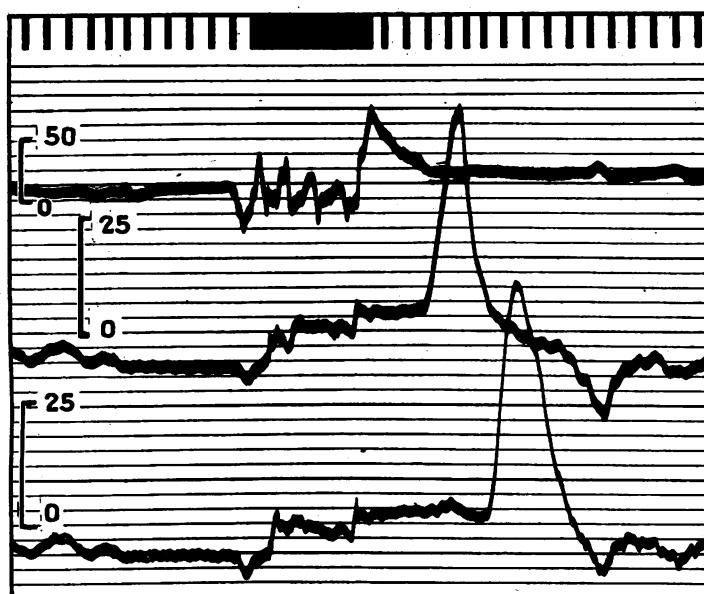


Fig. 2.—As in fig. 1. During signal shown in time record at top, fluid is being drunk in a continuous series of gulps. Note propulsive wave follows only the final gulp.

some 15 mm. Hg. With an inspiratory effort against a closed glottis, much higher pressures are generated. Fig. 4 shows a difference of 80 mm. Hg maintained for 5 seconds. There is no tendency for the pressures to equalise, as must happen if there were a leak between the two regions. The normal cardia is thus extremely resistant to regurgitant flow.

Localisation of the Cardia

The opening of a recording-tube is readily moved either way through the cardia even when a considerable pressure gradient is maintained. Only a few millimetres' movement are needed for the recorded pressure to change from high to low or vice versa. A characteristic spike of pressure usually appears as the opening passes from one region to the other. It is immaterial whether a tube with a lateral or terminal opening is used (fig. 5). Similar phenomena occur with a suitably placed tube with changes in respiratory posture, presumably as the cardia is pulled over the fixed tube. With mercury-tipped tubes the recording positions are easily identified on the radiograph. From the pressure record the functional position of each tube is known at the moment of exposure, so that the radiographic position of the functional cardia can be fixed within narrow limits (fig. 6).

Resistance of the Cardia to Forward Passage

It is notable that a very flexible polythene tube is easily passed through the cardia even when it is supporting a considerable inverse pressure during deep inspiration. The cardia's resistance to forward passage of fluid was investigated in the following way:

Pressures were simultaneously recorded above and below the cardia while the region was observed on the X-ray screen. The subject rapidly drank about 250 ml. of thin barium emulsion and the first appearance of the barium in the stomach was signalled. In four experiments the screen was photographed twice a second during the critical period, each exposure

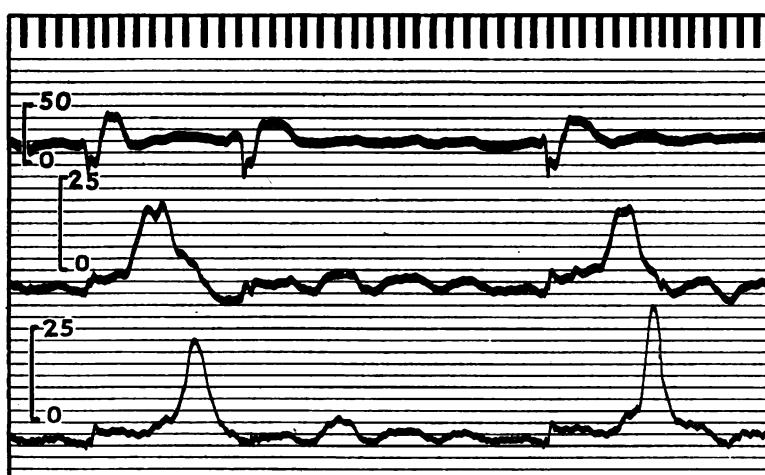


Fig. 1.—Pharyngeal swallows and oesophageal propulsive waves. Upper trace: pressure in pharynx. Middle and lower traces: pressures 9 and 18 cm. down oesophagus. Note that a pharyngeal swallow repeated too soon fails to initiate a propulsive wave. In this and subsequent records, time is marked at the top in seconds and pressures in mm. Hg.

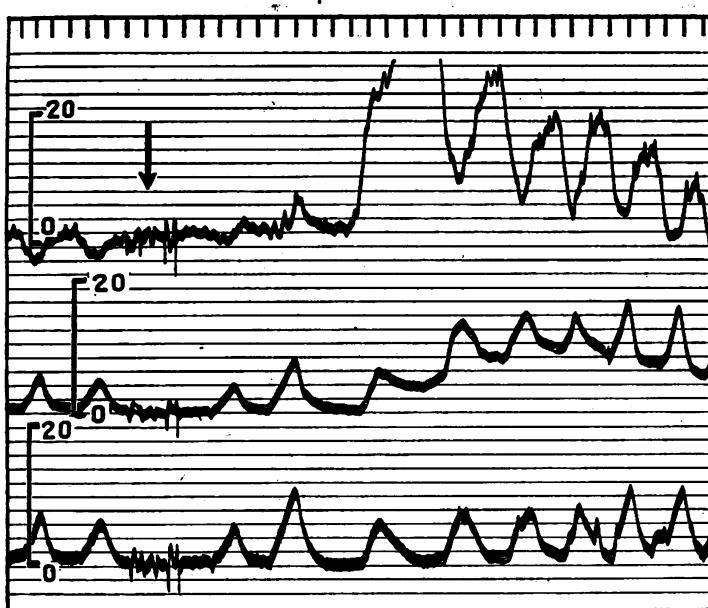


Fig. 3

Fig. 3—Upper trace: pressure on oesophageal side of cardia. Middle trace: pressure on gastric side, 1.5 cm. lower down. Lower trace: gastric pressure clear of the cardia. At arrow, a mouthful of water was swallowed. The lingering pressure rise in vicinity of cardia contrasts with the steady level in stomach. Exaggerated respiratory swings in upper trace suggest that tube is lightly gripped in cardia during expiration.

Fig. 4—Gastric pressures (above) and oesophageal pressures (below) during Müller's manœuvre.

being signalled. From the data it was possible to ascertain the pressure differences required before the fluid would pass through the cardia, and the resistance to the flow once it was established. It should be emphasised that during the whole period under consideration there were no propulsive waves in the oesophagus.

The results are typified by figs. 7 and 8. The descending barium rapidly annuls the previous negative pressure gradient across the cardia and within a second or less the fluid is streaming through a widely open channel, while the pressure in the oesophagus maintains a plateau. Before this happens the gradient swings briefly positive—in fig. 7 by about 4 mm. Hg above the free-flow plateau. The maximum pressure difference reached may be considered as the "yield-pressure" of the cardia. For some seconds after a propulsive wave has reached the cardia this yield-pressure is increased (fig. 9).

The height of the pressure plateau above the level before drinking starts, and the height of the fluid column during the steady-flow period, necessarily increase with increasing depth of inspiration—i.e., with the magnitude of the inverse pressure difference which must be annulled before any forward flow can occur.

When drinking ceases a propulsive wave is normally initiated and a few seconds later it reaches the lower oesophagus, sweeping the remaining contents into the stomach.

The conclusion from these experiments is that, except for the few seconds following a propulsive wave, the normal cardia offers only trivial hindrance to forward flow: the smallness of the yield-pressure and the rapidity of yield (about 0.5 sec.) scarcely suggest a sphincteric mechanism. The height of the column of fluid apparently supported by the cardia is adequately accounted for by the inverse pressure gradient.

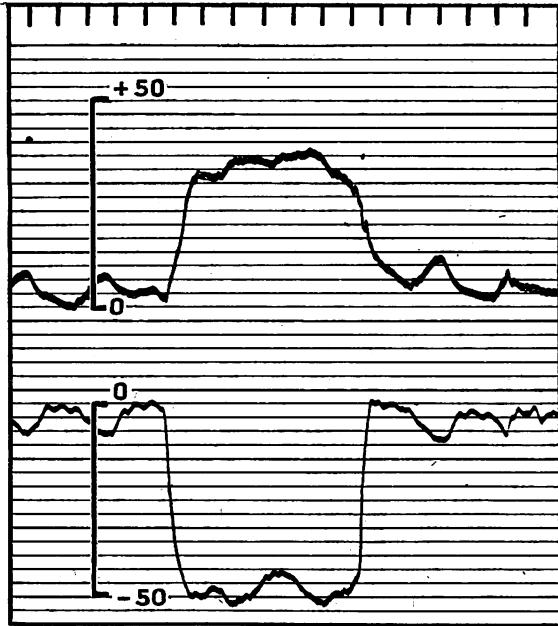


Fig. 4

Rôle of the Diaphragm and other Extragastric Structures

The large inverse pressures that we have described involve contraction of the diaphragm, and it is important to determine whether this can itself occlude the oesophagus. The following observations suggest that this is not so: at the end of a thoracotomy on 3 patients with lung-disease, a finger was passed alongside the oesophagus through the diaphragmatic hiatus, while the patient recovered from the muscular relaxant; even when vigorous diaphragmatic movements were regained, no constriction of the finger by the hiatus could be felt.

The rôle of other anatomical factors was investigated as follows:

In 2 patients it was necessary to mobilise the stomach as the first stage of radical operation for carcinoma of mid-oesophagus. When this had been done and the oesophagus was freely movable in the relaxed hiatus, a tape was passed round

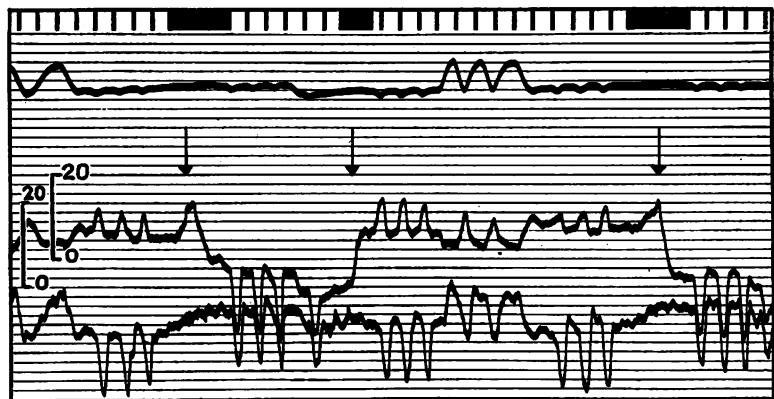


Fig. 5—Upper trace: pneumogram (inspiration downwards); larger excursions are normal respirations, smaller ones are inspiratory efforts with closed glottis to show position of recording sites. Middle trace: pressure at tube opening in vicinity of cardia. Lower trace: tube opening in oesophagus throughout. At signals shown in time record at top, tubes were advanced or withdrawn about 1 cm. Arrows indicate when tube crosses cardia.

the pylorus and the stomach inflated with air with a syringe. It was found that the cardia prevented the escape of air in spite of firm pressure on the body of the stomach. Air readily escaped, however, on manipulation of the cardiac region. During this procedure the stomach was not supported by the liver or other structures. The oesophagus made approximately a right angle with the slight convexity of the fundus. There was no visible groove or fold suggesting contraction of the main muscle layers.

It appears that support from adjacent structures or the maintenance of an acute angle of oesophageal entry are not necessary for cardiac competence. This is, of course, not to say that they may not assist it.

DISCUSSION

Our results show that from the point of view of function the cardia is a very localised region, extending over not more than 5 mm. This region has the characteristics of a valve—namely, very small resistance to forward passage, with the ability to resist retrograde flow in spite of large inverse pressures. The mechanism appears intrinsic to the neighbourhood of the anatomical cardia and to be independent of externally visible folding or kinking. The behaviour is unlike that of known smooth-muscle sphincters, and favours the existence of some form of flap or funnel valve. By exclusion, we have come to believe that the muscularis mucosae, which is well developed in this region (Thomlinson 1953), pulls the lax mucosa into some valvular form. The valve must be capable of active opening for eructation of gas, which we have observed to occur with only trivial rises in gastric pressure and also for vomiting. It is well known that the cardia yields no secrets post mortem, and visual confirmation in the living subject is desirable.

There has been some controversy over the part played by the diaphragm; the increased column of barium supported in the oesophagus during inspiration has been regarded as

evidence of diaphragmatic constriction. Both our direct and indirect evidence is against this notion, which we think to be based on an ignorance of the pressure changes involved and a misconception of the respective roles of gravity and of propulsive waves in the swallowing of liquids in the upright posture.

SUMMARY
The characteristics of normal oesophageal propulsive waves in the swallowing of liquids in the upright posture.

Fig. 7—Upper two traces : pressure in lower oesophagus. Lower trace : pressure in stomach. Barium drunk during long signal shown at top ; films exposed at short signals shown below this. Arrow indicates timing of first film showing barium passing into stomach.

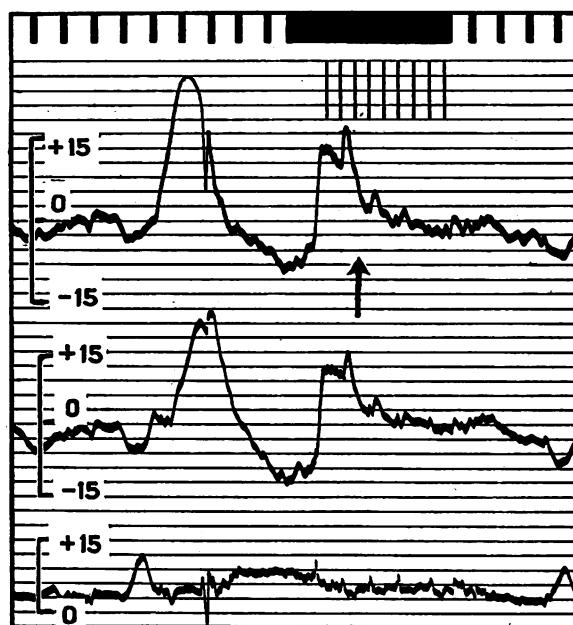
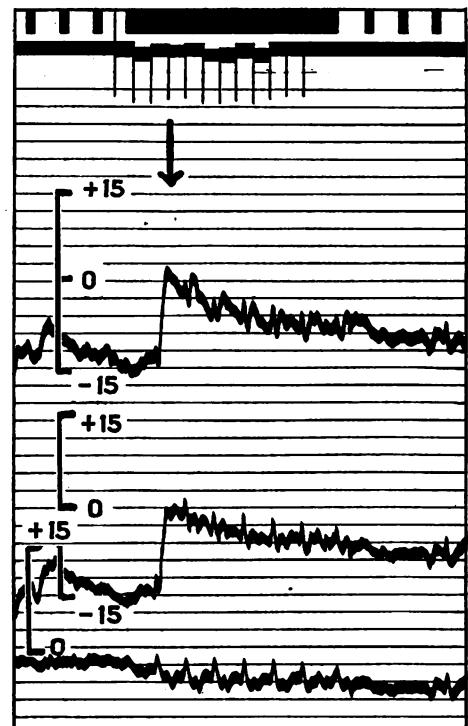


Fig. 9—As in fig. 7, showing effect of a recent propulsive wave on behaviour of cardia.

The normal cardia exerts little resistance to forward passage, but it has a great capacity for preventing retrograde flow. The area of the functional cardia is sharply localised. The cardia is considered to be a valve, probably formed by the action of the muscularis mucosae on the mucosa.

Evidence is produced that the contracting diaphragm does not occlude the oesophagus.

We are indebted for technical assistance to Mr. R. W. Halls and Mr. M. G. Ventom, and to members of the physics and photographic departments of St. Thomas's Hospital.

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THE OESOPHAGEAL LESION IN SCLERODERMA

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WHILE it is well known that in symmetrical progressive scleroderma (sclerodactyly) oesophageal lesions may produce dysphagia, it is less widely recognised that in this condition a disorder of oesophageal function is frequently demonstrable when the patient is unaware of any difficulty in swallowing. We describe here the disorder and its histological basis.

Material and Methods

Six consecutive patients with sclerodactyly were examined by radiography and their oesophageal contrac-

tions recorded as described by Dornhorst et al. (1954). All the patients had typical changes in the fingers; two had in addition certain features suggestive of dermatomyositis. None complained of dysphagia. Necropsy material from two further cases was available for histological study.

Results

All six patients had a definite abnormality of oesophageal function: five showed the same pattern differing only in degree; the sixth had, in addition, a stricture in the region of the cardia.

The characteristic defect was failure of the propulsive waves to continue normally into the lower half of the oesophagus. The upper half contracted with normal vigour; though usually for less than the normal time, and often with spontaneous iteration; but the contraction either failed entirely to propagate or became very feeble and incoördinate (fig. 1). The weakness of the lower oesophagus was manifest radiographically when the patient was observed swallowing in the supine, slightly head-down, position; the bolus was carried briskly to about the position of the tracheal bifurcation where its progress ceased. A further mouthful might push it on a little, but it would not enter the stomach until the patient stood up.

The microscopic appearance is of simple atrophy with minimal fibrous replacement of the main muscle-coats in the lower oesophagus—the muscularis mucosæ is unaffected. There is no sclerosis such as occurs in the dermis (fig. 2).

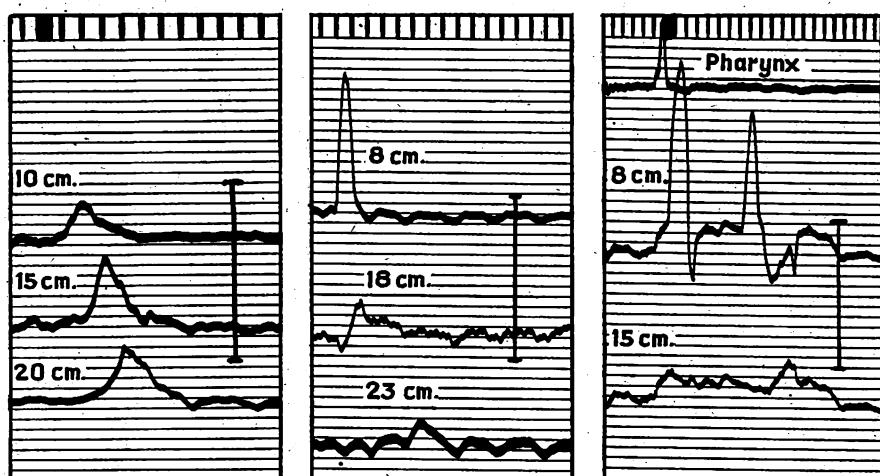


Fig. 1.—Oesophageal pressures recorded simultaneously at different sites. The distance of each site below the cricopharyngeal sphincter is marked on the trace. The vertical bars indicate deflection produced by 50 mm. Hg. Time marked in seconds.

(a) Normal propulsive wave for comparison. The wave, of rather less than average amplitude, is propagated into the lower oesophagus without decrement.

(b) Failing propagation in sclerodactyly. Note adequate force, but short duration of contraction of upper oesophagus.

(c) Iterative contraction in upper oesophagus with failure to propagate. The pressure changes in the lower oesophagus are probably entirely passive.

Discussion

Since all six unselected patients with sclerodactyly had oesophageal disorders though free from dysphagia, the association must be common. Radiographically, since there is no interference with the normal "gravity swallowing," the abnormality is easily overlooked if the patient is examined standing and a barium cream of average consistency is used. One of our patients had been reported as having a hypermotile oesophagus; measurement showed that the movements of the lower oesophagus, while quite numerous, were very feeble. Another had been described as swallowing much air but as otherwise normal: in fact there was complete paralysis of the lower oesophagus and hence no means of expelling air from it. Observation of anti-gravity swallowing is necessary for recognition of this disorder.

The microscopic appearance, radiography, and pressure measurements all point to simple muscle weakness and wasting in the lower half of the oesophagus as the essential lesion. No doubt oesophagitis, with reflux, stricture, &c., occurs as a complication in some patients.

Summary

Oesophageal disorder in sclerodactyly is common, but on radiographic examination may be overlooked unless anti-gravity swallowing is observed.

The essential disorder is weakness and wasting of the muscle of the lower oesophagus.

We are indebted to Dr. G. B. Dowling for his help in sending us patients with scleroderma.

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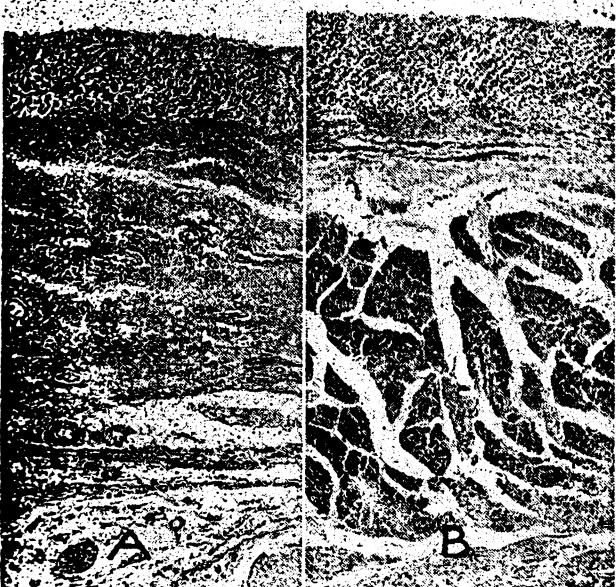


Fig. 2.—Two sections from the lower end of the oesophagus. A shows complete loss of the main muscle coats; while B, taken from 1 in. higher up the oesophagus, shows loss of the longitudinal coat only. In both the muscularis mucosæ is intact.

"... One of the purposes of a journal is to provide a means for the dissemination of the opinion of its readers. ... It is not likely that all the letters received can be published, therefore somebody has to select those most suitable for this purpose and to reject others. ... Fortunately, there will be many who will not approve the editor's decision, for that keeps all concerned alert and on their toes, but he is fortified by the knowledge that a measure of disapproval is inescapable, and that all he can do is to endeavour to see that it moves round as much as possible, and does not stagnate in one place."—*Brit. dent. J.* March 16, 1954, p. 144.

**THE BLOOD-C.S.F. BARRIER TO BROMIDE IN
DIAGNOSIS OF TUBERCULOUS
MENINGITIS ***

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It is now established that, given adequate treatment, the overriding factor in the prognosis of tuberculous meningitis is the stage the disease has reached at the outset of treatment. For example, in a series of 80 consecutive unselected cases treated at Oxford between December, 1949, and July, 1952, whereas the over-all mortality was 37·5%, no patient died among those 21 who were still fully conscious and rational and without focal neurological signs when their treatment was begun. Yet it is precisely in this, the most favourable, stage of the disease that diagnosis can be most difficult. As a result these favourable cases remain a small minority of the whole.

When evidence of active systemic tuberculosis is lacking, the clinical picture at this stage of the illness is simply one of mild meningeal inflammation. The abnormalities of the cerebrospinal fluid (c.s.f.) may be limited to a lymphocytic pleocytosis and some increase in the protein content, since the chloride content is seldom decreased and, not infrequently, even the glucose content is still within normal limits. The differential diagnosis is thus from virus infection of the central nervous system (especially pre- or non-paralytic poliomyelitis); from spirochaetal infections, such as syphilis and leptospirosis; from brain abscess and, occasionally, tumour; and from benign lymphocytic meningitis of unknown aetiology (Cairns et al. 1950). In the absence of any distinctive clinical or pathological features differentiation may be extremely difficult; yet, if the case is really one of early tuberculous meningitis, to withhold treatment until the nature of the disease has declared itself is often to wait until too late.

Recently we have been receiving an increasing amount of help in the management of these difficult cases from the results of studies on the passage of bromide from blood to c.s.f. The opportunity to make these observations arose during the course of larger studies on the aetiology of glaucoma and of schizophrenia. The bromide test used is a modification of that devised by Walter (1929). For a critical assessment of its reliability as a means of measuring barrier permeability see Hunter et al. (1954).

Methods

Sodium bromide is used as the test substance and is given by mouth or by intravenous injection. The oral dose for adults is 1·0 g. t.d.s. for three days and for children 0·25–0·5 g. t.d.s. for three days, depending on the size of the child. The intravenous dose for adults is 8 g. and for children 2–4 g. given at a single injection. The intravenous solution is made up by dissolving 8 g. of sodium bromide in 30 ml. of sterile distilled water. After oral administration two full days is allowed for equilibrium to become established between blood and c.s.f.; after intravenous administration twenty-four hours is sufficient. The intravenous solution is moderately

irritating, causing some patients to complain of local discomfort towards the end of the injection, and care must be taken to ensure that all the solution is delivered into the vein and none allowed to escape into the surrounding tissues. The sodium bromide has had no other detectable effect on the clinical condition of the patients. The bromide is excreted so slowly that this dose has proved sufficient to maintain measurable levels in blood and c.s.f. for several weeks.

When equilibrium has been established, samples of venous blood and of c.s.f. are collected into dry and

SERUM/C.S.F.-BROMIDE RATIOS IN "NORMAL" CONTROLS

Condition	No. of cases	Bromide ratio	
		Range	Mean
Psychosis	13	2·20–3·39	2·68
Glaucoma	6	1·95–2·97	2·52
Tuberculosis without meningitis ..	5	2·03–3·05	2·53
Total	24	1·95–3·39	2·61

chemically clean test-tubes. Venous blood 5 ml. and c.s.f. 3 ml. are sufficient to allow the estimations to be done in duplicate. The clotted blood is centrifuged and the bromide contents of the serum and c.s.f. are estimated. The results are expressed as the ratio of the serum-bromide level to the c.s.f.-bromide level (serum/c.s.f. bromide). This we call the bromide ratio.

All the ratios given here are based on lumbar c.s.f. Since the bromide content of cisternal and ventricular fluids is lower than that of lumbar c.s.f., ratios based on those fluids are not comparable with ratios based on lumbar c.s.f.

All the bromide estimations were made by an iodometric titration method (Hunter 1953).

Results

"NORMAL" CONTROLS

By this method of determination we find that, in the absence of detectable organic disease of the central nervous system, serum contains two or three times as much bromide as does c.s.f.—in other words, the bromide ratio is 2–3. These results (see table) were obtained from cases of various kinds of psychosis, from cases of glaucoma, and from cases of tuberculosis without evidence of meningitis.

These ratios are significantly lower than those reported by Walter (1929). This discrepancy is undoubtedly due to the different method used for the bromide estimations. Walter and his immediate followers used the gold-chloride method for their estimations. The bromide levels of several samples of blood and c.s.f. have now been estimated both by the gold-chloride and by the iodometric titration methods. Whereas the results obtained by the two methods in c.s.f. were in close agreement, some substance other than bromide was present in blood that reacted with the gold chloride to give the same brown colour. The serum-bromide levels, and consequently the bromide ratios, estimated by the gold-chloride method are too high (see Hunter et al. 1954).

We have now estimated the bromide ratio in several neurological disorders, especially tuberculous meningitis, non-purulent meningitis other than tuberculous meningitis, and during intrathecal tuberculin reactions. A full report of our findings is in preparation, but certain points of practical importance are briefly discussed here.

DURING INTRATHECAL TUBERCULIN REACTION

By the intrathecal tuberculin reaction is meant that wave of meningitis which follows the introduction of tuberculin into the c.s.f. of a Mantoux-positive person

* Based on communications given to the Association of British Neurologists and the Association of Clinical Pathologists.

† Working with a grant from the Medical Research Council.

with normal meninges and without active tuberculosis. This meningitis, which undoubtedly reflects a true specific antibody-antigen reaction, affects both the cellular and protein content of the c.s.f. and is, when fully developed, diphasic (Swithinbank et al. 1953). The reaction has a dramatic effect on the passage of bromide from blood to c.s.f. During the first phase of the reaction the serum/c.s.f.-bromide ratio falls to unity; in other words, the blood-c.s.f. barrier to bromide is abolished. The ratio remains at or below unity throughout the second phase of the reaction and then slowly begins to climb, but it is many weeks before the barrier is completely re-established. That the ratio is a reliable indicator of the permeability of the blood-c.s.f. barrier to bromide is shown by the fact that it is independent of the absolute amounts of bromide present in blood and c.s.f. (fig. 1).

The rise of the c.s.f.-bromide level is often, but by no means invariably, associated with a rise of the c.s.f.-protein level. At the beginning of the reaction the serum/c.s.f.-bromide ratio falls as the c.s.f.-protein level rises; but, as the reaction develops, the two tend to become dissociated, until finally the c.s.f.-protein level returns to normal before the bromide ratio. A dissociation between the c.s.f.-protein level

and a disturbance of the bromide ratio has been seen in other neurological conditions. The one condition we have so far found in which a low bromide ratio has invariably been associated with a high c.s.f.-protein level is spinal block. Whether the block has been due to spinal-cord tumour or to tuberculous meningitis, the ratio for the fluid below the block has always been about 1.

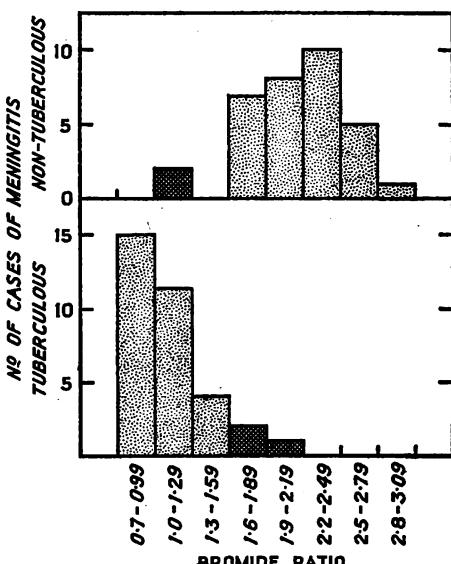


Fig. 2.—Bromide-ratio distributions in 33 cases of early proved tuberculous meningitis and in 33 cases of non-tuberculous "non-purulent" meningitis. For further explanation see text.

below the block has always been about 1.

TUBERCULOUS MENINGITIS

Active tuberculous meningitis appears to have the same effect on the blood-c.s.f. barrier as does the intrathecal tuberculin reaction. In our experience it has been the rule for the ratio to be profoundly depressed but to return to normal when the infection is brought under control. Even when intrathecal tuberculin was not used in treatment, values of 1 or less were common.

Moreover, this fall in the ratio appears to happen early in the illness.

For example, two young women were admitted to hospital at about the same time, both with miliary tuberculosis. As soon as the diagnosis was established radiographically, a routine lumbar puncture was done in each case. In the first the lumbar c.s.f. contained 2 cells per c.mm. and protein 35 mg. per 100 ml. The bromide ratio was 2.18—i.e., within normal limits. The patient made a straightforward recovery without ever developing any signs or symptoms of meningitis.

In the second case the lumbar c.s.f. contained 10 cells per c.mm. and protein 120 mg. per 100 ml., but the bromide ratio was only 0.99. The patient was treated for tuberculous meningitis, and the diagnosis was later confirmed when *Mycobacterium tuberculosis* was cultured from an early specimen of c.s.f. Shortly after conclusion of the intrathecal therapy the ratio had risen to 2.39; and at her last follow-up, seventeen months after the beginning of her illness, it was 2.97.

The results obtained in 33 cases of tuberculous meningitis are shown in fig. 2. The diagnosis was confirmed in all the cases by the isolation of *M. tuberculosis* from the c.s.f. This figure is restricted to estimations of the bromide ratio made during the first month of treatment, since this is a period for which it is certainly justifiable to treat suspected but unproved cases of tuberculous meningitis. None of these patients had received any intrathecal tuberculin before the bromide test, nor did any of them show evidence of a spinal block. These are, of course, necessary conditions for comparison, since the intrathecal injection of tuberculin can lower the ratio to 1 or less even in people with normal meninges, and the ratio is always low for the fluid below a spinal block.

OTHER VARIETIES OF NON-PURULENT MENINGITIS

In other varieties of non-purulent meningitis a fall in the bromide ratio comparable with that found in tuber-

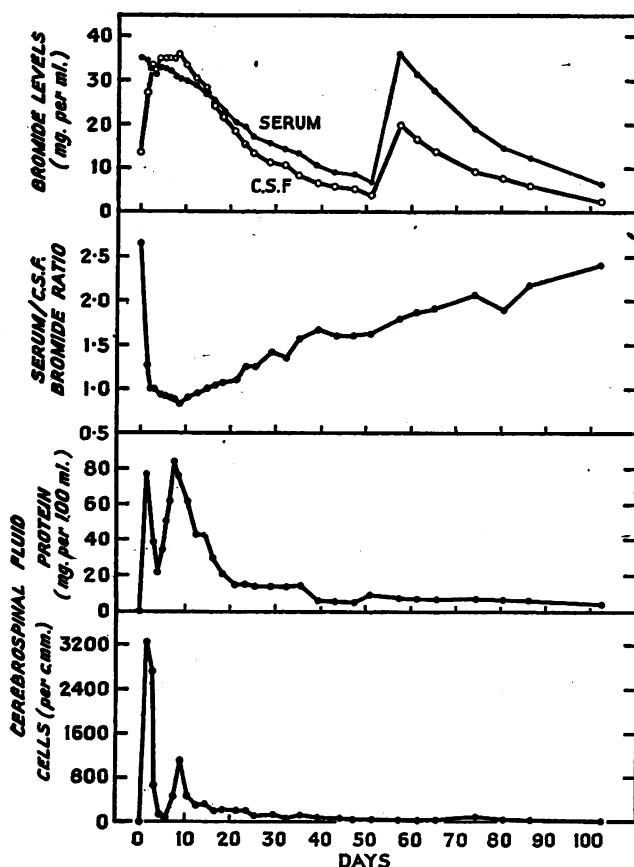


Fig. 1.—Intrathecal tuberculin reaction in a person with normal meninges.

Note (1) steady fall in serum-bromide level until 52nd day, when another three-day oral "course" (total 9.0 g. of sodium bromide) was given; (2) rapid rise in c.s.f.-bromide level after intrathecal injection of tuberculin on day 1; (3) abrupt fall of bromide ratio after injection of tuberculin, and its steady recovery, still incomplete after 102 days (increase in serum-bromide and c.s.f.-bromide levels between days 50 and 60 had no effect on ratio); (4) diphasic rise in the cell-counts and protein content of c.s.f. (during first phase serum/c.s.f.-bromide ratio falls sharply to 1 and only begins to climb as the second phase subsides).

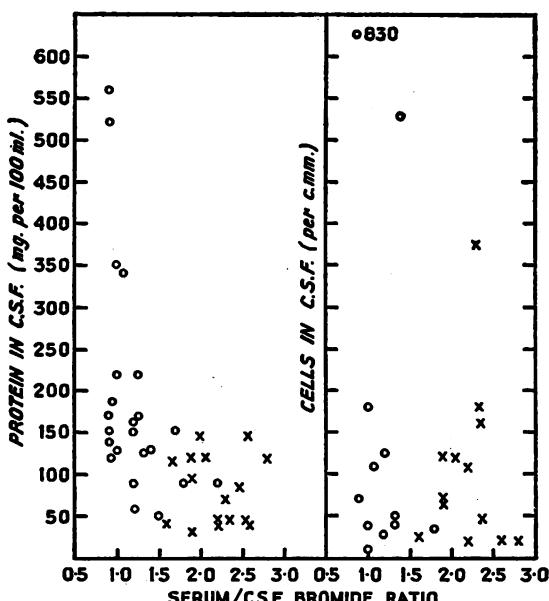


Fig. 3.—Serum/C.S.F.-bromide ratio plotted against amount of protein and cells in C.S.F. in tuberculous and non-tuberculous cases of meningitis. Findings in tuberculous cases are shown by circles and in non-tuberculous by crosses. For further explanation see text.

lous meningitis has proved exceptional. Even though the changes in the number of cells and the amount of protein in the C.S.F. were about the same as those in tuberculous meningitis, the blood-C.S.F. barrier to bromide was, on the whole, remarkably well maintained. This finding suggested that the bromide test might be used as an aid to the diagnosis of tuberculous meningitis. Accordingly the ratio was estimated in 33 cases of non-purulent meningitis that was not tuberculous. The composition of this group is shown in the following list, which includes many of those conditions from which the differentiation of early tuberculous meningitis can be most troublesome:

Diagnosis	No. of cases
Paralytic poliomyelitis	9
Choreo-lymphocytic meningitis (mouse-borne)	1
Neurosyphilis	2
Leptospirosis	1
Cerebral abscess	1
Intracranial tumour	1
"Lymphocytic meningitis" * of unknown aetiology	18
Total	33

* Includes probable cases of non-paralytic poliomyelitis.

The ratio distributions for the cases in these two groups are shown in fig. 2. In the great majority of the tuberculous cases the ratio was between 0.7 and 1.29, and in only 3 of the 33 was it higher than 1.6. The ratio distribution for the non-tuberculous cases shows a flatter peak, as might be expected in a group of mixed aetiology. But, by contrast with the tuberculous cases, in only 2 of the 33 was the ratio lower than 1.6. Thus, with 1.6 as the critical level, in 5 cases out of 66 the ratio fell out of place, giving an error of about 7%.

This difference in the bromide ratios of the two groups is largely independent of any differences in the amounts of protein and cells in the fluids (fig. 3). Except for a few tuberculous cases in which a very high protein content was invariably associated with a low ratio, the disturbance in both cells and protein was about the same in both groups of cases, and in the tuberculous cases a trivial increase of protein proved quite compatible with a low bromide ratio.

EFFECT OF INTRATHECAL CHEMOTHERAPY

Several of the patients in the non-tuberculous group were originally suspected of being tuberculous and were receiving daily intrathecal injections of streptomycin,

or of streptomycin and isoniazid, when the bromide ratio was estimated. In spite of this the ratios were not obviously depressed. We therefore conclude that this form of intrathecal medication has no significant effect on the blood-C.S.F. barrier to bromide.

Discussion

There is already a considerable amount of circumstantial evidence that the changes in the C.S.F. in tuberculous meningitis are the expression of spontaneous intrathecal tuberculin reactions—i.e., of a hypersensitivity or antibody-antigen response (Cairns and Smith 1952). The finding that the disturbance of the bromide ratio is identical in tuberculous meningitis and in the experimental intrathecal tuberculin reaction strongly supports this hypothesis. It also suggests that some mechanism other than a hypersensitivity effect must be at work in the production of the C.S.F. changes in many of the other varieties of non-purulent meningitis.

From the point of view of diagnosis we do not for one moment suggest that a low bromide ratio is pathognomonic of tuberculous meningitis. Nor must the result of the bromide test be considered in isolation from the other findings, clinical and pathological. But in doubtful cases where the picture as a whole is compatible with the diagnosis of tuberculous meningitis the finding of a low bromide ratio is strong reason for beginning treatment without further delay.

Summary

The diagnosis of tuberculous meningitis in its early and most favourable stage may be extremely difficult.

The bromide test for permeability of the blood-C.S.F. barrier is described, and evidence is presented that the barrier to bromide is more frequently and more seriously impaired in tuberculous meningitis than in other varieties of meningitis with comparable changes in the C.S.F.

The bromide test may therefore prove helpful in the early diagnosis of tuberculous meningitis.

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AMINO-ACIDURIA IN MARCH HÆMOGLOBINURIA

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MARCH hæmoglobinuria is an uncommon and apparently harmless transient disturbance after exercise in the upright posture. Most usually it affects young men, but Gilligan and Altschule (1950) have described the syndrome in a young woman and consider that it is commoner in females than is usually supposed. Because this disorder is benign and transient, our knowledge of its pathology is slight, although its clinical aspects have been fully described (Witte 1936, Gilligan and Blumgart 1941, Gilligan et al. 1941, 1943, Palmer and Mitchell 1943, Hobbs 1944, Kurz 1948, Lubran and Sakula 1949, Whitby and Britten 1950, Plumb 1951).

The colour of the urine is startling enough to bring the patient to his doctor. It is classically described as being

of a port-wine colour, but the patient's description of it as resembling black blood is equally apt. Associated symptoms are usually absent, though there may be slight aching in the loins. The haemoglobinuria is directly related to exercise in the upright posture; swimming or cycling never result in the syndrome. Gilligan and Blumgart (1941) have strikingly demonstrated the influence of posture by showing the inhibitory effect of increasing kyphosis on the degree of intravascular haemolysis. Usually the disturbance occurs after an unaccustomed degree of exercise—many cases have been described in young recruits to the Armed Forces—but the exercise threshold tends to be constant for each individual. Summation may be apparent, as in a patient we saw who only had the syndrome if he played football two days in succession. Discoloration is maximal immediately after exercise, and decreasing amounts of haemoglobin are found in urine passed during the next few hours. By the time the patient reaches hospital his urine is usually quite clear, and the diagnosis has to be made from the history, with laboratory tests to exclude other causes of haemoglobinuria and haematuria. After a period varying from a few months to several years the attacks disappear spontaneously, and these do not recur in later life.

Two main factors seem to produce this disorder:

1. Increased haemolysis. The plasma-haemoglobin is normal at rest but after exercise rises to abnormally high values; its level increases with the degree of exertion and falls as soon as the exercise is stopped (Gilligan and Blumgart 1941, Gilligan et al. 1943).

2. Renal tubular defect. By correlating the time of onset of haemoglobinuria with the plasma-haemoglobin values, it has been found that the renal threshold for haemoglobin in these patients is much reduced. This abnormality is probably not related to the exercise since a similar threshold is found during rest (Gilligan and Blumgart 1941, Gilligan et al. 1941). Gilligan et al. (1941) have shown in normal subjects that, once this peak is exceeded, excretion of haemoglobin will continue at levels as low as 50% of the normal threshold.

Material

While investigating a patient with a history of march haemoglobinuria, we observed that he was a natural excretor of β -amino-isobutyric acid. On the basis of this case and the known renal tubular abnormality in patients with march haemoglobinuria, we decided to examine for abnormal amino-acid excretion the urines of as many patients as possible who had had this complaint. The Army authorities kindly collected for us the case-notes of 24 patients who had been in hospital with symptoms suggestive of the syndrome during the past seven years. Owing to the nature of the disorder, haemoglobinuria was seldom observed in hospital, and "probable" cases of march haemoglobinuria were selected by the following criteria:

1. The patient must be a young man who gave a history of passing dark red urine directly related to exercise in the upright posture, with absent or only slight associated symptoms.

2. Absence of red blood-cells on microscopical examination of the urine was likewise essential.

3. At least one of the following investigations must have yielded supporting evidence: (a) oxyhaemoglobin found on spectroscopic examination of the urine with absence of red blood-cells on microscopy; (b) negative serological examination of the blood; or (c) negative radiographic and bacteriological examination of the urinary tract.

Of the 24 cases, 15 appeared from their notes to be "probables" and we were able to obtain early morning specimens of urine from 11 of these, making 12 in all with our original case.

Methods

Samples of early morning specimens of urine were obtained from the 12 patients and stored in a refrigerator with a crystal of thymol as preservative. Volumes of urine containing 0.015 mg. of creatinine were spotted on

RESULTS OF TESTS ON EARLY MORNING SPECIMENS OF URINE FROM 12 PATIENTS WHO HAD HAD MARCH HAEMOGLOBINURIA IN THE PREVIOUS SEVEN YEARS. THE RESULTS FOR CHEMICAL ANALYSIS OF CYSTINE ARE GRADED FROM 0 TO 4 ARBITRARY UNITS

Case no.	Cystine		B.A.I.B.	Generalised amino-aciduria
	Chem.	Chromat.		
1	3	++	+	+
2	4	++	+	+
3	2	+	+	0
4	1	+	+	0
5	2	+	+	0
6	2	++	+	0
7	3	+	+	0
8	4	++	+	0
9	3	+	+	0
10	1	+	Slight	0
11	1-2	+	Slight	0
12	2	+	0	0

to 20-cm. squares of Whatman no. 1 filter-paper and run as two-dimensional chromatograms, using phenol-water and collidine-lutidine-water as solvents.

Cystine was demonstrated chromatographically by oxidation with 30% (100 vol.) H_2O_2 and 0.1% ammonium molybdate, and chemically by the cyanide-nitroprusside test of Brand et al. (1930). A rough quantitative estimation was attempted by this latter test, grading the intensity of colour response in 0-4 arbitrary units. β -amino-isobutyric acid was identified by the following procedures:

1. β -amino-isobutyric acid (kindly presented to us by Mr. R. G. Westall) occupied a similar position on the chromatogram and also reinforced the unknown spot when both were put up together.

2. Hydrolysis with concentrated hydrochloric acid at 100°C for twenty-four hours did not change the chromatographic properties of the substance.

3. Similarly, it was not affected by oxidation with 30% (100 vol.) H_2O_2 and 0.1% ammonium molybdate.

4. "Copper runs" were done by the method of Crumpler and Dent (1949), these leaving the unknown spots unchanged.

Results

The results of the urinary analyses are shown in the accompanying table. Cystine was excreted in excess in every case. β -amino-isobutyric acid (B.A.I.B.) was present in 11 of the 12 cases, although in 2 of these the quantity was small. In 2 cases there was pronounced general amino-aciduria, including B.A.I.B.

As far as our methods would allow of quantitative assessment, the results suggested a correlation between the amounts of cystine excreted and the presence or absence of other amino-acids in the urine. Thus in both the cases with generalised amino-aciduria there was evidence of a larger excretion of cystine in the urine than in most of the other cases. Conversely only comparatively small amounts of cystine, although larger than normal, were present in the urines of the 3 patients who showed either an absence or only traces of B.A.I.B.

Discussion

Gilligan et al. (1943), observed increased haemolysis in 18 out of 26 marathon runners. Whereas the accepted level for normal persons at rest is less than 6 mg. haemoglobin per 100 ml. plasma, values of 15-44 mg. per 100 ml. plasma were found in their series; and 3 of the runners had actual haemoglobinuria. Patients with march haemoglobinuria have a tendency to abnormal intravascular haemolysis after relatively moderate exercise, although there would appear to be no clear-cut distinction between normal and abnormal (Witts 1936, Hobbs 1944, Lubran and Sakula 1949, Plumb 1951).

For haemoglobin to appear in the urine, haemolysis must occur to such an extent that the plasma-haemoglobin level is greater than the renal threshold for this substance. Conceivably this could occur with the normal renal threshold of over 135 mg. per 100 ml. plasma (although

such a state has not, to our knowledge, been described). Obviously haemoglobinuria would be more likely in the presence of a low renal threshold; and indeed haemoglobin has been found in the urine with plasma values of less than 100 mg. per 100 ml. (Gilligan and Blumgart 1941, Gilligan et al. 1943, Palmer and Mitchell 1943, Hobbs 1944, Lubran and Sakula 1949, Gilligan and Altschule 1950, Plumb 1951).

Many workers' estimates of the renal threshold for haemoglobin were based on plasma samples taken from their patients after the exercise had been completed. These figures were thus, perhaps, abnormally low; for Gilligan et al. (1941) have shown by intravenous injection of haemoglobin that, once the renal threshold has been exceeded, haemoglobin will continue to be excreted at much lower plasma levels. In the resting patient Gilligan et al. demonstrated an initial renal threshold of 30-75 mg. per 100 ml. plasma in patients with march haemoglobinuria, but their experimental method precluded any estimate of the specific effect of exercise.

This low but variable renal threshold to haemoglobin suggests that these patients have a renal tubular defect of differing severity. Our experimental findings indicate that this same defect involves tubular reabsorption of amino-acids. The degree of amino-aciduria cannot be correlated with the clinical severity of the syndrome, since the haemoglobinuria depends not only on the renal threshold but also on the amount of intravascular haemolysis.

In our cases increased urinary excretion of cystine was a constant finding. The two with the highest urinary cystine level showed a chromatographic pattern consistent with heterozygous cystinuria (Harris and Warren 1953). It would be interesting to assess the renal threshold to haemoglobin in other conditions associated with an excessive cystine excretion, such as the Fanconi syndrome, Wilson's disease, and homozygous cystinuria (Dent 1947, Uzman and Denny-Brown 1948, Cooper et al. 1950, Dent and Rose 1951). Urinary B.A.I.B. is almost as constantly associated with march haemoglobinuria as is excess urinary cystine. In a large majority of our cases B.A.I.B. was present in the urine, although it is found chromatographically in only about 10% of the general population (Harris 1953). We suggest that the reabsorption of cystine, B.A.I.B., and haemoglobin takes place in the same or adjacent sections of the renal tubule and that the low renal threshold in march haemoglobinuria is a non-specific tubular defect.

Summary

March haemoglobinuria is due to an association of two abnormalities: (1) increased intravascular haemolysis on exertion in the upright posture; and (2) lowered renal threshold to haemoglobin. This renal tubular defect also manifests itself in amino-aciduria.

It is suggested that cystine, β -amino-isobutyric acid, and haemoglobin are reabsorbed in the same or adjacent sections of the renal tubule, and that the low renal threshold in march haemoglobinuria is a non-specific tubular defect.

We should like to thank Dr. Harry Harris for his advice on the classification of the cystinurias. This work would not have been possible without the willing co-operation of the Army Medical Statistics Department and various regimental record offices. We are grateful to the A.D.M.S., Home Counties District, for permission to publish this paper.

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THE BRISTOL RESPIRATOR

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In this country we still largely depend on the Both respirators donated to the nation by Lord Nuffield. Possibly we would have been in a much worse case since 1947 but for the extraordinary foresight represented by these gifts, though up till then the supply sufficed so well that advances in respirator design may have been delayed. Despite any criticism, the Both machine has given invaluable service; and the Ministry of Health (1953) has advocated modification of this apparatus rather than the introduction of a new respirator.

In April, 1953, a review of resources for artificial respiration in this hospital showed that we were almost wholly dependent on Both machines already much depreciated by time and use; and we had no means of positive-pressure respiration. As an immediate priority the Clevedon respirator was developed (Macrae et al. 1953); and in August, 1953, work began on a new type of cabin respirator to improve on the Both machine.

Design

Advice was sought extensively from nurses much experienced in the use of respirators and from intelligent ex-patients. Nurses emphasised the sheer physical work involved in using telescopic machines, the space occupied by such machines when extended, the worry of working against time when the apparatus is opened, the relative immobility of the machine, and the almost complete uselessness of the hand ports lavishly provided on some respirators. Patients' criticisms applied to the appearances of the tank, the inflexibility of the neck seal, the suffocating sensation each time the tank was opened, and the equal discomfort of lung inflation through a face-mask.

The 'Bristol' respirator is shown in figs. 1-4. As will be seen (fig. 1), when ready for use this looks like a bed.

RESPIRATOR CABIN

The cabin has a rectangular box-type base, and it is fitted with a hinged and detachable dome at the head end and a long cover hinged at the foot end. This cover, which has six 'Perspex' windows giving clear vision to the whole of the inside, is balanced by means of a swinging weight and is secured in position by quick-acting lever clamps, one on each side.

The end panel is split longitudinally, the lower half being the head end of the box base while the upper half is part of a separately detachable component (fig. 3). This combination of end-pieces contains the neck seal, which is of reinforced sponge-rubber; if necessary, this can be replaced with an inflatable seal. The upper

DR. PARE, DR. SANDLER: REFERENCES—continued

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component is secured to the main box with quick-acting clamps, one on each side. The hand openings or doors (one either side) are fitted with rubber seals, to reduce air leakage when the hand is inserted, and with rubber gaskets and quick-acting clamps.

The hinged perspex dome connected to the end panel can be lowered over a patient's head and fastened by two lever clamps (fig. 4). When not in use the dome is held open by a hinged fork, or it may be removed by withdrawing the two hinge-pins.

The head rest (fig. 1) has a sponge-rubber pillow : it is circular except for a cut-away to provide extra clearance if necessary ; it has vertical and sliding adjustments and can be rotated ; it permits bronchoscopy.

A box, fitted externally to the foot of the cabin, has a sliding panel on which the air-duct

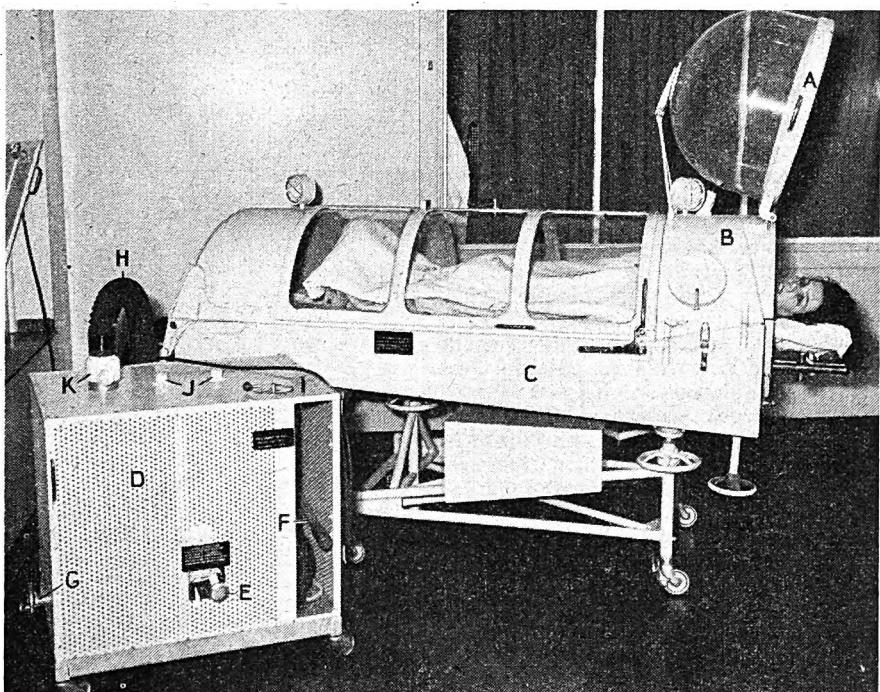


Fig. 2.—The respirator in use.

C, Box base. D, Pump unit. E, Motor-clutch lever. F, Telescopic manual operation handle. G, Respiration-speed adjustment. H, Flexible hose. I, Switches. J, Relief valves. K, Hose coupling.

from the pumping unit is fixed. Sliding this panel sideways selects either a duct to give vacuum to the cabin or a duct to give pressure to the perspex dome through a channel built into the cabin floor. The box is also fitted with valves to control the air-pressures supplied to either the cabin or the dome. An additional valve in the dome permits a controlled flow of air for ventilation and prevents condensation.

The cabin is fitted with two pressure-gauges, one showing vacuum inside, and the other connected by a pipe to record positive pressure in the dome when that is in use. These gauges are identical ; the scales (black for positive and red for negative pressure) indicate pressures of 0-35 cm. of water, positive or negative.

A drawer is fitted under the cabin on the undercarriage frame.

The respirator, supported on four castors fitted with foot-brakes, is easily moved by one nurse.

The dimensions are as follows :

Inside length of cabin ..	5 ft. 10 in.
Maximum inside breadth of cabin ..	2 ft. 5 in.
Diameter of dome ..	1 ft. 10 in.
Minimum height of bed from floor ..	2 ft. 8 in.
Maximum over-all width ..	2 ft. 10 $\frac{1}{4}$ in.

Adjustment of Cabin

The cabin is set in position on an undercarriage by means of three screw-jacks, two at the head and one towards the foot, mounted on a tubular hinged frame. The jacks are independent and attached to the underside of the cabin by universal joints and ballbearings ; that at the foot is fixed to a sliding plate. The greatest "upward" adjustment is 10° at the head and 23° at the foot end. Either side at the head can be tilted 15° sideways. Intermediate positions can be obtained within these maxima.

The mattress frame is mounted at the head on two screw-jacks connected together by a roller-chain.

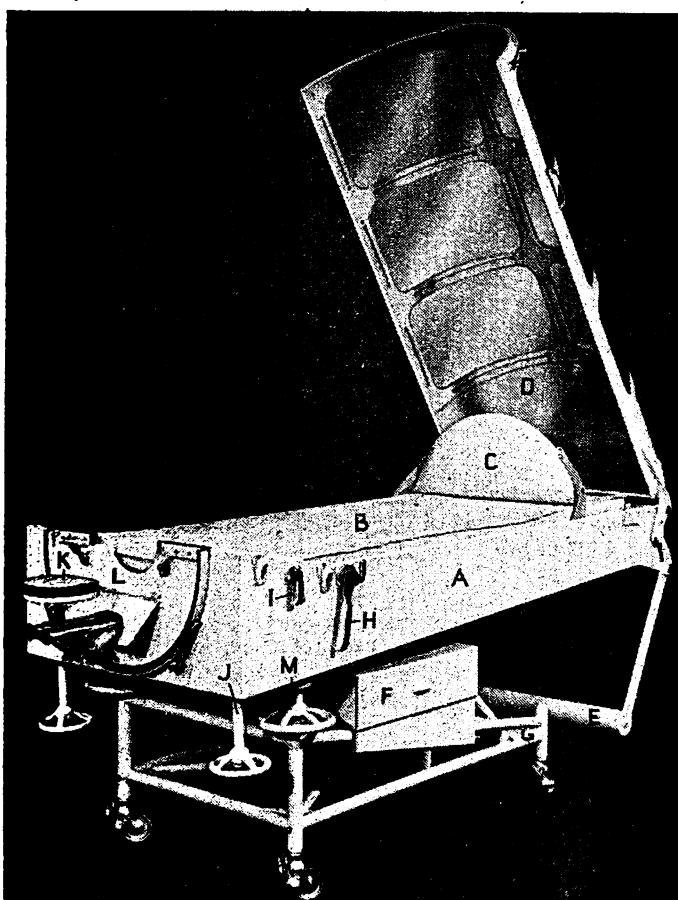


Fig. 1.—The respirator ready for a patient.

A, Box base. B, Bed. C, Foot rest. D, Cover. E, Counter-balance weight. F, Drawer. G, Undercarriage on locking-castors. H, Cover clamp. I, Detachable head-end component clamp. J, Adjustment vertical movement of bed. K, Head rest. L, Socket lower half neck seal. M, Screw-jack for left lateral tilt.

This provides a vertical movement of 5 in. and gives close control of the patient to suit neck-seal requirements. A foot rest, adjustable along the length of the mattress, is included (fig. 1).

THE PUMP UNIT

The pump unit is separate from the cabinet and readily detachable (figs. 2 and 5). It consists of a $\frac{1}{2}$ H.P. electric motor running at 1450 r.p.m., driving through a variable-speed pulley (expanding type), range 3 to 1, and a worm gearbox of 25 to 1. This gives final speeds of approximately 30–10 r.p.m.; variation between these limits is made by turning a small wheel to adjust the motor on slide rails.

The gearbox output shaft is fitted with a gear-wheel meshing into a similar wheel mounted on its own bearing shaft. These gears are mounted eccentrically, thereby giving a changing velocity ratio with an expiration to inspiration value of 4 to 3.

The pump itself is of the bellow type, consisting of two end-boards connected by leather. The top board of the bellows is supported on a base frame by three vertical tubes which also act as roller-

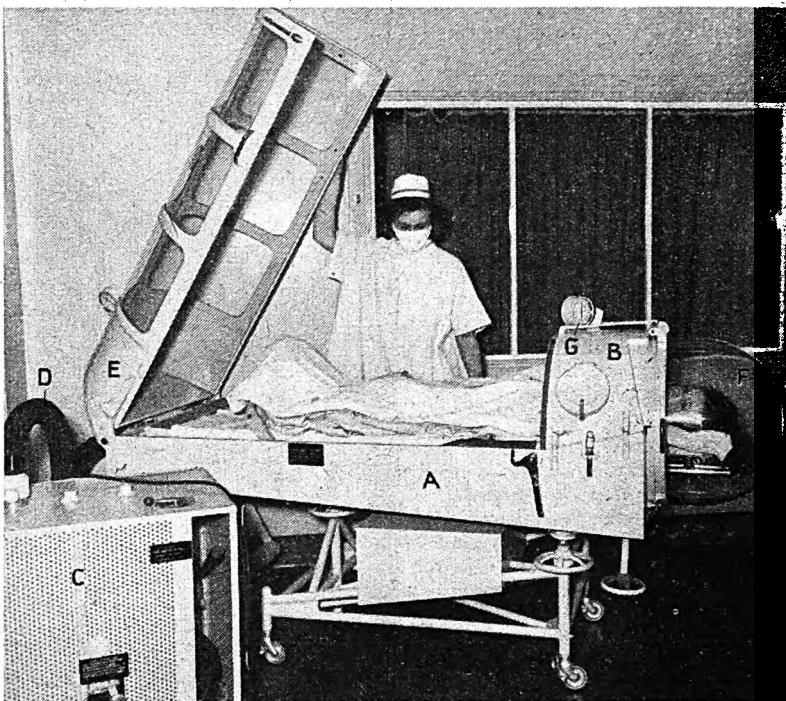


Fig. 4—The perspex dome in use.

A, Box base. B, Head-end upper component. C, Pump unit. D, Flexible hose. E, Cover. F, Perspex dome. G, Dome-pressure gauge.

guides. The top board is fitted with adjustable positive and negative pressure relief-valves and a detachable coupling for the air duct ($2\frac{1}{2}$ -in. flexible hose). The bottom board has a fitting to take a connecting-rod which is also attached to a lever on a layshaft to the side of the unit. On this shaft is another lever carrying a connecting rod attached to a pin in the face of the lower gear-wheel, thus imparting a reciprocating motion to the bellows.

The two levers on the layshaft are connected together by means of a dog coupling, sliding on a serrated sleeve whereby the motor can be disconnected and the pump operated manually by a lever positioned at one end of the shaft. This hand lever is normally within the casing which surrounds the unit, but can readily be withdrawn to operating position. The dog coupling is moved as required by a hand lever. The complete pump unit is enclosed in a casing and is mounted on four easily moving castors.

The Respirator in Use

The respirator was first used on Dec. 26, 1953. It has been used in five cases of respiratory paralysis, due to poliomyelitis, in adults. One patient, a State-registered nurse, did not recognise the apparatus as a respirator when she saw it ready for her reception. This patient, who was in the respirator for fifteen days, has nothing but praise for it, particularly on account of the comfort and the continuity of breathing provided by the positive-pressure dome.

The dome, which has been needed in three cases, has been a happy revelation to nurses accustomed to older types of respirator. It has been used for as long as forty-five minutes at a time—one patient fell asleep in it—and no ill effects have been reported or observed. Nursing has been unhurried, unworried, and accomplished in less time than the necessarily staccato performance with older types of respirator. One nurse can do all nursing tasks alone, except for major changes

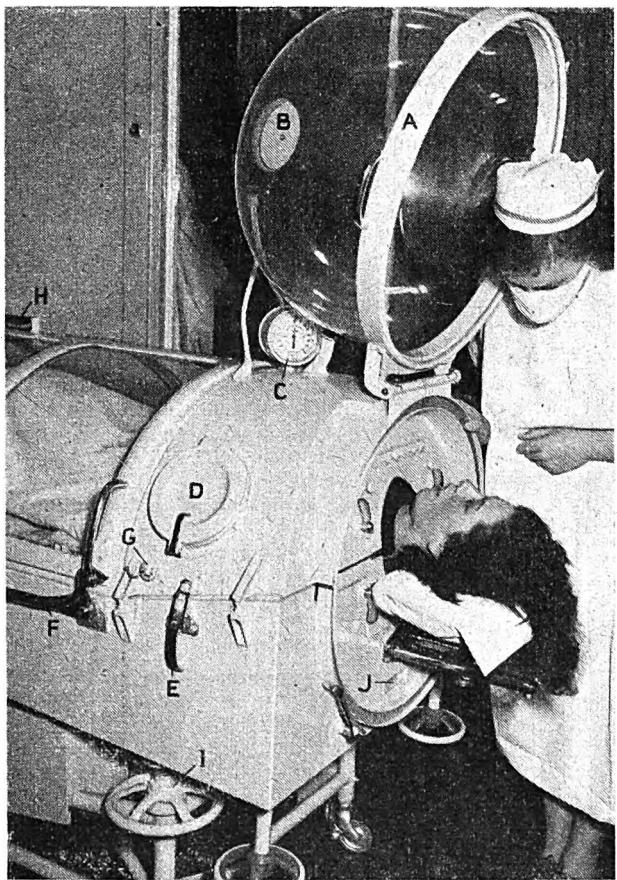


Fig. 3—The respirator in use.

A, Detachable perspex dome in "parked" position. B, Dome breather valve. C, Dome-pressure gauge. D, Hand-porthole cover. E, Head-end upper component clamp. F, Cover clamp. G, Porthole for tubing, &c. H, Inclinometer for longitudinal tilt. I, Screw-jack right lateral tilt. J, Duct for dome pressure.

of position ; and these are quickly completed by two nurses. It is helpful—and comforting—to be able to see the whole patient in the respirator.

Adjustments have proved easy ; and the application of various tilts has proved useful. Though the neck seal is firm, it bears no pressure from weight or angulation of the neck when the positions of the bed and of the head rest are suitably adjusted. The colour of patients has remained good, and they have slept well.

As a result of experience, we believe that this respirator would be further improved by providing hydraulic jacks instead of screw-jacks in the tilting mechanism, a quieter expanding pulley in the pump unit, an alarm

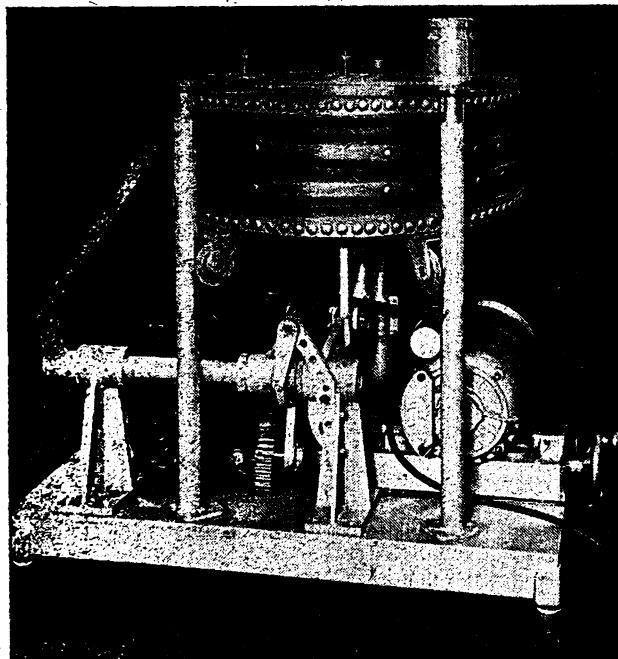


Fig. 5.—The pump unit.

system (already on order), and inflatable neck seals. So far the machine has proved reliable.

The production of this respirator has been a happy experience of co-operation. We thank the Bristol Aeroplane Company and the South Western Regional Hospital Board for great interest and encouragement in this work ; and are grateful for advice and unfailing help from Sister S. Williams, of Ham Green Hospital, and many others.

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"... we seem farther from the goal of 'social sciences' than ever we were. And the chief reason is not that, like the natural scientists, we have run into up-to-date complex inconsistencies and non-causal relationships in the phenomena we study, but that we have not yet reached the first stage of agreed classifications, nor agreed on definition and determination of the phenomena social scientists are supposed to study. ... The gulf between the psychologists, engaged with individuals, and the social psychologists is notorious ; indeed, social psychology in Britain can scarcely be said to have advanced for a generation, in spite of the advances in psychology as a whole. What exactly are these social scientists studying ; along what lines are their studies carrying them ; towards what goals ? The natural scientists today can still broadly answer such questions. The social scientists cannot." —*Times Literary Supplement*, March 26, 1954, p. 193.

A NEW CABINET RESPIRATOR

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IN June, 1952, the Birmingham Regional Hospital Board appointed a committee on which Captain G. T. Smith-Clarke, of Coventry, was invited to sit as consulting engineer to find means of improving the existing Both respirator. A performance specification issued by the breathing-machines committee of the Ministry of Health was used as a basis for discussion, and Captain Smith-Clarke agreed to modify one Both respirator to see how far the specification could be met. Eventually five Both respirators held by the Hospital Management Committee in Coventry were modified up to what was later known as stage 1 (Smith 1953a). The experience gained in the first stage revealed that more could be done to provide comfort for the patient and to reduce difficulties in nursing. The stage-2 modification followed, and this included a "split head" (Smith 1953b).

Success with the split head suggested to Captain Smith-Clarke that further advantage would accrue if the whole cabinet could be split so as to open alligator-fashion from the head end ; means for withdrawing the bed would then become unnecessary, and the patient would be immediately accessible in the most complete way. To do this demanded an entirely new cabinet, and in the autumn of 1952 a scale model was made of a split cabinet respirator to show the feasibility of this principle. At this stage local interest awakened, and various donors made contributions towards the cost of developing a prototype model which could be put into service in the Coventry group of hospitals. In addition during the coronation procession in Coventry about £800 was collected in the streets ; this was added to what became known as the Coventry Iron Lung Fund. Finance being thus assured, Captain Smith-Clarke arranged for a full-size prototype complete with a newly

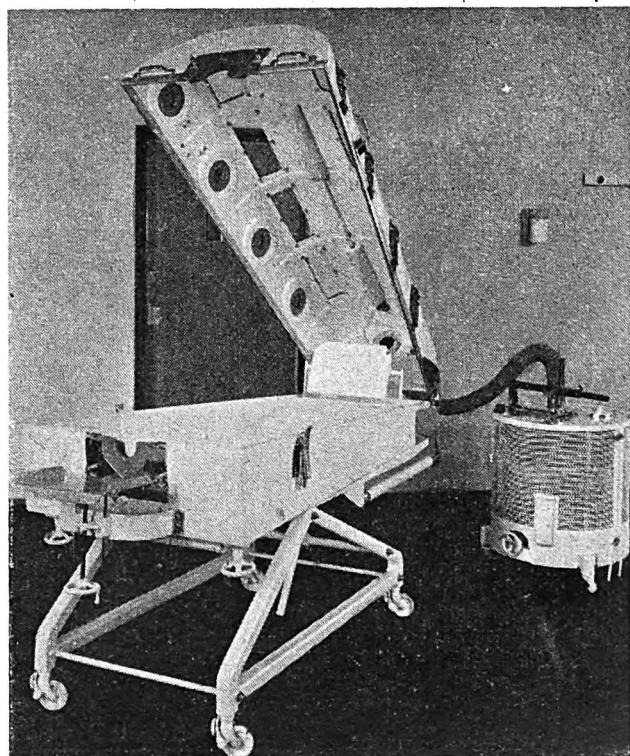


Fig. 1.—Respirator (open) and pumping unit.

designed pumping unit (figs. 1-3) to be made to his instructions.

The Respirator

The lifting section is moulded in one piece from fibre glass; the bed portion and the stand are made of aluminium alloy and steel.

The shape of the cabinet is such that the patient's head projects at the apex of an obtuse angle, thus ensuring that in both the prone and the supine positions the head-board slopes away from the patient's chin.

The two half-collars are held in position by clamping plates which are readily removable.

Means are provided externally to centre the patient's neck in the collar by raising the entire bed rather than merely a section towards the head-end. The double control fitted for this purpose can be used to give a small amount of lateral tilt to the bed if desirable.

A fully adjustable pillow support is provided, and by the removal of two pins the complete support can be slung down to allow hyperextension of the neck for bronchoscopy.

The top of the cabinet is hinged at the foot and can easily be opened and closed by a nurse, because it is counterbalanced by two arms containing compression springs. In the unlikely event of a spring breaking, the compression action would only allow a small drop, and in no foreseeable circumstances could the top fall unchecked. Guides are provided on the base to facilitate accurate reseating on closure.

The foot rest is as in the modified Both respirator.

The respirator can be tilted on a pivot from 10° head-up to about 25° head-down. The pivot is so placed that, on tilting head-down, the head of the patient remains in a convenient position for nursing. The mechanism for tilting is purely mechanical and positive, and is so arranged that a nurse can easily operate it.

A continuous seal on one plane is used, and the top is secured with two large quick-acting clips near the head end.

Hand ports are provided on each side, but no so called bedpan opening has been fitted, because the cabinet is so easy to open and close. Future models will, however,

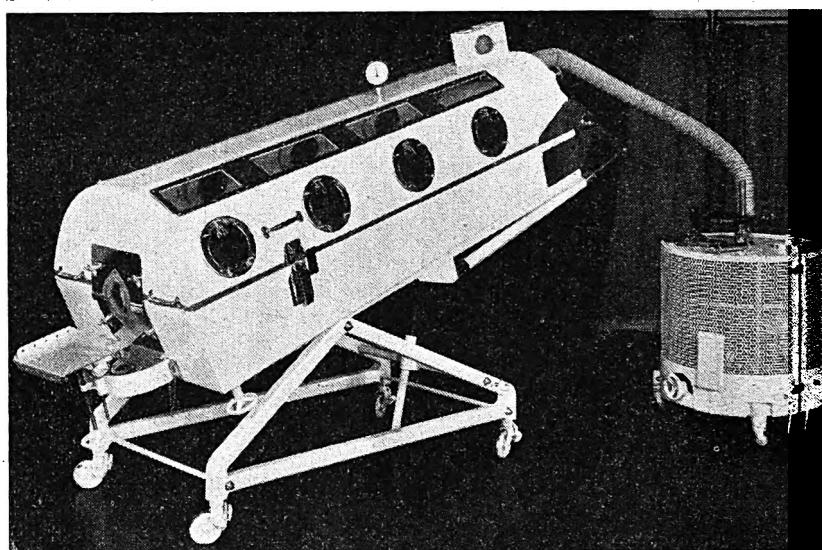


Fig 3—Respirator (closed) and pumping unit.

have such an opening in the position found very useful in this hospital for introducing nursing equipment usually other than bedpans—e.g., additional blankets, sand-bags, catheters, kidney dishes, woollen pads—and for giving hypodermic injections. A full view of the patient is provided by two rows of 'Perspex' panels.

A compound pressure gauge indicating negative and positive pressure is mounted centrally on the top of the cabinet; it can be rotated so as to be visible from any desired position.

A negative-pressure valve, giving fine adjustment with positive locking, is fitted on the foot end.

An automatic alarm indicates within less than 30 seconds, by a red light and a bell, any fall of pressure below the desired point; this is the same device that was fitted on the modified Both respirator.

The mattress is 70 in. long, 28 in. wide at the head end, and 18 in. wide at the foot end. The over-all external dimensions of the respirator are 8 ft. 1 1/2 in. long, 2 ft. 7 in. wide, 4 ft. high with top closed, and 7 ft. 6 in. high with top fully open.

Pumping Unit

Though it has many of the features of a normal pumping unit, this model has, instead of the conventional connecting rod, a sliding cross-head forming part of a lever pivoted to the base plate. This is so arranged as to provide a better breathing pattern than can be obtained with a connecting rod. The negative pressure is smoothly built up over an angle of about 170°, leaving 190° available for expiration. The use of the lever obviates the necessity for any other guiding mechanism on the bottom end of the bellows, thus abolishing the noise often arising at this point.

The hand-pumping gear is on the general lines of the system used in the fully modified Both respirator but has been made entirely fool-proof. Instead of removing a pin to allow of hand-pumping and replacing it when power is again available, the pin in the new unit remains always in place, being partially withdrawn and turned through 90°

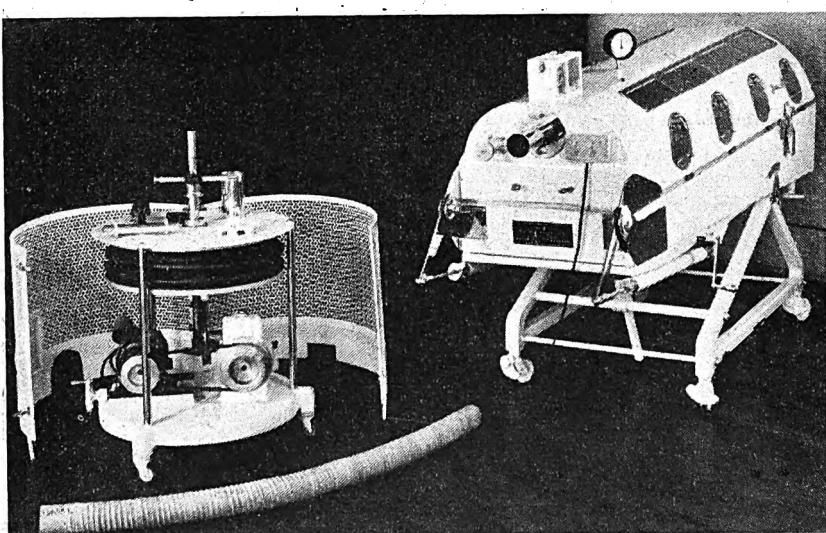


Fig. 2—Pumping unit and respirator (closed).

to lock it in the withdrawn position when hand-pumping is required. At the end of hand operation power-pumping can be re-started merely by reversing the 90° turn of the pin, when it will automatically spring into engagement as its socket on the moving central spindle comes into position. It is completely impossible to do anything wrong with this hand-pumping mechanism.

Positive pressure is controlled by a non-return disc valve located on the pump unit. Smooth adjustment without fear of accidental alteration is given by a screw with knurled head and a knurled locking nut.

The whole of the pumping unit has been designed on exceptionally strong lines to allow of long periods of use with minimal servicing. With positive and negative controls both at maximal setting the pressures attained are + 19 and - 25 cm. water. A perforated guard, which can be opened and folded back, gives access to the motor and bellows without having to remove the pressure hose. The prototype pump has a continuously variable gear giving speeds of about 12-25 cycles a minute, but it is believed that for general purposes a five-step pulley with a very easy method of changing the belt will be preferable. A five-step pulley will probably be provided on the standard respirator with the continuously variable gear available as an extra if required.

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BILATERAL HÆMORRHAGIC EFFUSION COMPLICATING ACUTE PULMONARY MONILIASIS

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From the Medical Division, Tidworth Military Hospital

PULMONARY moniliasis, though rare, is probably commoner than is generally supposed. In a study of over a thousand sanatorium patients with pulmonary disease Keiper (1938) attributed no less than 2.9% of the infections to monilia. Acute pulmonary moniliasis following the exhibition of antibiotics is described by, among others, Ormerod and Friedmann (1951), Wolff (1952), and Browne (1954).

CASE-RECORD

Pte. A, aged 21, was transferred to Tidworth Military Hospital on Dec. 8, 1953.

Three days previously he had been admitted to a neighbouring medical reception station with retrosternal pain and shortness of breath of a few hours' duration; he had little cough, and it was unproductive. On admission to the reception station he had a temperature of 102°F, and signs of consolidation at the base of the right lung. A diagnosis of pneumonia was made, and penicillin treatment was begun. Next day his temperature was 104°F and the pain in his chest was worse. Despite treatment with sulphadimidine his temperature again reached 104°F, and he was acutely ill; the signs of consolidation at the right lung base persisted.

When admitted to Tidworth Military Hospital he had had about 500,000 units of penicillin intramuscularly and about 6 g. sulphadimidine by mouth. He said that he had had drenching sweats during the past three nights. His previous history was not relevant: before being called up, he had been working as an electrician.

He was now acutely ill, and orthopnoeic though not cyanosed. His temperature was 99.4°F. The mouth and fauces were normal and no enlarged glands were found. His cardiovascular system was normal: blood-pressure 120/90 mm. Hg. In his chest, impaired tactile vocal fremitus,

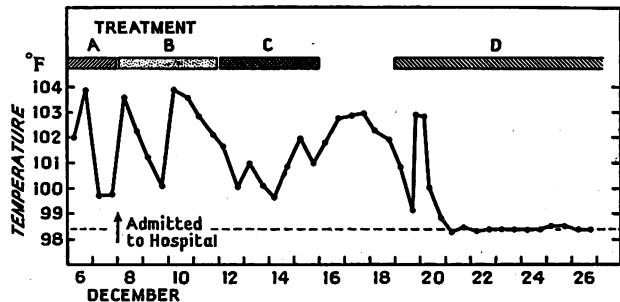


Chart showing patient's temperature in relation to treatment given : (A) sulphadimidine 6 g. and penicillin 500,000 units ; (B) penicillin 4,800,000 units ; (C) aureomycin 4 g. ; (D) potassium iodide gr. 80 daily

dullness to percussion, and diminution in air-entry at the right base suggested consolidation with effusion. Radiography showed consolidation at both bases, especially the right. All other systems appeared normal, and the optic fundi showed no changes.

Sputum culture and examination revealed no predominant organism and no acid-fast bacilli with Ziehl-Neelsen staining. The white-cell count was 12,900 per c.mm. (polymorphs 72%, lymphocytes 18%, monocytes 10%).

From admission until Dec. 11 he was given intramuscular penicillin 200,000 units in saline solution four-hourly. Nevertheless his condition deteriorated rapidly. On Dec. 10 his respiration-rate was 40 per min. and he was in great distress, being confused, cyanosed, and at times delirious. On the right side bronchial breathing could be heard as high as the 4th intercostal space posteriorly. He was placed in an oxygen tent. That night his temperature rose to 104°F (see figure) and he was sweating profusely, though feeling cold. At 10.30 P.M. he had a sharp haemoptysis and coughed up about an ounce of sputum, much bloodstained. A report on this sputum stated that it contained spores and (?) mycelia.

On Dec. 11 penicillin was discontinued, after a total dose in Tidworth Military Hospital of 4,800,000 units. During the next four days aureomycin 4.0 g. was given.

On Dec. 14 there were signs of fluid on the right side of the chest, and a diagnostic aspiration yielded 60 ml. of fluid, bloody but not turbid. The report on this was :

Micro-organisms.—None seen on Gram or Ziehl-Neelsen staining. *Cultures.*—Forty-eight-hour cultures (blood agar aerobic and anaerobic) sterile.

Cytology.—Red blood-cells 5800 per c.mm.; white cells 17,200 per c.mm. (polymorphs 66%, lymphocytes 34%).

Chemistry.—Protein 3.0 g., sugar 130 mg. per 100 ml.

On Dec. 16 a further 60 ml. of fluid (deep orange in colour) was removed. The sputum now yielded *Staphylococcus albus*, *Neisseria catarrhalis*, and *Streptococcus viridans*, and in addition a few monilia (candida) colonies. Culture on Sabouraud's medium produced a heavy pure growth of *Candida albicans*, and on four subsequent occasions this organism was grown from the sputum.

From Dec. 15 onwards no antibiotics were given, and from Dec. 19 the patient received potassium iodide gr. 80 daily. The effect was dramatic: his temperature fell to normal within thirty-six hours (see figure) and he felt much better. By this time, however, there were signs of effusion on the left side, confirmed by radiography. Aspiration on the left side (Dec. 21) yielded 35 ml. of orange-yellow fluid containing red blood-cells 5600 per c.mm., and white cells 10,900 per c.mm. (polymorphs 58%, lymphocytes 34%, monocytes 8%). No organisms were seen, and culture on blood agar and on Sabouraud's medium was sterile after forty-eight hours. At two further aspirations on the left side a further 25 ml. of orange-red fluid was removed. The report for Jan. 5 was :

Micro-organisms.—None seen on Gram or Ziehl-Neelsen staining. *Cultures.*—On blood agar (aerobic and anaerobic) negative.

Cytology.—Red blood-cells 14,400 per c.mm.; white cells 5900 per c.mm. (polymorphs 28%, lymphocytes 68%, monocytes 4%).

Chemistry.—Protein 3.0 g., sugar 130 mg. per 100 ml.

Improvement continued. On Jan. 20 radiography showed complete resolution at the right base and only pleural thickening on the left diaphragm, and on Feb. 1 the only abnormality seen was a pericardio-phrenic adhesion on the left side.

The patient has remained perfectly well and after a period of convalescence has gone back to full duties. He has not returned for follow-up, and it is not known whether or not his sputum still contains *C. albicans*.

COMMENT

Castellani in 1905 was the first to report primary bronchomoniliasis (Castellani 1910). He later maintained that the condition could be diagnosed only if tubercle bacilli were absent from the sputum and monilia constantly present (Castellani 1928). Ikeda (1936) distinguished three main groups of pulmonary moniliasis :

- (1) *Mild*.—Cough and scanty sputum.
- (2) *Moderate*.—Cough, sputum, and low-grade fever.
- (3) *Severe*.—Dyspnoea, night sweats, cough, sticky glairy sputum; exacerbation resembling acute lobar pneumonia; chest pains, haemoptysis.

Cases of pleural exudate have been described (Koerth et al. 1941, Warr 1931).

In the case we report here, our reasons for diagnosing moniliasis were : (1) the absence of leucocytosis at height of the illness; (2) the absence of tubercle bacilli in the sputum; (3) the presence of *Candida albicans* in the sputum; (4) the resemblance of the symptoms and signs to those described by Ikeda as characterising the severe form of pulmonary moniliasis; (5) the failure to respond to antibiotics; and (6) the dramatic response to iodides (Wylie and De Blase 1944).

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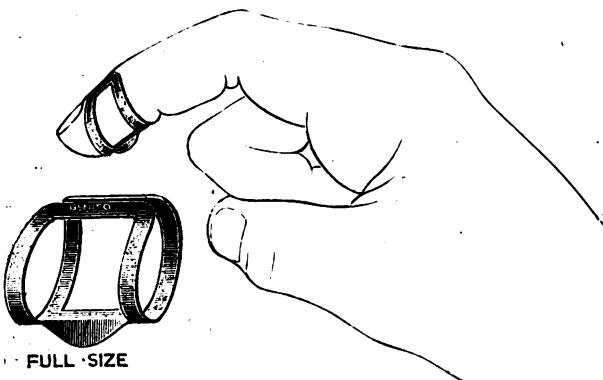
New Inventions

A KNIFE FOR MITRAL VALVOTOMY

In most cases of mitral stenosis it is possible to enlarge the mitral orifice adequately by splitting the commissures with the index finger. Sometimes the commissures do not yield to this force and have to be cut. Since this is a blind procedure, it is very important to retain a sense of touch so that it is the commissure that is divided and not any other part of the valve.

The instrument illustrated here has a small crescentic cutting blade made in one piece with a steel spring clip which can be slipped over the tip of the index finger. A rubber stall is worn over the instrument to assure that it does not come off the finger; the blade cuts through the rubber of the fingerstall as it engages the commissure.

This instrument allows the sensitive tip of the finger to explore in advance of the knife, and ensures that the blade is applied in exactly the right place and in the right direction. Worn in the manner illustrated, with the blade over the pulp of the finger, it is used for dividing the anterolateral commissure. To cut the postero-medial commissure it may be reversed so that the blade is over the finger-nail.



FULL SIZE

For the design and manufacture of this instrument I am indebted to the late Mr. R. Schranz, whose sudden death last year was such a sad loss to British thoracic surgery. It is made and supplied by the Genito-Urinary Manufacturing Co. Ltd.

VERNON C. THOMPSON
F.R.C.S.
London, W.1

Medical Societies

ROYAL SOCIETY OF MEDICINE

Clinical Aspects of Immunity

AT a meeting of the section of medicine on March 23, Sir HENRY COHEN, the president, introducing the speakers, commented on the appropriateness of discussing immunity problems during the centenary year of Ehrlich's birth.

Prof. A. A. MILES, discussing bacterial immunity, dealt mainly with the selection of appropriate antigens for active immunisation and with difficulties of clinical trials of new prophylactics.

Prof. A. W. DOWNIE surveyed virus infections, and he contrasted diseases such as poliomyelitis in which only a few persons exposed to infection developed clinical symptoms, with measles and smallpox in which nearly all persons encountering the infective agent for the first time developed the disease. In smallpox the fall in temperature and apparent improvement in the patient's condition was associated with the appearance of antibodies in the blood-stream and the disappearance of free virus particles, but the virus already present in the tissue cells was protected from antibody attack and caused the later symptoms and finally death. Hence it was important that protective antibodies should be administered to contacts before the end of the normal incubation period and before the viruses gained access to the tissue cells.

Prof. B. G. MAEGRAITH spoke on protozoal infections and offered advice on the treatment of different malaria patients. A patient such as an Indian seaman who was likely to be exposed to fresh infection should have his immunity preserved; he should be treated with a drug such as mepacrine which would clear up the current attack by removing parasites from the blood-stream without affecting the reservoir of exoerythrocytic forms. On the other hand, in, for example, a National Service-man returned from Korea or Malaya it was necessary to eradicate the infection completely, and drugs such as proguanil which dealt with the exoerythrocytic forms should be used. It had been found accidentally that a milk diet suppressed malarial infections, and this accounted for the fact that in malarial districts breast-fed infants escaped infection, while after weaning young children were highly susceptible to malaria until immunity developed. Thus dietary and other factors could influence resistance to disease without affecting basal immunity.

Both Prof. ROBERT CRUICKSHANK and Mr. A. FELIX, D.Sc., F.R.S., commented on the interference by antibiotics with the development of immunity following bacterial infections. Relapses occurred since these antibacterial agents rapidly reduced the number of infecting organisms below the level at which they provided sufficient antigenic stimulus to immunise the patient. This was seen particularly in infections with haemolytic streptococci, typhoid bacilli, and brucella.

Dr. DOUGLAS McCLEAN, who had recently returned from a conference on immunisation arranged by the World Health Organisation, made a plea for the establishment in this country of a pool of gamma-globulin from the plasma of persons who were convalescent from various diseases, or who had been recently immunised. Globulin from Service recruits recently vaccinated would be valuable for the treatment of smallpox, and globulin

from rubella convalescents could be used for the protection of pregnant women.

In winding up the discussion, the PRESIDENT felt that in clinical trials adequate controls could be maintained without withholding valuable treatment from those needing it. He questioned whether some bacterial antigens were really entities or merely names without substance.

Reviews of Books

Modern Trends in Dermatology

2nd series. Editor: R. M. B. MACKENNA, M.D. Camb., F.R.C.P., physician, dermatological department, St. Bartholomew's Hospital. London: Butterworth. 1954. Pp. 327. 6s.

THIS is a complementary volume to the first series published five years ago. Progress in dermatology in these years has been extensive, and this book gives a clear idea of the most important advances. Of the 17 chapters, 7 are by dermatologists and the remainder by writers in other specialties directly or indirectly related to dermatology. In his introduction Dr. MacKenna wisely advises the reader not to follow the classical custom of beginning at the beginning and going on until he comes to the end: for the subject matter, though in orderly arrangement, is diverse, and the reader will find himself subjected to abrupt changes of thought—leaping from psychosomatic medicine to anatomy, or from cortisone to beta rays.

Especially good chapters, with a practical bearing, include those by Shooter on the use of antibiotics, Sulzberger and Rose on cortisone and corticotrophin, Pillsbury and Kligman on cutaneous bacteriology, Baer on cross-sensitisation, Haserick on lupus erythematosus, and Dowling and Wetherley-Mein on cutaneous tuberculosis. Banks gives the book a good start and a broad outlook with his opening chapter on the changing pattern of skin diseases since the 16th century, and outlines prospects for the future with special reference to an ageing population.

Altogether this is a stimulating and thought-provoking work, a worthy companion for its five-year-old sibling. References are comprehensive.

Le Leptospirosi

MARIO AUSTONI, aiuto dell'istituto di patologia medica e incaricato di malattie infettive nella Università di Padova. Padua: Tipografia del Seminario di Padova. 1953. Pp. 706. L. 5000.

Professor Austoni's extensive monograph falls into two parts. In the first, which deals with leptospires as micro-organisms, he describes their morphological and cultural characteristics.

He agrees with Bergey's *Manual of Determinative Bacteriology* in placing the genus in the order Spirochaetales, and the family Treponemataceae. He holds that the genus is most conveniently subdivided according to antigenic composition since that is a specific and stable character. By contrast, association with carrier-hosts, and differences in pathogenicity, in geographical distribution, and in the clinical picture in man are not sufficiently characteristic to be of value for this purpose. But each species of leptospire has its carrier-host of election, and differences in the ecology of these hosts and in their associations with man and domestic animals is of importance in choosing the most appropriate preventive measure. Hence Professor Austoni has therefore included a chapter on carrier-hosts.

The second, and much the longer, part of the monograph is concerned with leptospires as pathogens. It is no easy task to give a comprehensive survey of leptospirosis in man and animals, for more than thirty different species (or serological types) are known. A single type may produce quite different pathological changes in different species of animals, and strains of the same serological type may evoke different illnesses in individual hosts. Nevertheless there are certain essential features common to all forms of leptospirosis—e.g., the importance of urine-contaminated water in transmission, and the potential capacity of all species to attack the liver,

kidney, and meninges—and Professor Austoni has skilfully used these features in drawing a general picture of the condition in man. He then takes each of the more important species of leptospires separately, and shows how their differences are reflected in the epidemiology and the clinical manifestations of the disease they produce. This plan has some disadvantages, since the different aspects of infection with a single species are not treated as a complete entity: the casual reader, interested perhaps in one form of leptospirosis, may find difficulty in piecing the details together. But the method obviates endless repetition, and has allowed Professor Austoni to make good use of a wealth of material.

The monograph is well printed on good paper with many illustrations. The bibliography contains nearly 3000 references.

Anatomy and Surgery of Hernia

LEO M. ZIMMERMAN, M.D., professor of surgery and co-chairman of department of surgery, Chicago Medical School; BARRY J. ANSON, PH.D., professor of anatomy, Northwestern University. Baltimore: Williams & Wilkins. London: Baillière, Tindall, & Cox. 1953. Pp. 374. 76s 6d.

THIS is a well-produced, profusely illustrated, readable, and informative book on the condition which most commonly needs to be submitted to surgery—hernia. It has been written jointly by a professor of surgery and a professor of anatomy, and, as they say, "the anatomical studies go beyond the usual morphological descriptions." Indeed, more than 40 pages are dedicated to a detailed description of the abdominal wall before the anatomy of hernia is specially considered. In the opening chapter due credit is given to the pioneer work of Marcy. Each type of abdominal hernia is considered separately and thoroughly, and a special chapter is devoted to hernia in general. Good judgment is shown in reviewing the various methods of treatment in vogue. The injection treatment is not recommended (except for very special cases), and concerning the use of fascial sutures the authors do not commit themselves.

This is too big a book for the student, and the junior surgeon would probably ask for greater detail on the operative relief of strangulation; in fact, it is a work of reference for the experienced surgeon. But there are no illustrations in it to equal any of the plates in the classical book on hernia by Astley Cooper (who appears in the references to the historical section simply as "Cooper, A. P.").

Hypertensive Diseases

Causes and Control. H. A. SCHROEDER, M.D., F.A.C.P., associate professor of medicine and director, hypertension division, department of internal medicine, Washington University School of Medicine. With contributions from G. S. GRESSEL, M.D., D. F. DAVIES, M.D., K. M. PERREY, jun., M.D., and D. F. GIBBS, M.R.C.P.E. London: Henry Kimpton. 1953. Pp. 610. 75s.

THIS book will be welcome. All but a few chapters are the work of Dr. Schroeder, who, besides being an authority on its complex subject, has a talent for exposition.

The first half is mainly a documented survey of what is known about the pathogenesis of hypertension. In discussing renal pressor factors Dr. Schroeder tells how he and his colleagues isolated phentrenasin, an amine compound which is said to be the only pressor agent consistently found in the blood of hypertensives but not of normotensives.

The rest of the book describes hypertensive conditions and their treatment. Three main types—neurogenic, nephrogenic, and endocrine—are postulated. Dr. Schroeder's conception of endocrine hypertension is broader than the conventional one, but he makes out a good case for it. Some of his cases of neurogenic hypertension, however, would not ordinarily be regarded as truly hypertensive, for at rest their blood-pressure was normal. Dr. Schroeder may be right in so labelling them, but he does not give evidence that these intermittent hypertensives deteriorate, as is implied by calling their condition stage I of neurogenic hypertension. The absence of an adequate discussion of prognosis is in fact a disappointing feature of the book: our knowledge of the natural history of hypertension is admittedly not great, but he does not do it justice.

Dr. Schroeder makes a strong claim for the efficacy of oral treatment with a combination of 1-hydrazinophthalazine

('Apresoline') and hexamethonium. The effect on 250 patients over a period of two or three years is said to have been "little short of miraculous."

This is not a book for the student or intern, for much of it is controversial; but those with experience of hypertension will find it thought-provoking and important.

Carcinoma of the Female Genitalia

By HANS LUDWIG KOTTMAYER, M.D., chief, gynaecological section, Radiumhemmet, Stockholm. Baltimore : Williams & Wilkins for Vanderbilt University. London : Baillière, Tindall, & Cox. 1953. Pp. 213. 33s. 6d.

In Sweden a cancer campaign is in progress, and cancer detection departments have been established at the three main clinics, where anybody who fears he has cancer can be examined. Kottmeier notes that, at the Radiumhemmet, fundamental changes in technique and methods of treatment are never made until the new technique in use has received a thorough trial; and the success obtained at this centre is no doubt largely due to this policy. The uncritical use of irradiation has brought radiotherapy into disrepute in some other countries; and radioactive isotopes and supervoltage X-ray therapy may lead to a similar situation. As yet we know very little indeed about the use of these agents, and the need for caution is great.

Kottmeier reviews the various methods of estimating dosage-distribution in the pelvis, in the treatment of cancer of the cervix, and describes his own work in this field. In his view, combined radium and X-ray therapy is the treatment of choice. Almost 20% of stage-I cases have metastases, and it is here that X-ray treatment can play an important part. Charts and tables illustrate 5-year survival-rates, incidence of rectal and bladder injuries, and the sites of recurrences in apparently healed cancer of the cervix.

Cancer of the body of the uterus is on the increase. In Sweden its ratio to cancer of the cervix is 1 : 2·4, and hysteroscopy has demonstrated that cervical involvement in cancer of the body is commoner than is generally believed. The results of radium treatment in this type of cancer, followed in cases of failure by surgery, compare favourably with the best results obtained by surgery alone. A 5-year survival-rate of 80·7% for cases in stage I, and 72·2% for cases in stage II, at the Radiumhemmet, compares favourably with the 64·7% 5-year survival-rate in cases treated surgically by Meigs and Morton. The claim that it is possible to control lymph-gland metastases by surgery and not by radiation is met by comparing statistics for cases treated surgically by Bonney in England and cases treated radiologically at the Radiumhemmet.

No-one interested can fail to profit from the information and instruction contained in this book. The text is profusely illustrated with statistical tables, charts, radiographs, and photomicrographs.

Introduction to Electronics for Physiological Workers

I. C. WHITFIELD, B.Sc., Ph.D., lecturer in physiology, Birmingham University. London : Macmillan. New York : St. Martin's Press. 1953. Pp. 236. 18s.

BOOKS such as this, which introduce electronics to physiological workers, are particularly useful now that medicine and physiology have assimilated many of the techniques of the exact sciences. It is an advantage to the physiologist to have some theoretical knowledge of light current engineering—electronics, as it has come to be called—since he has to employ thermionic valves for many measuring purposes.

There are books which describe circuits and electrophysiological techniques useful to physiologists; but, in attempting less, Mr. Whitfield's book possibly achieves more. He explains the elements of the subject lucidly and with practical understanding; and the student who works conscientiously through this book will begin to think in terms of electronic methods and electrical measurements, and will thus be enabled to devise apparatus to meet his particular needs. He should, however, remember that this is an abbreviated course, and should use caution in attaching electronic apparatus to himself or his patients without expert help. The chapters on noise and interference are especially commendable, and could only have been written by someone with much practical knowledge of the subject.

Vitamins and Hormones

Advances in Research and Applications. Vol. II. Editors : ROBERT S. HARRIS, professor of biochemistry of nutrition, Massachusetts Institute of Technology, Cambridge, Mass.; G. F. MARRIOTT, professor of medical chemistry, University of Edinburgh; KENNETH V. THIMANN, professor of plant physiology, Harvard University, Cambridge, Mass. New York and London : Academic Press. 1953. Pp. 356. \$8.50.

THIS eleventh volume, built up on the lines of the preceding ones, contains 8 articles written singly or jointly by 13 experts in their own fields; and it will appeal to physicians and physiologists because it contains more of direct human interest than some of its predecessors.

A historical and rather critical article on the biochemistry and physiology of vitamin D, by R. Nicolaysen and N. Eeg-Larsen, is matched by a good one on ascorbic acid by A. P. Meiklejohn. L. W. Mapson has contributed an article on the function of ascorbic acid in plants, and S. Zubiran and F. Gomez-Mont have a section on endocrine disturbances in chronic human malnutrition which is largely an account of their own clinical findings in Mexico. Many will read with interest the account of the biochemistry of the thyroid gland by J. Gross and Mrs. Pitt-Rivers, which includes all the recent work on the active triiodothyronine. The remaining articles deal with the relation of pantothenic acid to adrenal cortical function, the evaluation of procedures for the cytological localisation of ketosteroids, and the synthesis of cortisone and related steroids. The last, by C. Djerassi, will be appreciated by the select few, but it is not exactly fireside reading.

This volume carries a cumulative subject index for the last 5 volumes and its own subject and author index. The editors have spared themselves no trouble which might enhance the reputation of their series, and are to be congratulated on the result.

Practical Procedures in Clinical Medicine (2nd ed. London : J. & A. Churchill. 1954. Pp. 484. 32s.).—The second edition of this practical account of biochemical and radiological investigations in clinical medicine includes procedures and techniques which have come into general use since the first edition appeared in 1950. Dr. R. I. S. Bayliss has again aimed at providing enough detailed information to enable residents and others to carry out many of the investigations described; more complex tests are described less fully, but their physiological basis is clearly stated. It is interesting that the four pages of clear description of the electrocardiographic leads included in the 1950 edition are now reduced to about half, while several pages are devoted to cardiac catheterisation—not previously dealt with. Many of the subjects, such as a fairly full posological table and a section on dietetics, seem rather outside the scope of the title. The chapter on radiology in clinical medicine remains most helpful, and this edition will certainly retain its predecessor's popularity, especially among housemen and those sitting for higher examinations.

An Introduction to Pathology and Bacteriology for Medical Students in the Tropics (2nd ed. London : Staples Press. 1953. Pp. 390. 50s.).—This book, originally written by the late Dr. E. C. Smith and now revised by Prof. R. Kirk, is intended for medical students in tropical schools. It was conceived as an introduction to, not as a substitute for, the existing textbooks, and it is not a "practical manual" but an exposition of the intimate relation between pathology and bacteriology, and between these subjects and clinical medicine.

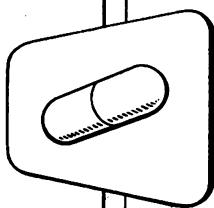
The pathological section comprises chapters on disturbances of metabolism and circulation, inflammation, tumours, infection and resistance; but the remaining sections also contain much pathology. There are chapters on bacteria and the diseases caused by them, pathogenic fungi, viruses and rickettsiae, spirochaetes, protozoa, and helminths. Others follow on diseases of the blood, the endocrine organs, the liver and other abdominal organs, and four appendices deal with lymphadenopathy, post-mortem technique, stains, and culture media. So large a range of subjects obviously can only be dealt with in outline, but the virtue of the book is that it brings these subjects conveniently together, and it is well fitted for use in conjunction with lectures which amplify and explain the terms and processes here succinctly described. The illustrations (photographs, photomicrographs, and coloured drawings) are very good.



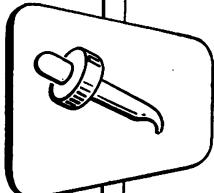
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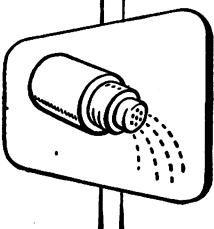
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THE LANCET

LONDON : SATURDAY, APRIL 3, 1954

Who is to Pay for Mistakes?

In the litigation of the past few years an unedifying situation has occasionally arisen in which a hospital authority, in defending itself against a charge of negligence, has provided evidence against its own medical staff. Moreover, under an instruction issued in 1949 by the Ministry of Health, a hospital authority which has to pay damages to a patient is expected to reduce its own pecuniary loss by obtaining, through legal process, a contribution from any member of its staff whom it regards as negligent. Thus administrators and doctors, who should always be partners in a common task, have sometimes become antagonists, whether actual or potential, to the detriment of the service. In the hope of putting a stop to this state of affairs, the medical defence societies and the British Medical Association have asked the Minister to withdraw his 1949 instruction, and this has now been done. Under an agreement embodied in the Ministry's circular which we summarise on p. 727, hospital authorities are told to consult with the defence societies—preferably before the court hearing—and if possible reach agreement on the proportion of damages that each should pay in the event of damages being awarded. If the defence society and the hospital authority cannot agree, each is to pay half.

The first reaction to these arrangements will be one of relief. Given the amicable co-operation on which we may fairly count, they should reduce friction and will often lead to fairer decisions. Our impulse, then, is to congratulate the Ministry and the professional organisations on a success for good will and common sense. But before expressing unreserved approval we should perhaps examine the implications a little more closely. Is there not some risk that, perhaps imperceptibly, the new system may weaken the independence of the profession? Professional freedom and professional responsibility are two sides of the same medal; and if the doctor is to be free he must also be responsible—responsible not only for his successes but likewise for his failures. If it should ever come to be thought that the State, as his employer, ought to pay the cost—or even part of the cost—of his mistakes, he must to that extent become its employee, and be bound to do its bidding.

Do the new arrangements really contain this risk? We do not, of course, know exactly how they will work; but presumably if a defence society thinks that its member really has been negligent, and that the responsibility rests on him alone, it will offer to pay all the damages awarded. So far so good. If, on the other hand, it thinks that, though its member is to blame, some part of the responsibility rests on non-medical members of the hospital staff or on the administration, it will offer to pay only an appropriate share of the damages. Again that would be right. But if, as may often happen, it feels that, though there has been an accident and the patient has suffered thereby, the doctor has been more unlucky than culpable, may it not be tempted to urge that the damages should be paid by the hospital—that is to say,

by the service rather than by the profession? The reputation of the profession could be in no safer hands than those of the wise and experienced people who run our defence societies; but unless they are provided (as they should be) with funds sufficient to make money no object, they can hardly be expected to insist on paying in full damages which the Ministry is ready to share. The temptation to avoid, on behalf of their members, apparently unnecessary obligations will surely be enhanced by the provision that, if no agreement is reached, the Ministry and the profession shall each pay half. Should such friendly compromise ever become the norm, regardless of the merits of the individual case, then indeed will our professional position be imperilled.

Are we exaggerating? Is there any real threat to this position? Consider the following passage from Mr. SPELLER's handbook¹ published this week by the Royal College of Nursing:

"All the staff of the teaching hospital, medical and non-medical alike—with the possible exception of part-time consultants—are servants of the board of governors, i.e., they work under a contract of service. The staff of a non-teaching hospital, with the same reservation, are servants of the regional hospital board, though, except in the case of senior medical staff, the power of appointment and dismissal is, by regulation, delegated to the hospital management committee. Throughout these notes, therefore, we shall for practical purposes treat the hospital management committee as the employer or master."

Unhappily these words do fairly represent legal opinion in England (though not in Scotland) today; and, unless this English opinion is reversed by the House of Lords, it looks as though the profession either will have to accept the relationship of hospital authority and doctor as that of "master and man" or will have to negotiate a change in the terms of service of the N.H.S. so that doctors are paid through professional bodies and not by lay boards. Meanwhile it should, we believe, be careful to do nothing that might weaken the principle that the doctor, being responsible first and foremost to his patient, must use his own judgment in discharging that responsibility and must accept the consequences of his errors. When the other day we insisted on this professional freedom of judgment,² the *Manchester Guardian*³ argued that where, in what he held to be the interest of the patient, a surgeon deliberately took a risky course, his decision would be upheld by any good hospital authority. That is true; and the good "employer" of doctors will certainly want to back them when some personal issue of conscience is presented thus forcibly—in some sort of *cause célèbre*. But this will not necessarily prevent a slow change of climate in which caution and conformity flourish and control takes root. If, over the years, it were accepted that hospital authorities ought to go shares in any damages awarded against their doctors, they would be justified in introducing more and more small rules for doctors—indeed they would feel obliged to do so. A situation would thus arise which the Ministry of Health has so far scrupulously avoided, in which clinical work was exposed to lay regulation; and even if (as is doubtful) such regulation

1. Law Notes for Nurses. By S. R. SPELLER, LL.B., secretary and director of education, Institute of Hospital Administration. London: Royal College of Nursing, 1A, Henrietta Place, Cavendish Square, W.I. Pp. 36. 3s. 6d.

2. *Editor*, March 20, 1954, p. 607.

3. *Manchester Guardian*, March 20, 1954, p. 4.

sometimes prevented negligence, the damage it would ultimately do to the work of doctors would far outweigh, for the public, the advantage thus gained. Fortunately this situation is one which, through the defence societies, we can, if we wish, avert. If we think professional freedom more important than money—if we are not prepared to sell our professional birthright—we must insist that when we do make mistakes we pay for them ourselves.

The Curability of Cancer

WHILE we acclaim new methods of treating cancer by radical surgery and radiotherapy, the death-rate from that dread disease abates little. The comparative mortality index, which allows for changes in the age structure of the population, shows for men a rise of 6% in cancer mortality between 1938 and 1950, and for women a fall by the same amount. The small disparity between the sexes is almost entirely due to the relatively greater increase in the frequency of death from cancer of the lung among men. Even among women, however, the decline is small enough to give point to Professor MCKINNON's analysis¹ of our apparent failure in cancer control. In Saskatchewan, despite a long and intensive educational programme for the early detection and treatment of cancer, the death-rate from cancer of the breast shows no downward trend. This disappointing stability, MCKINNON finds, is shared by another Canadian province where no special measures have been taken. In Massachusetts, where an active drive for early diagnosis and treatment has been in progress since 1926, the trend of breast-cancer mortality, he says, is almost identical with that in England and Wales. Twelve years ago LOMBARD and MACDONALD² took a more optimistic view of the trend in Massachusetts, compared with that in the rest of the United States; but the small and equivocal improvement they claimed was disappointing in view of the apparent success of health education in persuading women to report suspicious masses in the breast. In Massachusetts the average delay between first sign and first consultation dropped from six months in 1926 to four months in 1948. In Connecticut similar methods resulted in a rise in the proportion of cases with "localised" breast cancer from 44 to 51% between 1940 and 1949, while five-year survival-rates increased from 21·7 to 27·6% between 1935 and 1944. Yet over these years the death-rate from breast cancer in the Connecticut population showed no sensible decline. Possibly simultaneous alterations in factors affecting both true and reported incidence may have masked a beneficial effect of cancer education and early treatment. With improved death certification there is greater likelihood of the breast, rather than an organ of metastasis, being named as the primary site.³ Again, a fall in the birth-rate may increase the proportion in the population of middle-aged nulliparous, who are especially prone to the disease. These and other factors could neutralise the results of therapeutic success and keep the death-rate steady. But that these influences should be precisely equal and opposite seems unlikely. Some better explanation is required.

1. McKinnon, N. E. *Lancet*, Jan. 30, 1954, p. 251.

2. Lombard, H. L., Macdonald, F. A. *N. Engl. J. Med.* 1942, 226, 81.

3. Bigelow, G. K., Lombard, H. L. *Ibid*, 1934, 210, 527.

The basic reason for aiming at prompt detection and treatment of cancer is that the survival-rate is greater in cases treated before metastatic spread is apparent than in those with metastases: if only it could be taken in time, the argument runs, cancer of the breast would usually be curable. There is an implicit assumption that nearly all neglected cancers enlarge and spread by the lymphatics, and that radical treatment will cure a small localised, recently discovered, tumour. MCKINNON, however, takes the opposite view, concluding that in "most, if not all, lethal breast cancer remote spread takes place via the blood-stream before interference is practicable"; and in this heresy he is not alone. The survival-rates after different periods of delay before seeking medical advice often show a curious paradox. Thus SWYNNEERTON and TRUELOVE,⁴ reviewing 395 cases of gastric carcinoma, showed that the greater the delay and the longer the history of symptoms, the greater was the survival-rate; and their findings are neither novel nor singular. BLOOM,⁵ for example, showed that, in patients with cancer of the breast who had had symptoms for six months or less before operation, the five-year survival-rates were certainly no better than for patients who had had symptoms for a year or more. KREYBERG⁶ cites reported series where symptoms had been noticed for less than four weeks and yet the five-year survival-rate was only 50%. He notes, too, that the size of the primary tumour is no guide to its curability; two-thirds of patients reporting with tumours of the breast which were smaller than a hazel nut already showed metastases.

This apparent paradox is explained by the overwhelming importance of the growth-rate of the tumour. In ascribing to early treatment the higher survival-rate in stage-I breast cancers compared with those in stage II, we assume that we are comparing like with like. But the apparently curable stage-I cancers may consist of slowly metastasising tumours, whereas those first seen in the late stages may mostly be rapidly invasive and metastatic tumours whose brief initial stage escaped notice. In other words, the stage of the disease is a function, not of time, but of the tumour type. As LEES and LEES point out,⁷ when inoperable or untreated cases are followed up until death⁸ the natural survival-time proves longest in just those cancers—of breast, rectum, or cervix uteri—which are usually thought to be most amenable to treatment. LEES and LEES note, too, that the variability between individuals in survival-time is proportional to the mean survival-time for all untreated patients with the same type of cancer. In cancer of the breast a patient may survive for a long time even without treatment, and individual instances of long survival after operation are therefore no proof of the operation's efficacy. Such differences, found even in inoperable patients, bespeak major difference in tumour malignancy or host susceptibility, and they suffice to explain the unexpected association between length of delay before treatment and five-year survival—for example, in cancer of the stomach. MACDONALD and KOTIN⁹ have re-stated views suggested by

4. Swynnerton, B. F., Truelove, S. C. *Brit. med. J.* 1952, i, 287.

5. Bloom, H. J. G. *Brit. J. Cancer*, 1950, 4, 347.

6. Kreyberg, L. *Ibid*, 1953, 7, 157.

7. Lees, J. C., Lees, T. W. *The Treatment and Classification of Cancer*. Edinburgh, 1952.

8. Greenwood, M. *Rep. publ. Hlth med. Subj., Lond.* 1926, no. 33,

p. 18.

9. Macdonald, J., Kotin, P. *Surg. Gynec. Obstet.* 1954, 98, 148.

KORTEWEG in 1880. In the period of delay a "natural selection" of cancers of relatively low malignancy takes place through the elimination, by the patient's death, of the more rapidly metastasising tumours. Any group of patients operated on shortly after the onset of symptoms will contain both rapidly metastasising and relatively much less malignant tumours. With longer delay patients with more rapidly lethal cancers will die, leaving a higher proportion of less serious tumours.

Because of the supposed need for early diagnosis and treatment, chest radiographs and self-examination of the breast have been suggested as appropriate methods of detection. If recent experience is typical, however, by the time definite abnormality appears on the radiograph,¹⁰ most cases of pulmonary cancer have progressed too far for successful resection; and an apparently normal radiograph can be followed by death within a year. As KREYBERG suggests, there may be an intermediate group of cancers amenable to early excision, but if the disheartening views on the rapid lethality of most cancers and the irrelevance of early treatment are to be believed, no great improvement in mortality can be expected from such measures. It would be much better to treble the tax on tobacco.

In ordinary practice other considerations arise. The palliative effect of local resection of tumours causing physical difficulties is indisputable. On the other hand hazardous and mutilating radical operations for removal of the breast are less clearly desirable: as Professor MCKINNON emphasises in a letter in this issue, survival-rates after simple excision, radical mastectomy, and irradiation are depressingly uniform.¹¹ Vital statistics give only a general indication of the results of treatment; and the statistical pitfalls of assessing the value of treatment by comparing the results in consecutive series of patients in the same hospital, or of different series at different centres, are now well known. BLOODGOOD¹² pointed out that education of the public will bring to the hospital an increasing number of patients with a mass in the breast which is not a lethal cancer at all but which, when included in reported series, will inflate the survival-rates. Similarly, the inclusion of different proportions of such tumours in series treated in different clinics can cause wide divergences in survival-rates which are unrelated to the different methods of treatment.¹³ Neither by clinical examination nor by biopsy can such tumours be unerringly classified as benign or malignantly metastatic, and the histopathologist's opinion (which is subject to little-studied "observer-error") cannot be relied on to equate the clinical material on which rival claims are based. Cancer registration may, when complete, provide useful epidemiological evidence. But since it lacks the essential feature of random allocation of treatment to patients it is no effective substitute for the carefully controlled clinical trial now practised in other branches of medicine.

Our basic approach may be wrong: the attempt to treat cancer as a local rather than a general disease may be as irrational as treating syphilis by excising the primary chancre. Although there is no clear

evidence either way, the value of drastic remedies is uncertain enough to justify, as a first step, treating half our patients in a controlled trial by simpler methods. By a progressive elimination of the more drastic remedies whose value is not confirmed by clinical trial, we may eventually assess the place of local measures in the treatment of cancer. Surely the time has come for a realistic and unbiased appraisal?

Dyspnoea and the Work of Breathing

By dyspnoea is usually meant excessive subjective respiratory effort. As patients' judgments are not always reliable it is natural to seek an objective measure of effort in the work performed in breathing. This work is used partly in moving the chest wall and abdominal viscera, but mostly in expanding the lungs and in driving air through the bronchioles; and this part can now be measured fairly easily. As long ago as 1927, VON NEERGAARD and WIRZ¹ pointed out that simultaneous records of intrathoracic pressure and respiratory airflow enabled the work to be further analysed into a portion used in overcoming the retractile force of the lung and another overcoming the resistance to movement. By such analysis one could assign to the patient's lungs and air-passages a pressure-volume characteristic (elastance) and a pressure-movement characteristic (viscance), and so calculate the work entailed by a specified pattern of respiration. By direct measurement of intrapleural pressure and airflow, VON NEERGAARD and WIRZ obtained excellent records in a few subjects; but since their method was difficult and potentially dangerous it was not widely used. The theory was developed by FENN and his colleagues,^{2,3} who showed that for a given net (i.e., total less dead-space) ventilation the respiratory work passed through a minimum as the rate was varied. This optimum rate increased with increasing net ventilation and also if elastance was increased with respect to viscance. With the introduction by DORNHORST and LEATHART⁴ of a simple and convenient method of recording intrathoracic pressure through a fine oesophageal tube, these theoretical ideas can now be safely applied to the investigation of patients.

A recent series of papers by CHRISTIE and his colleagues⁵⁻⁷ demonstrates that in patients with emphysema and cardiac dyspnoea the work of breathing is increased—because of increased viscance in the former and increased elastance in the latter. Moreover, in normal people and in cardiac patients, at rest and during exercise, the actual respiratory-rates were close to the calculated optimum. Loss of lung distensibility during cardiac dyspnoea is probably related to an increase in pulmonary capillary blood-pressure, but the exact mechanism is obscure. The high viscance of emphysema is probably due to hindrance to airflow, since FRY et al.⁸ found very good agreement between the calculated and observed increase on breathing an argon/oxygen mixture which

1. von Neergaard, K., Wirz, K. *Z. klin. Med.* 1927, **105**, 35, 51.
2. Rahn, H., Otis, A. B., Chadwick, L. E., Fenn, W. O. *Amer. J. Physiol.* 1946, **146**, 161.
3. Otis, A. B., Fenn, W. O., Rahn, H. *J. appl. Physiol.* 1950, **2**, 592.
4. Dornhorst, A. C., Leathart, G. L. *Lancet*, 1952, ii, 109.
5. McIlroy, M. B., Marshall, R., Christie, R. V. *Clin. Sci.* 1954, **13**, 127.
6. Marshall, R., McIlroy, M. B., Christie, R. V. *Ibid.* p. 137.
7. McIlroy, M. B., Christie, R. V. *Ibid.* p. 147.
8. Fry, D. L., Ebert, R. V., Stead, W. C., Brown, C. *Amer. J. Med.* 1954, **16**, 80.

was denser and more viscous than air. These workers also confirmed the remarkable rise in airway resistance as emphysematous lungs are emptied,⁹ which is probably due to collapse of bronchioles in the absence of elastic tension from surrounding lung.¹⁰

In the common forms of dyspnoea, then, breathing is in fact harder work ; but this is not the whole story since the capacity for respiratory work is often impaired as well. The importance of this factor is seen, for example, in poliomyelitis with respiratory involvement, where a mild increase in airway resistance due to bronchitis may cause urgent dyspnoea because the patient can scarcely manage the work needed to maintain ventilation. In emphysema, too, the force that can be applied to the lungs often falls off quickly with movement, and this is one of the factors limiting vital capacity and maximal respiratory work.¹⁰ So the patient is entitled to have his effort assessed in relation to his own possible maximum, and this is the basis of the "dyspnoea index" of HUGH-JONES and LAMBERT,¹¹ where the patient's actual ventilation during standard exercise is compared with his maximal

breathing capacity. This formula does justice to those patients whose ventilation on exercise is above normal : these usually have mild mechanical trouble but, because of diffuse lung changes, a considerable decrease in the effectiveness of ventilation ; they are apt to be regarded as neurotic.

Dyspnoea in organic disease can therefore be taken as reflecting an increased excitation of the respiratory centre, whether or not this results in greater respiratory work, and whether or not the greater work results in greater ventilation. The sensation would be excessive in quantity but normal in quality. However, it is as well to remember the possibility of dyspnoea arising from some abnormal sensation : for example, an adrenaline infusion produces a moderate hyperpnoea involving no great effort,¹² but accompanied by a peculiar sense of respiratory unease quite distinct from that in other forms of hyperpnoea though probably akin to that felt by patients with psycho-neurotic effort intolerance. In conditions such as mitral stenosis both types of dyspnoea may co-exist and make clinical assessment difficult. In such cases the oesophageal tube may be of practical value.

9. Dayman, H. *J. clin. Invest.* 1951, 30, 1175.

10. Dornhorst, A. C., Kelly, H. B. *Lancet*, Feb. 6, 1954, p. 290.

11. Hugh-Jones, P., Lambert, A. V. *Brit. med. J.* 1952, i, 65.

12. Whelan, R. F., Young, I. M. *Brit. J. Pharmacol.* 1953, 8, 98.

Annotations

AUREOMYCIN IN ATYPICAL PNEUMONIA

FOR five years aureomycin has been thought to benefit patients with primary atypical pneumonia. This view has rested largely on accounts of small trials which have not been suitably controlled. Sometimes the diagnosis was in doubt, and the effect of treatment was usually evaluated only by decrease in fever and malaise. Two carefully controlled studies have lately been made in the U.S.A., but the authors come to opposite conclusions.

Major Walker, of the William Beaumont Army Hospital, Texas,¹ investigated the effects of aureomycin during an epidemic at Fort Bliss, Texas, where the patients were mainly young soldiers in basic training. Age, sex, race, physique, nursing, nutrition, and other variables were as uniform as they could possibly be. Duration of disease before treatment, severity, and symptoms were very similar in treated and untreated groups. Initial diagnosis was based on gradual and progressive development of fever, malaise, frontal headache, cough, and substernal pain, with or without physical and radiographic signs of alveolar pneumonia. Great care was taken to exclude such diseases as tuberculosis, ooccosis, bacterial pneumonia, histoplasmosis, Q fever, and psittacosis. The 212 cases diagnosed as primary atypical pneumonia were divided at random into two groups ; one group was treated with 0.5 g. aureomycin six-hourly until the temperature had been normal for at least three days, while the other group received no chemotherapy and served as a control. Walker found no significant difference between the two groups in the time taken for recovery. Comparison of duration of fever, physical signs, radiographic appearances, and major symptoms such as headache, malaise, cough, chest pain, and fever also showed no difference between the treated and the untreated patients. From this carefully controlled trial it would seem that aureomycin has no beneficial effect on primary atypical pneumonia.

Meiklejohn and his collaborators,² in California, examined the effect of various antibiotics on 146 young soldiers during an epidemic of primary atypical pneu-

monia. Only 30 were treated with aureomycin ; the rest were given chloramphenicol, oxytetracycline (terramycin), or penicillin. The statistical treatment was less thorough than that of Walker's series, and the principal criterion of chemotherapeutic activity was a fall in temperature. Meiklejohn and his co-workers admit that a large proportion of patients will recover soon after admission to hospital, regardless of treatment ; but they conclude that aureomycin is effective, and that chloramphenicol and oxytetracycline are no less useful. Penicillin in their hands gave disappointing results.

There are possible explanations of these apparently contradictory conclusions. Walker gave his patients aureomycin late in the disease—not until the fourth day—and the results might have been better if it had been given earlier. Eaton³ showed that aureomycin given to rats immediately after inoculation with the sputum of patients with primary atypical pneumonia inhibited the subsequent development of pulmonary consolidation. Meiklejohn and his collaborators treated their patients much earlier in the course of the disease ; three-quarters of them were treated in the first or second day. Another explanation is that the virus may not have been the same in the two epidemics, one but not the other responding to chemotherapy. For the present it seems wise to treat primary atypical pneumonia with one of the orally administered antibiotics, such as aureomycin, oxytetracycline, or chloramphenicol, as soon as the diagnosis is made.

DUPUYTREN'S DISEASE OF THE FOOT

Dupuytren's contracture of the palmar fascia is a well-known disorder, but an analogous process involving the plantar fascia is less familiar. Pickren et al.⁴ cited 104 reported examples and added 16 of their own ; and Pedersen and Day⁵ have now described the clinical and pathological findings in 6 further cases.

There are important anatomical differences between palmar and plantar fascia.⁴ Plantar fascia is much longer, narrower, and thicker ; it arises from the anteromedial margin of the calcaneus and extends distally beneath the plantar fat and superficial to the muscles, tendons,

3. Eaton, M. D. *Proc. Soc. exp. Biol., N.Y.* 1950, 73, 24.

4. Pickren, J. W., Smith, A. G., Stevenson, T. W., Stout, A. P. *Cancer*, 1951, 4, 846.

5. Pedersen, H. E., Day, A. J. *J. Amer. med. Ass.* 1954, 154, 33.

1. Walker, S. H. *Amer. J. Med.* 1953, 15, 593.

2. Meiklejohn, G., Thalman, W. G., Walligora, D. J., Kemp, C. H., Lennette, E. H. *J. Amer. med. Ass.* 1954, 154, 553.

nerves, and vessels. The fascia fans out towards the forefoot, and the superficial fibres terminate in the superficial transverse ligament. Deeper, heavier components branch off before this and are inserted into the distal ends of the metatarsals in conjunction with the annular ligaments of the flexor tendons. Extension into the toes is absent or rudimentary; hence there is generally no counterpart in the foot to the flexion of the fingers which characterises Dupuytren's contracture of the palmar fascia. For this reason, Pedersen and Day prefer to speak of Dupuytren's disease when the foot is involved, while Pickren et al. called the condition "fibromatosis of the plantar fascia" because a nodule of proliferating fibroblasts is the presenting feature. A tumour-like nodule may also form in the palm; and pathologically there is no essential distinction between the processes in hand and foot. In the foot, however, in the absence of contractures and perhaps of pain, a nodule may easily escape notice, and the disorder may well be commoner than is realised.

The characteristic nodule (or nodules) in the plantar fascia is usually found on the medial side, near the highest point of the longitudinal arch,⁵ where it produces a visible and sometimes even prominent tumour. The mass may grow rapidly from the start, or begin to enlarge after long apparent inactivity. One or both feet may be involved. Of the 16 cases reported by Pickren et al., Dupuytren's contracture was also present in one or both hands in 6, while the condition of the hands was normal in 8, and was not recorded in the remaining 2; the thickened fascia was only occasionally adherent to the skin. Males seem to be affected more often than females, and the process may start in patients as young as 5 years of age. As in Dupuytren's contracture of the hand, a familial tendency can sometimes be discovered. In some cases there is exceptional liability to keloid formation, and the disease also has a curious and unexplained predilection for epileptics.

Pickren et al. described the lesion as consisting of lobulated, irregular, nodular thickenings of the plantar fascia together with the adjacent fat and fibrous tissue. The average size of the nodules was about $3 \times 2 \times 2$ cm.; they projected from the fascia chiefly towards the plantar surface, but sometimes deeply towards the dorsum of the foot. The medial aspect of the fascia was chiefly involved. Invasion of tendons, nerves, vessels, or bones was never seen. Microscopically the normal broad, cell-free collagen bands of the plantar fascia terminated in nodules of young fibroblasts and interdigitated with other bundles of highly cellular new tissue. No capsule was observed, and the marginal fibroblasts merged into the surrounding tissues. In the nodules and bundles spindle-shaped cells were sinuously interwoven, curving abruptly at sharp angles; the cells were closely packed, with scant intercellular collagen. Infiltration with leucocytes was rare. Occasionally large numbers of mitotic figures were seen. Pedersen and Day believe that the formation of nodules is a response to degeneration of the plantar fascia. They found nodules, never in areas of normal fascia, but only where the collagen fibres showed fibrillation, fragmentation, and hyalinisation. They interpreted increased numbers of thick-walled small vessels and focal collections of round cells as a response to a primary degenerative process, possibly related to trauma.

These careful histological studies, though yielding no fresh clue to aetiology, should help to prevent the unfortunate misdiagnoses which have occasionally led to unnecessary amputation.^{4,5} The danger is of interpreting the histological changes as fibrosarcomatous; the suspicion of malignancy may seem to be confirmed when a new mass appears at the site from which a nodule has earlier been removed. Fibrosarcoma of the plantar fascia is exceedingly rare,⁴ and local "recurrences" of Dupuytren's disease do not take place if it is correctly

treated by excision of the entire plantar fascia. Mistakes are less likely in cases where contracture of the hands provides a pointer to the true nature of the plantar lesion.

NEW TANK RESPIRATORS

In patients with paralytic poliomyelitis the chief cause of dangerous respiratory insufficiency is paralysis of the intercostal muscles and/or the diaphragm. In such cases, provided that there is no paralysis of swallowing, treatment in a tank type of respirator is still the safest and most efficient method from the point of view of both the heart and the lungs. Formerly the patient began to receive artificial respiration only when he was in extremis, perhaps with widespread pulmonary collapse; but nowadays the vital capacity is commonly recorded at intervals of an hour or so while paralysis is spreading, and the respirator is used to rest weakening respiratory muscles long before serious embarrassment develops. It is essential, however, that tank respirators should incorporate modern improvements in design, and that those who use them should be well trained.

Improved types of tank respirator were developed quickly in the U.S.A. during the late war, but it is only in more recent years that improvements have been developed in this country. Some of these improvements are described in two papers, from Coventry and Bristol, published on earlier pages of this issue. These advances have depended on the work of many people, especially perhaps the members of the Breathing Machines Working Party of the Ministry of Health. Such a working party, however, has little authority to develop new apparatus, and it is noteworthy that these new machines have been developed without financial assistance from the Ministry.

In these respirators the first striking change is the "split front," which was first suggested by Bourdillon et al.¹ and was adopted by Messrs. Siebe Gorman.² A machine designed in Australia by Both incorporated a split of the whole cabinet and also of the rubber collar. Each of the new respirators is of this "crocodile" type, with which it is possible to dispense not only with the sliding stretcher but also with the difficult manoeuvre of pushing the patient's head through a hole in the front plate of the machine. Further, it has been found that the split rubber collar can be still airtight, and is both comfortable and easy to adjust to the neck contour. Another advantage of the crocodile type is the ease of full access to the patient and the freedom with which passive movements can be applied to the upper limbs: the tight shoulder-muscles commonly observed in respirator cases can thus be easily avoided. One danger of respirator treatment is that the patient tends to be nursed too much on his back; but these new models are adjustable over a wide range so that the lateral and semi-prone postures are feasible when the patient is handled by a skilled team.

There remains the question of how to provide positive-pressure breathing to the face when the cabinet is opened. The Bristol respirator incorporates the dome system used in some American makes and also by Christie and Espen³; but the design is necessarily complex, and some will prefer Captain Smith-Clarke's simpler and much cheaper construction reported from Coventry by Dr. Galpine. Patients treated in this Coventry machine will depend on some other apparatus for positive-pressure breathing when the cabinet is opened, and Captain Smith-Clarke has designed a small bellows for this purpose which is operated by the main pump unit.⁴ The latest type of "Beaver" machine for positive-pressure breathing, approved by the Ministry of Health, or the pump designed by Russell and Schuster,⁵ can also

1. Bourdillon, R. B., Davies-Jones, E., Stott, F. D., Taylor, L. M. *Brit. med. J.* 1950, ii, 539.

2. See Russell, W. R. Poliomyelitis. London, 1952.

3. Christie, A. B., Espen, J. R. *Lancet*, 1953, i, 1027.

4. Galpine, J. F. *Ibid* (in the press).

5. Russell, W. R., Schuster, E. *Ibid*, 1953, ii, 707.

be used. In the absence of a dome, positive-pressure respiration can be maintained through a closely fitting face-mask or, better, through a mouth-piece of the type used with B.M.R. machines.

It is dangerous to use the tank type of respirator when there is paralysis of the pharynx as well as of respiration. In paralysis of this combined type, Lassen's method⁶ of positive-pressure breathing through a cuffed tracheotomy tube is probably the most likely to prevent fatal respiratory insufficiency.

OLD PEOPLE LIVING ALONE

SOLITARY old people, holding to their independence, are almost the only real poor left in this country; and their poverty makes heavy demands on their failing powers. Dr. Gordon Scott and Mrs. C. R. S. Williams,⁷ in a review of eleven North Oxfordshire villages, found that even in the relatively small population of 7500 there were at least 135 people aged sixty-five and over living alone. The survey was undertaken at the request of the Oxfordshire Association for the Care of Old People, which made a grant towards the cost. Mrs. Williams, who did the field work, visited 107 of the old people, of whom 79 were aged seventy-one or more. Broadly speaking, the older the people the less satisfactory were their home conditions: only 39 of the 107 had water inside the house; 56 of the remainder had a tap or well reasonably near the house; 11 had to go some distance for water, and 7 of these were aged seventy-six or more. The remaining old person got her water from the river. Only 75 of the 107 had electricity in their homes; 6 had gas; but 24 relied on lamps and 2 (aged over seventy-five) on candles.

Fuel is dear; and though 43 had been able to afford logs last winter to supplement their coal ration, 18 complained that they had been short of fuel and 26 spoke of the heavy expense. It seems possible that some kept themselves warm only by going short of food. Only those who were visiting the doctor could get medical certificates for extra fuel. Many found themselves in difficulties when it came to buying clothes or replacing household articles which were worn out: in general they had just enough for their day-to-day expenses with nothing over; 22 found it difficult to manage. Only 10 had any private means; 46 were receiving National Assistance, and as a result of the survey a further 5 were given it. At the time of the survey 24 were under treatment from their doctors, but 46 others complained of rheumatic pains, and 39 of sleeplessness—caused in most cases by pain. Some needed spectacles, or new spectacles; but of 19 in this situation, 11 were not physically fit to make the journey to have their eyes examined. Only 6 were very deaf, all of them over seventy, but they found it a serious handicap.

About a fifth had no visits from relations, and about a tenth had hardly any visitors at all. Health visitors seemed to call only on those who were using home helps. Most of the old people, however, were in touch with relations, either receiving visits from them, or going to stay with them from time to time. Many relied on good neighbours for help and friendship. Only 14 complained that loneliness was their biggest problem, and 50 said they had no special problems. They were nearly all greatly attached to their independence, and ready to bear much to retain it. In spite of narrow means and such inconveniences as an outside water-supply and no indoor sanitation, nearly all of them kept their homes in clean and shining order.

The impression is left of tremendous "gameness"—of a will to live and savour life. Dr. Scott believes that married couples on National Assistance are better off than those living singly, and suggests that an extension of the cheap milk scheme to old people living alone

would help to narrow the gap. He proposes also that local authorities, through their health visitors, should keep an eye on all old people over seventy living alone; and these, he thinks, should be able to claim a supplementary allowance of coal.

Might it not also be possible, surely, to improve their amenities in various inexpensive ways—by bringing an outside tap inside, for instance; by providing 'Elsan' closets indoors (if indoor sanitation is out of the question), and by sending a man to empty it at regular intervals; or by wiring for electric light, where this is available. Such things do not cost nearly so much to install as special bungalows cost to build; and they have the advantage of leaving the old person in surroundings to which he is accustomed, and which he often prefers.

PERIPHERAL AUTONOMIC NERVOUS SYSTEM

Meyling,¹ extending Leeuwe's work, has given his view of a new concept of peripheral autonomic innervation. This may be briefly summarised in two parts:

1. The viscera contain a peripheral nerve net composed of branching "autonomic interstitial cells" (A.I.C.). These are small ganglion cells; their processes form a syncytial network in which conduction is aysynaptic and impulses are spread with a decrement. Like the larger autonomic ganglion cells these A.I.C. develop from neuroblasts. Neurofibrils are present in the A.I.C., and Nissl's granules can be stained; oxidases and peroxidases similar to those in sympathetic ganglion cells can be demonstrated. After section of the orthosympathetic and parasympathetic nerves, this network of A.I.C. retains its identity; thus in man the network will persist after section of the postganglionic fibres or after sympathetic ganglionectomy. The network innervates every effector cell—e.g., every smooth-muscle cell of the gut wall.

2. This A.I.C. nerve net is linked both to the efferent fibres of the orthosympathetic and parasympathetic systems and to the visceral afferent fibres. The individual efferent post-ganglionic fibres come to lie over portions of the all-pervasive A.I.C. network and, in their finest branches, form synaptic end-knobs or end-loops on the surface of the A.I.C. Afferent fibres in the same way have a synaptio connection with these A.I.C. This means that the A.I.C. network acts as a mediator between the nerve-fibres and the tissues.

The story of these "autonomic interstitial cells" goes back to Ramon y Cajal's description in 1894 of the "neurones sympathiques interstitiels" which he demonstrated by the Golgi method in the intestinal villi and elsewhere. Since then the nature of these cells has been disputed: some, with Boeke, Jabonera, and others, have regarded them as nervous; some, like Dogiel and Nonidez, have considered them connective-tissue elements; and some, like Lawrentjew and Schabadasch, have thought them accessory nerve-cells of the lemnoblast (Schwann cell) type. Miss C. J. Hill, in her classical paper on the innervation of the intestinal wall, came to no conclusion about their nature.

The nature of the peripheral nerve net and of the termination of the postganglionic fibres has been variously pictured; some workers have denied the existence of any true syncytial network, while others have held that this exists but have disagreed on its character. Some have held that the final branchings of the postganglionic fibres end in a diffuse network, others that each postganglionic fibre ends discretely. All agree that orthosympathetic and parasympathetic fibres pass to smooth muscle in many of the viscera, but there is still little agreement on the nature of the terminal innervation of the smooth-muscle cells. Some of these differences are due to the difficulty of studying these fine structures.

Meyling's hypothesis, if accepted, will have very extensive implications. It may help towards the solution of the vexed questions of the nervous and humoral control of blood-vessels. It may also add to our understanding of the differences between the immediate and the late results of sympathectomy.

6. Lassen, H. C. A. *Ibid.* 1953, i, 37. Russell, W. R., Smith, A. C., Spalding, J. M. K. *Ibid.* (in the press).

7. *Oxford Times*, March 12, 1954.

1. Meyling, H. A. *J. comp. Neurol.* 1953, 9, 495.

Special Articles

HOSPITAL BEDS FOR CHILDREN AN ESTIMATE OF NEEDS

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THERE is yet no formula by which the need for hospital beds can be accurately calculated. Other things being equal, the need should depend only on the incidence and type of illness in the town or district concerned. But other things are never equal. The customs of the people, the houses they live in, the habits of the doctors, and the quickness of the hospital staffs in dealing with their patients vary from place to place and from time to time.

Of all institutions where the sick are treated, the greatest variability of staffing, of method, and of custom is to be seen in children's wards and in children's hospitals. Nor is it only a matter of staffing, method, and custom. For example, some hospitals open children's wards, not to meet a clinical need, but to satisfy a nurse-training scheme or some other professional demand. These and other variable factors suggest to us that we should attempt the estimate of hospital beds for sick children that we offer here.

The Investigation

Our estimate is based on surveys that we made in 1943 and 1944, and which we repeated in 1950. The basis of the surveys was the child population in Newcastle upon Tyne in those years. From this total sample of about 50,000 children aged 0-12 years we identified each child who went to hospital or nursing-home. By personal examination of the records, the age of the child, the duration of the stay in hospital, and the nature of the illness were established; and duplicate admissions or transfer from one hospital to another were eliminated.

In our enumerations there was a possible source of error through some Newcastle children having been admitted to hospitals in other towns. The child away from home on holiday or at a boarding-school may have taken suddenly ill, or parents may have wished their child to be treated in another city. After examination of this possible source of error we conclude that its effects are so small that it does not materially affect our estimate.

The investigation took into account all children resident in the city under the age of 13 years, but in 1950 we extended it to include the children aged 13 years and 14 years. Ten hospitals and four nursing-homes were involved in one or both surveys, some of which were situated outside the city.

The standard of record-keeping in the hospitals was high, but their methods of classification of diseases were not sufficiently informative for our purpose; so we designed and used a classification and record which indicates more clearly than the traditional classification the type and scope of the work undertaken by the hospitals. We consulted the information collected by the Regional Hospital Board for the Ministry of Health on their S.H.3 return, but this was of no value to us.

LOCAL FACTORS

In interpreting the results we would ask the reader to keep in mind certain factors favouring an economical use

of beds in Newcastle, which might not obtain some other places.

(1) The hospital accommodation for children was ample, and there was no waiting-list for admission, except for tonsillectomy and operation for squint.

(2) The threshold of admission to hospital was high, because of the prevailing hospital policy that whenever possible the sick child should be treated at home.

(3) This policy was reinforced by the provision of a daily outpatient consultation service to which the family doctors could refer their patients immediately. Conducted by senior and experienced consultants, this service reduced the demand for beds.

(4) The children were admitted mainly to children's hospitals or children's departments arranged and staffed as combined clinical units, in which personal consultations between paediatric physicians, surgeons, and specialists were so promptly obtained that time and anxiety were saved.

(5) In these children's hospitals and departments all children were examined by an experienced paediatric resident at the time of admission to hospital, and the allocation of patients in wards and beds was under his control with consultant advice immediately available. These measures eliminated outbreaks of those infective illnesses for which children's wards are often closed, and in other ways contributed to a full and efficient use of bed accommodation throughout the periods of survey.

(6) In two hospitals time was saved by using, for the nursing of sick children, the Babies' Hospital method of "mother-nursing" which shortens the child's length of stay in hospital.

(7) Newcastle being a regional and university city, its hospitals are self-sufficient in their consultant and specialist services. Therefore the estimates we make are for similar cities. For those towns and districts which are not self-sufficient in paediatric and specialist services, and from which transfer of cases to a regional centre will take place, a reduction in the estimate is required.

(8) If our estimates are to be used for policy and plans in the future, the changing trends of mortality must be noted. The disappearance of diphtheria (185 admitted in 1943, and 0 in 1950), the diminished hospital needs for scarlet fever (495 in 1943 and 26 in 1950), are on the credit side. On the debit side is the long stay in hospital for modern forms of treatment of children with tuberculous meningitis; but it can be predicted that after ten years there will be a steady reduction in the number of children coming to hospital for treatment of tuberculosis. On the debit side also is the increase in tonsillectomy, but it is within the bounds of possibility that a changing attitude towards this operation will diminish greatly the demand that it shall be done.

(9) A local policy about scarlet fever exercises a paramount influence on the need for hospital beds. In Newcastle the policy, which we hold to be the right policy, is to admit to hospital only those children with scarlet fever, the severity of whose illness indicates the need for hospital treatment. In some other towns all cases of scarlet fever are admitted to hospital, however mild the illness may be.

THE POPULATION

Estimates can be based on (a) the total population (table I), or (b) the population of the age-groups under

TABLE I—POPULATION OF NEWCASTLE

—	Total	Children
1943	254,890	49,800 under age of 13
1944	262,920	50,400 " " 13
1950	294,800	{ 57,800 66,130 " " 15

TABLE II—ANNUAL BIRTHS AND BIRTH-RATE

—	Live annual births	Newcastle birth-rate	National birth-rate
1943	4548	17.8	16.5
1944	5359	20.4	17.6
1950	5051	17.14	15.8

* Holding a research grant from the Scientific and Research Committee of the Newcastle Regional Hospital Board.

TABLE III—ANNUAL ADMISSIONS IN AGE-GROUP 0-12 YEARS

—	Total	For tonsillectomy	For scarlet fever
1943 }	3743	890	495
1950	3980	1482	26

study (table I), or (e) the birth-rate (table II). Our final estimates are based on the first of these and are expressed as rate per 100,000 of total population. This is probably the best method of comparing one town with another, but for strict comparison the governing factor of birth-rates should also be considered.

The Findings

There is so little variation between the years of 1943 (3782 admissions) and 1944 (3704 admissions), that the

TABLE IV—ANNUAL ADMISSIONS IN AGE-GROUPS

—	Infants (0-12 mos.)	1-4 yr.	5-12 yr.	13-14 yr.	Total
1943 }	419	1293	2031	(not counted)	3743
1950	449	1197	2334	260	4240

figures for these two years are dealt with as an annual average of 3743 children (aged 0-12 years) admitted to hospital in each year, which is 7.48% of the childhood population in that age-group, or 1410 per 100,000 of the total population. In 1950, 3980 children aged 0-12 years were admitted, which is 6.85% of children in that age-group, or 1350 per 100,000 of the total population. In 1950 there were in addition 260 children aged 13 or 14 admitted to hospitals. These figures show that 1 child in 15 is admitted to hospital each year, which is equivalent to every child being admitted to hospital once before the age of 15.

The admissions for tonsillectomy and scarlet fever may play so large a part in the figures that they must be considered separately. In the years 1943 and 1944 the average annual admission for tonsillectomy was 890, and in 1950 it was 1482. For scarlet fever the numbers were 495 in 1943 and 1944, and 26 in 1950 (table III).

An analysis of admissions is given in tables IV and V, and we recommend that annual reports of children in hospital should be presented in this way and extended so that each category of illness is related to age-groups, to length of stay, and to results. This information is necessary if the type of clinical work in hospitals is to be judged.

The ages of children (table IV) are grouped in these three categories: (1) infants (aged 0-12 months); (2) pre-school children (aged 1-4 years); and (3) schoolchildren (aged 5-12 or 5-14 years).

Our estimate of the lengths of stay, which we use later, were made from the following groups: (1) for a period of less than a month; (2) for one to two months; (3) for two or three months; and (4) for three months or more.

Calculation of Bed Requirements

For Tonsillectomy

In 1943 and 1944 there were 890 annual admissions of children to hospital for tonsillectomy. In 1950 there were 1482 up to the age of 12, and 1574 up to the age of 14. The 1950 figure represents a higher-than-normal level when waiting-lists were being worked off. As an estimate for the future we will take a figure of 1200 tonsillectomies a year in children up to the age of 12 years, and 1250 up to the age of 14 years. This represents 1.8% each year of the child population at risk, and 24.7% of the annual births. Assuming that each child spends

either two or three days in hospital and that each bed used for this purpose accommodated 2 patients a week, 12 hospital beds would suffice for these 1200-1250 children admitted for tonsillectomy—i.e., 4 beds per 100,000 of the population.

Length of Stay

A distinction must first be made between the admissions to "acute" hospitals and the admission to "long-stay" hospitals, or children's sanatoria; but the latter form so small a part of the whole (30 admissions in 1943 and 88 in 1950), that we will confine our estimate of long-stay beds for children to the statement that about 35-45 will be required for a population of 300,000, or 12-15 per 100,000 of the population, assuming that the average stay in that kind of hospital is six months; but this estimate will vary according to the clinical policy of the hospitals, and its adjustment to the wishes and capabilities of the parents. This estimate of long-stay beds may be on the high side.

For all other categories of illness (i.e., excluding tonsillectomy and long-stay illnesses in special hospitals, for which we have already made a length-of-stay estimate) we have calculated an average length of stay expressed as the number of children per bed per year, by analysing the records of three fully staffed and active children's departments or hospitals, which admit about 4000 children a year with all types of medical, surgical, and special illnesses. A few of them (40 in the year) were in the wards for more than three months, and 150 for one to three months, but these were included in our calculation of the "average length of stay."

The average length of stay (excluding those in hospital for tonsillectomy) was just over fourteen days. From this we estimate that each hospital bed would accommo-

TABLE V—ANNUAL ADMISSIONS TO "ACUTE" HOSPITALS FOR CHIEF CATEGORIES OF DISEASE

—	1943-44 (0-12 yr.)	1950 (0-12 yr.)	1950 (13-14 yr.)
Scarlet fever ..	495	26	0
Diphtheria ..	185	0	0
Measles, pertussis, &c.	143	62	0
Pollomyelitis ..	10	65	1
Meningococcal infections ..	34	27	0
Upper respiratory infection .. (Including tonsillitis and otitis media)	140	364	28
Lower respiratory infection .. (Including pneumonia)	230	161	0
Acute gastro-intestinal conditions .. (Including dysentery)	213	126	0
Acute abdominal surgery			
Appendicitis ..	42	67	14
Intussusception ..	13	28	0
Pyloric stenosis ..	15	21	0
Others ..	8	8	2
Trauma			
Burns ..	55	33	0
Head injuries ..	56	49	3
Fractures ..	76	80	8
Poisons ..	7	8	0
Minor injuries ..	114	65	0
Planned surgery			
Tonsillectomy ..	890	1482	92
Eye operations ..	40	114	16
Plastic operations ..	12	32	0
Other planned surgery .. (Including orthopaedic)	127	232	9
Sepsis ..	140	70	5
Osteomyelitis (or suspected) ..	19	28	0
Tuberculosis			
Meningitis or miliary ..	26	30	1
Bone and joint ..	11	10	0
Others ..	90	37	3
Other conditions			
Acute rheumatism or chorea ..	24	21	4
Nephritis ..	11	16	0
Venereal diseases ..	7	3	1
Miscellaneous skins including impetigo ..	110	17	2
Bronchiectasis, asthma, and emphysema ..	17	28	1
"Feeding problems" ..	25	14	0
Other alimentary disorders ..	50	74	
Acute unknown infections ..	33	36	

date 23 patients a year, making due allowance for turnover and other adjustments.

In 1950 for the Newcastle children in the age-group 0-12 years there were 2410 admissions for illnesses in this category of medical, surgical, and special diseases. According to our estimate, 105 beds would be required for these. Adding the group of children aged 13-14 years, 110 beds would be required.

Final Estimate

Assuming that existing conditions continue, Newcastle, with its population of 295,000, including 66,130 children in the age-group 0-14 years, will require—for all types of illness other than those admitted to sanatoria or similar long-stay hospitals—the following number of hospital beds:

For tonsillectomy	12
For other illnesses	110
Total	122

In other terms this is 42 beds for children aged 0-14 years, per 100,000 of the total population. In addition we have tentatively suggested that 12-15 beds per 100,000 of the population would be required for long-stay cases in special hospitals.

Final Comment

This estimate of 42 children's hospital beds per 100,000 of the population is for an industrial town in the North of England with a high birth-rate and a high morbidity incidence. It is a tight estimate: to be on the safe side, the figure should be set at 50 per 100,000. On the other hand, fewer beds would be needed in some other towns, and considerably fewer in those districts or towns which are not self-sufficient in specialist and paediatric staffs.

This number of beds suffices for all hospital treatment of children, other than for what goes on in sanatoria and maternity hospitals.

In a university town which is a teaching and specialist centre still more beds will be required to meet regional needs.

This estimate may serve as a guide to the use of beds. We have found that hospital beds for children are used more effectively—i.e., with a higher turnover in numbers—and with greater satisfaction to patients, to parents, and to staff, if the children's wards are grouped and arranged together in children's departments or hospitals, of convenient size, which bring the medical, surgical, and specialist staff into a close and unavoidable working relationship. This way works better than scattering children's beds in specialist departments.

While our estimate may serve as a numerical guide, it cannot be used to judge the quality or value of clinical work, or the relationship of staffs and the arrangement of their responsibilities, on which so much depends in children's wards. The worth of these is measured, not by time-motion studies or by enumeration, but by the judgment of those who are fit to judge.

ESTIMATES FOR 1954-55

THE National Health Service estimates for 1954-55¹ allow for gross expenditure in England, Wales, and Scotland totalling £504,789,835, compared with £489,771,648 in the past year. Appropriations-in-aid (including contributions from the National Insurance Fund) are estimated at £71,656,350, compared with £70,094,770; and thus the net cost is £433,133,485, compared with £419,676,878—an increase of £13,456,607. The gross totals, which include grants for Civil Defence services, are made up as follows:

	1954-55 (£)	1953-54 (£)
Hospital, specialist, and ancillary services	321,492,525	310,511,603
General medical, dental, pharmaceutical, and supplementary ophthalmic services	140,296,000	135,215,520
Grants to local health authorities	23,198,010	21,558,020
Training services, &c.	1,605,200	1,689,750
Broadmoor Institution and mental-deficiency hospitals	1,498,200	1,504,000
Liabilities arising from establishment of N.H.S.	5,753,500	6,435,030
Superannuation	7,391,500	6,162,500
Civil Defence services	2,675,200	5,926,315
Other services	789,700	769,010
	£504,789,835	£489,771,648

Capital expenditure by hospital boards is estimated at £12,300,000 in 1954-55, compared with £9,975,000 in 1953-54 (an increase of £2,325,000), and maintenance expenditure at £295,820,000, compared with £287,496,558 (an increase of £8,323,442).

The grant-in-aid to the Medical Research Council¹ is put at £1,947,109 in 1954-55, compared with £1,805,856 in 1953-54. Of the total, £102,428 is for building. The grant for general expenses (amounting to £1,844,681 after deduction of £115,509 in receipts) is compounded as follows: administration, £68,532; provision for general scientific purposes, £18,400; National Institute for Medical Research, £386,187; research units and external scientific staff, £1,142,131; special grants to institutions, &c., £177,340; temporary research grants and training awards, £197,600.

Public Health

DOES INFLUENZA SPREAD WITHIN THE HOUSEHOLD?

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THERE is nowadays a general belief that influenza is spread by direct transmission of the causal organism from person to person. Less than a century ago, however, most of the careful students of the disease dismissed this explanation of influenza epidemics because it did not agree with their experience of the behaviour of the disease. Hirsch (1883), in a fine survey of the then available information, said:

"...there is not the slightest cogent reason for supposing that the several parts of an influenza pandemic stand in a genetic relation to one another, or that it is a question of the conveyance of a disease-producing substance from place to place."

"...The question whether influenza is communicable or contagious has given occasion to a lively controversy. In more recent times the great majority of observers have answered it decidedly in the negative, not so much on the strength of the many single observations which tell against the communicability of the disease, as on the ground that the spread of influenza can be shown to have taken place quite independently of intercourse. To this argument I may add the fact that it has not spread more quickly in our own times, with their multiplied and perfected ways and means of communication, than in former decades or centuries."

The transformation of medical opinion began in 1892 when Pfeiffer described *Haemophilus influenzae*, and the

1. Civil Estimates for the year ending March 31, 1955. Class v: Health, Housing, and Local Government. H.M. Stationery Office. Pp. 154. 5s. 6d.

* Working at the Institute of Social Medicine, Oxford for much of the time during which this paper was in preparation.

TABLE I.—INFLUENZA AMONG 385 PERSONS IN 100 HOUSEHOLDS BY SEX

—	Males	Females	Total
First cases ..	55 (55%)	45 (45%)	100
Subsequent cases ..	102 (46%)	121 (54%)	223
Escaped ..	28 (45%)	34 (55%)	62
Total ..	185 (48%)	200 (52%)	385

$\chi^2 = 2.62$ with 2 d.f. $0.30 > P > 0.20$.

outstanding epidemiological problems began to be less clearly visible in the cloud of controversy about the validity of the claim that Pfeiffer's bacillus was the causal organism of influenza. Just over forty years later the aetiological problem seemed to be settled by Smith, Andrewes, and Laidlaw (1933) who

(1) Transmitted the disease to ferrets by intranasal instillation of filtered nasal washings from a human case of epidemic influenza.

(2) Transmitted the disease from ferret to ferret both by natural contact and by intranasal instillation of filtered material.

The ensuing spate of research on viruses has established that epidemics of clinical influenza are usually associated with the presence of one or more of the group of influenza viruses, and there seems good reason to suppose that these organisms cause the disease. But this important knowledge by itself advances us little in unravelling the complex reasons for the appearance and disappearance of influenza epidemics.

The time is ripe for an assessment of the epidemiology of influenza against the background of the bacteriological and virological knowledge which has accrued during the last sixty years. Is it now possible to adduce statistical evidence that influenza is spread directly from person to person? The present paper examines the pattern of the disease in households during a recent epidemic.

Investigation

The data were collected during the influenza epidemic of 1951 in a general practice in and around Cirencester. Owing to the considerable burden of work some desirable statistics were omitted. For example, those concerning the extent of the epidemic in the practice as a whole and the proportion of households which escaped attack. However, a close watch was kept on 100 households in which at least 1 case of influenza was known to have occurred; the households were not otherwise subject to any conscious selection. The sex and age of each member of these households were recorded, with the date of onset and the "worst" day for those who contracted the disease. The material analysed below is very slightly different from that given in a provisional report (Hope Simpson 1951).

An element of uncertainty always attaches to the clinical diagnosis of influenza. All the cases upon which this study is based occurred during an epidemic of influenza, the symptoms were similar to those reported from other parts of the country, and of 69 paired samples of sera taken during the epidemic (although not all from these households) more than 80% were positive for influenza virus A. It therefore seems likely that most of the recorded cases were true influenza but that an unknown proportion were other diseases; also some atypical cases of influenza may have been diagnosed as other conditions.

The 100 households contained 385 individuals. Since the basis for selecting a household was the occurrence of a case of influenza, 100 of these individuals represented first cases in the household. (In a few households the first 2 cases started on the same day, and 1 was chosen at random as the "first" case.) Of the other 285 individuals, 223 (78%) subsequently manifested

influenza within fifty days of the first case in the household. Two women and a man, all aged over 75, died of the disease. In the ensuing analysis the 385 individuals are studied first, and then the 100 households.

SEX AND AGE

It was shown by Hope Simpson (1951) that the individuals in the affected households had a similar age-distribution to those in the practice as a whole. The same applies to the proportions of the sexes in the sample and in the practice. Thus there is nothing about the age and sex of the people in affected households to distinguish them from other people in the practice.

Within these households the individuals fall naturally into three groups: the first cases, the subsequent cases, and those who escaped. These three groups are compared in table I as regards sex and in table II as regards age. There appears to be a slight preponderance of males among the first cases, but this may be no more than a chance fluctuation; that is to say, there is no real evidence that one sex or age-group was more likely than another to manifest the first case of the disease in the household, nor, when the disease was present, that one sex or age-group was affected more than another. Further, since less than a quarter of those exposed to influenza in the household escaped, the level of immunity was low. There is no evidence that immunity was related to sex or age.

Influenza thus seems to have attacked male and female, old and young, indiscriminately. The figures offer no evidence about possible lines of the spread of the disease in the way that the data on measles (Hope Simpson 1951) and the common cold (Lidwell and Sommerville 1951) indicate the rôle of the school-child in introducing the disease into the household.

SIZE OF HOUSEHOLD

The 100 households ranged in size from 2 to 11 persons. Table III shows the numbers of first and subsequent cases

TABLE II.—INFLUENZA AMONG 385 PERSONS IN 100 HOUSEHOLDS BY AGE (YEARS)

—	Less than 15	15-24	25-44	45-64	65 or more	Total
First cases	22 (22%)	10 (10%)	34 (34%)	23 (23%)	11 (11%)	100
Subsequent cases ..	60 (27%)	29 (13%)	74 (33%)	42 (19%)	18 (8%)	223
Escaped ..	9 (15%)	9 (15%)	24 (39%)	15 (24%)	5 (8%)	62
Total ..	91 (24%)	48 (12%)	132 (34%)	80 (21%)	34 (9%)	385

$\chi^2 = 6.67$ with 8 d.f. $0.70 > P > 0.50$.

and of those who escaped, according to the size of the household. The final column shows the percentage of those exposed to risk who were subsequently attacked. The percentage is least for households of 4 (in which 3 persons were exposed to the risk of subsequent attack) and rises for smaller and larger households. This apparent association between size of household and subsequent attack-rate just attains statistical significance at the 5% level, and so warrants further investigation.

NUMBER OF SUBSEQUENT CASES

Methods

Certain widespread diseases, such as measles, chickenpox, mumps, and smallpox, have epidemiological features which are characteristic of direct person-to-person spread of the disease. In continuing this investigation of influenza it is useful to analyse the behaviour of one of these diseases—namely, measles—side by side with that of influenza, so as to compare their epidemiological features more closely.

The data on measles were collected, in the same area as those on influenza, in a series of epidemics from

Jan. 1, 1947, until March 31, 1952. All known cases in each outbreak have been included. The sex and age of each "susceptible" member of affected households were recorded, with the date of fullest development of rash for those who contracted the disease. A "susceptible" member was someone who gave no history of previous attack.

For the investigation of the number of subsequent cases of influenza the household is taken as the unit of study and is characterised by the number of persons in it and the number of cases of influenza which occurred after the first case. For measles the household is characterised by the number of susceptible members aged under 15 years, and the number of cases of measles which occurred among them after the first case. Tables IV and V give the basic data in this form.

Apart from the possibility of fresh introductions of a disease into a household, there are two main ways in which subsequent cases of that disease could arise:

(1) All members of the household are exposed to the risk of contracting the disease, but the agent does not spread directly from person to person. An example of this class of

TABLE III—INFLUENZA AMONG 385 PERSONS IN 100 HOUSEHOLDS BY SIZE OF HOUSEHOLD

No. of persons in household	First cases (i.e., no. of households)	Subsequent cases	Escaped	Percentage subsequently attacked
2	20	18	2	90
3	26	38	14	73
4	24	51	21	71
5	18	54	18	75
6	9	39	6	87
8	2	13	1	96
11	1	10	0	
Total	100	223	62	78

For differences between subsequent cases and those who escaped
 $\chi^2 = 11.46$ with 5 d.f. $0.05 > P > 0.02$.

disease would be typhoid fever from a well serving several households, where the subsequent hygienic precautions were sufficient to prevent secondary cases arising from infected clothing and excreta. Another example would be an illness caused by an organism which lay dormant in each person but recrudesced from time to time in response to suitable stimuli affecting several households.

(2) The second way in which subsequent cases could arise is by spread of the disease from person to person within the household, as in measles. The distinction is essentially between a disease which is not spread directly from person to person (class 1) and one which is (class 2).

For each of these two classes of diseases it is possible (with certain assumptions specified below) to make a theoretical prediction of the proportion of households of a certain size in which 0, 1, 2, &c., subsequent cases occur. If these predictions are compared with the pattern

TABLE IV—ACTUAL AND EXPECTED NUMBERS OF HOUSEHOLDS OF 3-5 PERSONS ACCORDING TO NUMBER OF SUBSEQUENT CASES OF INFLUENZA

No. of cases of influenza after first	Number of persons in household (i.e., persons exposed to risk plus one)								
	3			4			5		
	Actual	Expected (binomial)	Expected (chain binomial)	Actual	Expected (binomial)	Expected (chain binomial)	Actual	Expected (binomial)	Expected (chain binomial)
0	1	1.9	4.4	3	0.6	3.2	1	0.1	1.4
1	12	10.2	5.2	3	4.3	2.4	2	0.8	0.7
2	13	13.9	16.4	6	10.5	6.8	4	3.8	2.4
3	12	8.5	11.7	9	7.6	4.8
4	5.7	8.7
Total	26	26.0	26.0	24	23.9	24.1	18	18.0	18.0

TABLE V—ACTUAL AND EXPECTED NUMBERS OF HOUSEHOLDS WITH 3 AND 4 SUSCEPTIBLE CHILDREN UNDER 15 YEARS OF AGE, ACCORDING TO NUMBER OF SUBSEQUENT CASES OF MEASLES

No. of cases of measles after first	Number of susceptible children in household (i.e., persons exposed to risk plus one)					
	3			4		
	Actual	Expected (binomial)	Expected (chain binomial)	Actual	Expected (binomial)	Expected (chain binomial)
0	4	1.3	4.5	2	0.2	1.2
1	7	12.4	6.1	1	1.6	0.9
2	32	29.3	32.5	1	5.3	3.4
3	9	5.9	7.4
Total	43	43.0	43.1	13	13.0	12.9

observed for particular diseases—in this instance influenza and measles—it may help us to decide whether the causal agent is being transmitted directly from person to person. For a disease in class 1 an appropriate theoretical model to try is a simple binomial distribution. For a disease which spreads directly from one person to another (class 2) an appropriate model to try is a chain of binomials (Greenwood 1931).

Results of Analysis

The results of the calculations for the simple binomial and the chain binomial are given in tables IV and V. The principal difference between them is that, for a given size of household, the chain binomial yields larger expected values than the simple binomial when few or many subsequent cases occur. It seems, although the data are scanty, that the chain binomial fits the observed pattern better than the simple binomial for influenza households of 4 or 5, whereas the position is reversed for households of 3. For measles households of 3 or 4 the chain binomial also fits much better than the simple binomial. Households of 2 are not included in the table, because the chain binomial and the simple binomial predictions are identical for these households.

The effect of fresh introductions of the disease into households may be referred to briefly. In the absence of evidence to the contrary it is assumed that they did not occur very often. The effect of a few such introductions would be to increase the average number of subsequent cases. Apart from this increase the form of a simple binomial distribution would remain unchanged. The effect on a chain binomial is not quite so plain, but this distribution is unlikely to be seriously deformed. In other words, in drawing conclusions from tables IV and V, any fresh introductions of influenza or measles into the households may be ignored. There are, however, other reasons why it may not be valid to apply these two formulae to the data.

Applicability of the Simple Binomial

The simple binomial is an appropriate model for diseases of class 1 only if the risk of a subsequent case of the disease is uniform throughout all the households of a given size. It has already been shown that the incidence of influenza in the epidemic as a whole did not vary appreciably with sex or with age, and the mortality from influenza does not appear to be affected by social status (Registrar-General 1938). We have thus no evidence against the applicability of the simple binomial to influenza. Measles is referred to below.

Applicability of Chain Binomial

The chain binomial in its simplest form rests upon two assumptions: (1) each person without the disease runs the same risk of being infected by the first case as by any subsequent cases; and (2), as for the simple binomial, the risk is uniform throughout all households of a given

size. In the original application of the theory Greenwood (1931) found that the chain binomial agreed satisfactorily with data on measles in the form of our table V, whereas the simple binomial did not. This was confirmed by Wilson et al. (1939), but by a more detailed analysis they showed that the agreement was no more than fortuitous. In fact the first of the two assumptions, that each person without the disease runs the same risk of being infected by the first case as by any subsequent cases, was untenable. Those exposed to the first case of measles were substantially more likely to succumb than those exposed to subsequent cases.

In a further analysis Greenwood (1949) showed that the second assumption, that the risk is uniform throughout all households of a given size, was also untenable. The risk that an individual would catch measles from a home contact varied from one household to another of the same size.

As regards influenza, the uniform incidence with sex and age suggests that the second assumption may not be unrealistic, and that in influenza the risk may be uniform throughout households of a given size; but it is arguable that the first assumption—that the risk is equal for each of the persons in the household—is unlikely to hold for any disease if it is transmitted directly from person to person. The secondary cases, which are infected by the first case, will tend to include the members of the household who have the least individual resistance. Accordingly, those who remain uninfected will less readily fall victims to the secondary cases, and so on. No direct check can be made to see whether this is happening with influenza, since, unlike measles, the cases do not obviously group themselves in "generations." In fact, if they did so, we should not be trying to obtain evidence about the infectiousness of influenza in so tortuous a fashion.

Discussion

We are thus left in some uncertainty whether the satisfactory fit of the chain binomial to the influenza data in the larger households is fortuitous or whether it is real evidence in favour of the direct spread of the disease from person to person. On the other hand, the failure of the simple binomial in these households encourages us to reject the hypothesis that influenza is not infectious.

Before considering the different pattern presented by influenza in the small households it is desirable to recall an earlier finding. Other influences excepted, a consequence of the simple binomial theory is that the subsequent attack-rate is independent of the size of the household. Similarly, a consequence of the chain binomial is an increase in subsequent attack-rate with increase in size of household. The figures in table III suggest that neither of these patterns represents the whole truth for influenza. Thus, even if we can accept one of these two theories as a description of the method of spread of influenza within a household, it becomes necessary to examine other influences which may affect to a different extent households of different sizes.

Most people would prefer the explanation that influenza is infectious to the possibility that it is not. But in relation to our evidence this raises two difficulties: (1) the failure of the chain binomial to fit the data for households of 3 (there are too many instances where only 1 of the 2 persons at risk were attacked); and (2) the high subsequent attack-rate in households of 2. In the present sample most of the households of 2 consist of a married couple. The explanation might be that there is an inherently greater risk of one partner in a marriage infecting the other than of either infecting any other member of the household. If this were so it would help to account not only for the high subsequent attack-rate in households of 2 but also for the preponderance of households of 3 in which only 1 of the 2 persons at risk was attacked. In larger households the

effect might be less noticeable because of the larger numbers at risk. There is another possibility: the doctor may have been called more readily to a household of 2 when both members were incapacitated by influenza than if only 1 was. A bias of this kind would lead to a spuriously high subsequent attack-rate in the chosen sample of households of this size.

And there this approach to the problem must be left. We have gone as far as, perhaps further than, the available information warrants. For progress on these lines considerably more data are required.

INTERVAL BETWEEN CASES

So far, all the analyses have been devoted to the frequency of occurrence of subsequent cases and none to their timing. For many infectious diseases—e.g., measles, chickenpox, and infective hepatitis—there is a reasonably constant serial interval between the infecting and the infected cases. This interval represents the duration of the reproductive cycle of the causal organism (Hope Simpson 1952) and will show itself only if the duration of infectiousness of the first case is short, and if the incubation period does not vary too widely. If it is possible to uncover a serial interval between cases of influenza in the same household it will show that the disease is passing directly from person to person, and at the same time determine the duration of the reproductive cycle of the causal organism. Failure to uncover the interval may be due either to the fact that the disease does not spread directly from person to person, or to the other factors indicated above.

Evidence from Households with 3 or more Cases

Methods for studying intervals between cases were investigated by Greenwood (1946), who envisaged the use of data on separate households like the present material. The approach adopted here is to enumerate the intervals between successive cases according to their duration, in households with 3 or more cases, and to compare them with what would be expected if the timing of the cases between the first and the last were purely random. The relevant theory is sketched by Greenwood (1946) on pp. 100–101 of his paper. For influenza the intervals between the dates of onset and those between the "worst" days of the disease were enumerated separately, since one might give a more precise indication of any serial interval than the other. There were certain gaps in the information, particularly for "worst" days. The duration of 171 intervals between dates of onset and of 134 between "worst" days could be determined. For measles the intervals between the days of fullest appearance of the rash were enumerated. The duration of 151 intervals could be determined.

If there is a chain of infection, which is indicated by a serial interval, there will also be instances where 2 or

TABLE VI—COMPARISON OF ACTUAL AND EXPECTED INTERVALS BETWEEN SUCCESSIVE CASES OF INFLUENZA IN SAME HOUSEHOLD

Duration of interval (days)	Interval measured between			
	Days of onset		"Worst" days	
	Actual	Expected	Actual	Expected
0	34	34.8	20	29.8
1	33	29.1	34	23.9
2	25	24.2	23	18.7
3	21	18.6	11	13.7
4	7	13.6	10	9.1
5	10	9.4	3	6.3
6–7	14	13.1	10	8.7
8–9	6	9.2	8	6.0
10 or more	21	19.0	15	17.9
Total	171	171.0	134	134.1

χ^2 with 8 d.f. 6.55 12.23
Chance probability 0.70 > P > 0.50 0.20 > P > 0.10

TABLE VII—COMPARISON OF ACTUAL AND EXPECTED INTERVALS BETWEEN DATES OF MAXIMAL RASH OF SUCCESSIVE CASES OF MEASLES IN SAME HOUSEHOLD

Duration of interval (days)	Number of intervals	
	Actual	Expected
0 ..	26	16.9
1 ..	22	15.9
2 ..	16	14.9
3 ..	9	13.9
4 ..	4	13.0
5 ..	4	12.1
6 ..	7	11.2
7 ..	6	10.4
8 ..	7	9.4
9 ..	10	8.3
10 ..	13	6.3
11 ..	10	5.8
12-13 ..	8	6.1
14 or more ..	9	6.7
Total ..	151	150.9

χ^2 with 13 d.f. = 36.65.

$P < 0.001$.

more cases are infected by a single earlier one, and these will tend to occur close together in time. Thus in addition to a preponderance of intervals corresponding approximately to the serial interval there would be an excess of very short intervals. Any fresh introduction of the disease into the household might blur, but should not completely obscure, these tendencies. The comparisons of the actual intervals with those expected from a random distribution of cases are given in tables VI and VII. For influenza the intervals between dates of onset show no important deviations from the random pattern. There is a preponderance of intervals of one or two days between the "worst" days of successive cases, but this cannot be regarded as being of any aetiological importance, because the deviations are within chance limits, as the χ^2 -test shows. On the other hand, the analysis for measles shows a definite serial interval.

This examination of intervals therefore gives no evidence how influenza may be transmitted within the household. If it is passing directly from person to person, there must be considerable variability in the length of the incubation period, or each person must remain infectious for a period which is comparable in length with the incubation period; or, of course, both of these factors may apply.

Evidence from Timing of Influenza Cases in Household compared with that in the Whole Epidemic

The timing of the influenza cases may be examined in another way. If there is no connection between the cases which occur in a household, their distribution in time might reflect the time scatter in the epidemic as a whole, or in this sample of it. Statistically the point can be tested quite simply by an analysis of variance, which shows beyond reasonable doubt that the cases within a household tend to occur closer together in time than would be expected from the scatter of all the cases studied. (The ratio of the variance estimate between households to that within households is 3.11, with 89 and 219 degrees of freedom, for the dates of onset, and 2.82, with 89 and 199 degrees of freedom, for the worst days of the disease. Each chance probability is less than 0.001. Some cases were omitted from the analysis because one or other of the requisite dates were unknown.)

Although this analysis demonstrates some connection between the cases of influenza which occur within a household, it gives no indication of what that connection may be. A process of infection within the household is by no means the only possibility. The finding may be alternatively expressed by saying that the members of one household tend to be afflicted at a different stage of the epidemic from members of another; a disease spread by contaminated food or drink, by an insect, or by

some other vector might well reach different households at different times and present just the same picture.

Discussion

Does the mechanism of person-to-person spread explain what is known about the epidemiology of influenza? Of the large number of facts which need explanation the most salient and difficult are probably these—that influenza may come as an epidemic or a pandemic in two successive years or even more often, or it may disappear for twenty or thirty years or more; and that when it returns, after either a short or a long interval, it attacks with a high rate irrespective of age and apparently irrespective of previous attacks.

This is indeed a puzzling picture. If we postulate a lack of immunising properties, why do epidemics disappear at all? If numerous different strains of virus are responsible which give little or no cross-immunity—i.e., if there are numerous different diseases all more or less identical clinically—why do epidemics disappear for such a long time; and, having thus been absent, why do they ever reappear? If the sudden appearance of a mutant is responsible for the great outbreaks it should very soon become apparent to the laboratories. But where in the meantime are the parent strains lurking?

In the face of so many perplexities about this important disease there is urgent need for more precise information about the extent and distribution according to age, sex, previous attacks, and geography of each outbreak. Diagnostic difficulties are formidable for the field worker, even with facilities for virus studies. It seems, nevertheless, that this is the only way in which the problems can be solved; even imperfect attempts may supply evidence and experience, pointing the way to more successful studies.

In view of the clear-cut results with some other diseases it seemed reasonable to look for evidence of direct transmission in careful family studies of influenza. In the present study there is a vivid contrast between the clarity of the answer for measles and the equivocal results for influenza; yet if influenza is spread directly from person to person it must be at least as infectious as measles. This makes the lack of clear evidence all the more remarkable. The fit of the prediction by the chain binomial with the actual experience in the larger families suggests that influenza may be spreading from person to person inside the family; but, if this is actually happening, how can we explain the lack of a secondary wave of cases, such as occurs with measles and other diseases in which direct person-to-person spread is certain? One explanation would be that a large number of the cases included were not in fact influenza. Or it may be that the incubation period in influenza varies widely, or that the period of infectivity is of similar duration to the incubation period. Such factors could easily obscure the evidence of direct spread.

Then again the evidence provided by family studies depends on the family acting as a self-contained community transmitting the disease more readily than the community as a whole, with the result that entries into the family from outside after the first case tend to be relatively rare events. Perhaps influenza is so highly infectious that the family ought not to be treated as a community separated from the general community, because entries from outside happen with such ease that cases subsequent to the first case in the family are often re-entries. This is unlikely to be the complete explanation, because many of the intervals between subsequent cases in families were long; hence the opportunity of catching a disease as infectious as influenza inside the family would have been greater than waiting for a re-entry from outside. The more infectious the disease the more likely it seems that the picture inside the family would

be of a first case among susceptibles, followed by a generation including the majority of susceptibles at risk, and that is not found in influenza. In measles, for example, more than 70% of the susceptibles at risk in the family take the disease at the first opportunity (Hope Simpson 1952).

These points being taken into consideration, there seem to be two alternative explanations :

(1) Influenza is transmitted directly from person to person, but this feature is unrecognisable in family studies as a result of factors such as a widely variable incubation period, or a period of infectivity of similar duration to the incubation period, or a combination of them.

(2) Influenza epidemics do not depend on the mechanism of direct person-to-person spread.

The problem cannot be settled with the material that we have studied here. In any future epidemic it would be profitable to collect in addition data for households selected at random and to compare them with data for households selected because they have at least 1 case of influenza.

Summary and Conclusions

In an attempt to decide whether influenza is spread directly from person to person the pattern of influenza during the 1951 epidemic was studied in 100 households which experienced at least 1 case of the disease. The households contained 385 persons.

Influenza appeared to attack males and females, old and young, indiscriminately. The attack-rate among those exposed to the first case in the household was 90% for households of 2, dropped to a minimum of 71% for households of 4, and thereafter rose with increasing size of household.

The distribution of multiple attacks in households with 4 or 5 members was more nearly in conformity with that to be expected from a direct spread of the disease from person to person than with a hypothesis which precluded this method of transmission. Suggestions are made which might explain certain anomalies in households with 2 or 3 members.

Within each household the cases of influenza tended to occur at the same stage of the epidemic. This does not necessarily mean that influenza is spread by personal contact in the household.

No evidence could be found of any serial interval between successive cases of the disease within the same household.

The experience in households with cases of measles was analysed for comparison with that in the influenza households. It shows clear evidence of direct person-to-person transmission of measles.

The data available here are tantalisingly scanty. Much could be learnt from a larger study on similar lines of influenza as well as of other diseases.

We wish to express our appreciation of the late Dr. W. T. Russell's interest in this study and his early work upon the records. Miss Janet Edmonds and Miss Joyce Dawson, of the Epidemiological Research Unit staff, put in a great deal of painstaking work to ensure that the records were as complete and accurate as possible. We should also like to thank the sick families for their patient and helpful co-operation.

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Mr. Bevan on "A Municipal Hospital Service"

The *Municipal Journal* asked Mr. Aneurin Bevan, as the Minister responsible for the creation of the National Health Service, to discuss their suggestion that hospitals should be transferred to local government.¹ In his reply Mr. Bevan² admits his regret that in framing the health service he was unable to make more use of local-government machinery. But not even the larger local authorities are big enough to carry some medical specialties; nor could facilities for treatment be allowed to vary according to local finances, and national financial responsibility conflicts with local government administrative responsibility. Though he believes that it is a defect of the N.H.S. that the administrative agents are selected by the Minister instead of being elected by the people, he recognises that it is inevitable until the present units of local government are fundamentally revised.

True local government, he holds, must be "so near to the people as to ignite and keep their interest." The present borough and district councils are too small for efficiency and the administrative counties too large for democracy to flourish. In his view the ideal set up would be some 240 authorities, most of them covering a population of about 75,000. Except in the big towns, each should include rural as well as urban areas. They should be all-purpose authorities with a diversity of important functions sufficient to attract the best kind of councillor and large enough to command efficient teams of officers.

Local authorities of this standing could, he believes, appropriately assume responsibility for the administration of the hospitals as agents of the Minister. They would make all staff appointments except specialists—who would be appointed on the recommendation of a regional advisory body. But Mr. Bevan is firm that no local finances should be levied, for this would destroy the unity of the service. He also stipulates that local authorities should make full use of voluntary workers, otherwise he foresees that power may merely be transferred from "offices in Whitehall to those in the town hall." He believes that now the fears of the doctors have been largely assuaged they would be more disposed to "set aside the traditional antagonism between the clinicians and the medical officers of health."

Report on Detergents

In May last year the Minister of Housing and Local Government appointed a committee, with Sir Harry Jephcott, M.Sc., as chairman, "to examine and report on the effects of the increasing use of synthetic detergents and to make any recommendations that seem desirable with particular reference to the functioning of the public health services." This was a heavy assignment and the committee still have much work to do, but so many people are keenly interested in the subject that an interim report³ has been published.

There are four reasons why people have been worried about detergents: they may cause dermatitis and have other dangers to health; they may cause corrosion of domestic equipment and plumbing; there have been reports of excessive foaming at a number of sewage works; and foam on the rivers into which sewage effluents are discharged has given rise to concern for the purity of the river water. On these questions, the committee have collected evidence from many sources. Both synthetic detergents and soap-powders can cause dermatitis in certain cases, but there has been no significant increase, the report says, in this complaint since synthetic detergents came into common use. The committee's advice to housewives is: choose the detergent that suits you best: do not use more than you need; and always rinse and dry the hands thoroughly afterwards. The possibility that traces of detergent may

1. See *Lancet*, March 13, 1954, p. 568.

2. *Municipal Journal*, March 12, 1954, p. 544.

3. Interim Report of the Committee on Synthetic Detergents. H.M. Stationery Office. Pp. 7. 4d.

be ingested from crockery and in other ways is being examined, but there is so far no evidence that ill effects may be caused by this means. The committee do not think that corrosion will lead to widespread difficulties, particularly if sinks are well rinsed after each washing.

The most serious problem is the effect of detergents on sewage treatment and the disposal of effluents. A number of methods for suppressing foam formation at sewage works have been tried with some success—notably in the U.S.A. But further research is necessary before any one method can be recommended for general use in this country. Meanwhile, foaming is not at present sufficiently serious to justify alarm, though it may become more troublesome with increasing use of synthetic detergents of the present types, and it certainly calls for speedy remedy. Moreover, the presence of detergents may be adding to the existing difficulties of producing an effluent up to the required standard; and, if so, the report adds, this is cause for serious concern, and special attention is being given to this question.

The committee sum up their deliberations as follows:

"Available evidence . . . does not justify any immediate alarm in users or the public health services. There is definitely nuisance at some sewage works, however, and there are other and more serious possibilities in relation to the efficiency of sewage treatment, the condition of rivers, and the purity of water-supplies. All these matters require and will receive most careful examination."

Medicine and the Law

NEGLIGENCE CLAIMS AT HOSPITAL

WHEN the negligence of a doctor leads to a successful claim for damages against a hospital authority, that authority has been enjoined by the Ministry of Health¹ to take legal action to make the doctor pay part of the damages. Where doctor and hospital authority are both accused of negligence, the authority, in exonerating itself, has sometimes thrown blame on its own staff; and this has been found to "prejudice that successful conduct of the defence which is in the interest of doctor and hospital authority alike." Accordingly the Minister, after consultation with the British Medical Association and the medical defence societies, has modified present procedure.² In future, where the doctor is a member of a defence society and that body accepts responsibility for him, any payment made to the plaintiff is to be apportioned between the doctor and the hospital authority as agreed privately between them or, in default of agreement, in equal shares.

Where both the hospital authority and one or more hospital doctors are cited as defendants, the following arrangements will apply:

(1) Any defendant may, on notifying the other(s), decide to settle the case out of court at any stage in the proceedings, but if he does so, he must accept sole liability for payment of the whole sum for which the case is settled; but each defendant shall pay his own costs.

(2) If the defendants decide to explore the possibility of settlement out of court (and a settlement is ultimately effected), the payment made to the plaintiff shall be borne between the defendants agreed to be liable in such proportion as they may agree between themselves or, in default of agreement on the proportions, in equal shares.

(3) If the defendants agree to defend the action in court the procedure should be as follows:

- (a) the defendants should try to agree before the action comes to court on the proportion in which any damages and costs which may be awarded to the plaintiff shall be borne between them;
- (b) if this proves impossible, the defendants should try to reach such agreement after the trial of the action;
- (c) failing agreement under (a) or (b) the damages and costs awarded to the plaintiff shall be borne in equal shares between such defendants as are held liable.

(4) In exceptional circumstances where some important legal or professional principle is involved, any defendant may

give notice to the other before delivery of defence by either party that paragraphs 1-3 above shall not apply; and the normal legal processes will then be open to all defendants.

Where either the hospital authority alone or a hospital doctor alone is cited as defendant in the action, the defendant will have complete discretion whether to fight the action or to attempt to settle it out of court. The hospital or the doctor solely cited shall not take legal action to obtain a contribution from the other, nor cite the other unless requested so to do, when the request shall be conceded forthwith. The defence societies recognise, however, that there will be cases where, although one of their members has not been cited, they might properly be asked to make a contribution towards any payment made by the hospital authority to the plaintiff, because the action or inaction of the practitioner in question was a material factor in the negligence complained of. Conversely, in actions in which a hospital doctor alone is cited, there may be circumstances in which the defence society asks the hospital authority to make a similar contribution. In either case the procedure should follow the principles set out in paragraphs (2) and (3) above, as if the party not cited were a defendant.

The success of the new arrangements (the Ministry says) clearly depends on mutual confidence between the defendants and a fully cooperative attitude on the part of both parties from the beginning, and hospital authorities are urged to bear this in mind. There should be full consultation at the request of either party in the formulation of the defence. In any case where there is a possibility of a contribution being requested from a hospital authority or a doctor who has not been cited, full information about the incident and the possibility of such a request should be exchanged at the earliest opportunity.

What is a Hospital?

Last December Mr. Justice Vaisey had to decide the fate of the Royal Midland Counties Home for Incurables at Leamington.¹ If it was a "hospital" within the meaning of the National Health Service Act, it would rest in the Minister; if it was not, it would preserve its independence. The object of the home, it may be remembered, was to give relief to persons of good character and of limited or reduced income, suffering from incurable or chronic diseases or incapacity due to injury or wounds. The rules refused admission to patients suffering from insanity, imbecility, epilepsy, cancer, or pulmonary tuberculosis, past or present. Following the findings of an arbitrator, the learned judge came to the conclusion that the Leamington home was not a "hospital" within the Act. On Thursday last, however, his decision was reversed by a majority in the Court of Appeal.²

What, for the purposes of the Act, is a "hospital"? Section 79 says it is "any institution for the reception and treatment of persons suffering from illness . . ." and "illness" is defined as including "any injury or disability requiring medical or dental treatment or nursing." Mr. Justice Vaisey adopted the arbitrator's finding that the only treatment at the Leamington home was palliative treatment and treatment for casual ailments; there were nurses but their nursing was not part of medical treatment.

The Master of the Rolls has now held that the arbitrator and Mr. Justice Vaisey took too narrow a view. "Treatment," he says, in relation to a "hospital" means not only medical treatment but also nursing in the sense that patients are looked after by persons professionally trained to look after the sick. Reading the definitions of "hospital" and "illness" in section 79 together, the court could bring the Leamington home

1. Circular R.H.B.(49)128.
2. Circular H.M.(54)32.

1. *Lancet*, Jan. 2, 1954, p. 54.
2. *Times*, March 26, 1954.

within the Act as an "institution for the reception and treatment of persons suffering from . . . any . . . disability requiring . . . nursing." Lord Justice Romer agreed with the Master of the Rolls. A minority judgment, however, came from Lord Justice Denning, not for the first time. He dissented on the ground that a realistic view should be taken of what went on at Leamington. Most of the patients got about in wheel-chairs or on sticks; they were folk who would be looked after in their own homes by relatives, if the relatives could manage it; they stayed on at Leamington for years, and quite half of them went away for holidays. The staff did all they could to make life bearable for these incurables; they administered sleeping-tablets or aperients when necessary, but the amount of drugs and dressings was far less than would be used in an ordinary hospital. The Act, said the Lord Justice, drew a sharp distinction between "treatment" and "care"; care was the homely art of making people comfortable; the arbitrator had found that "such treatment as was given was merely subsidiary to the real purpose of the home," and his finding ought not to be lightly disturbed. Lord Justice Denning ended by expressing the opinion that, as the case was on the borderline, the court should decide in favour of the independence of the institution. "The voluntary, charitable institutions have served the country so well

that Parliament could only have meant to take them over when the overriding public interest demanded it."

Leave to appeal has been granted. At present two judges have voted for State vesting and two for independence. The House of Lords must tell us which two are right.

The Case of the Plaster Cast

On March 20 we summarised the proceedings at Nottingham when a child of 6 was awarded £5000 damages because her leg had suffered injury while enclosed during January in a plaster cast. A correspondent who was present in court takes issue with us on our statement that "the parents were not told of the serious condition of the child until the following June." According to a newspaper report the judge remarked that "not until six months after the plaster had been taken off were the parents told fully of the child's condition"; but in using the word "fully" the judge may well have been thinking of a complete explanation of the extent of the injury and the probable outcome. Our correspondent points out that soon after the orthopaedic surgeon saw the girl on Feb. 24 she was transferred to another hospital for further treatment and the parents at this time were well aware that the condition of the leg was unsatisfactory, though the final disability could not then be forecast.

Parliament

QUESTION TIME

Regional Hospital Boards—Administration

Mr. STAN AWBERY asked the Minister of Health if he was aware that the areas covered by the regional hospital boards were unwieldy and too wide for maintaining the necessary close touch with the people and patients, and that it would be preferable to establish smaller all-purpose areas in which the local knowledge of committee members of conditions and circumstances could play a more important part; and if he would consider this problem with a view to altering the administration.—Mr. IAIN MACLEOD replied: The close contact that needs to be maintained with local opinion and with patients is provided by hospital management committees, and I am not aware that the areas of regional hospital boards are too large for the purposes they are designed to serve. But this is a matter which will no doubt be considered by the committee now sitting under Mr. Guillebaud's chairmanship.

Deaths from Coal-gas Poisoning

Relying to a question Mr. MACLEOD said that provisional figures of deaths from coal-gas poisoning registered in the 12 months ended Sept. 30, 1953, were 569 by misadventure and 2061 by suicide.

Sale of Worthless Products

Mr. W. D. CHAPMAN asked the President of the Board of Trade whether he was aware that worthless products claimed, respectively, to be a cosmetic lotion, a slimming aid, an eyelash grower, and a bust-improver, had been exposed for sale in Birmingham shops, and that their true contents had been described in a report of the Birmingham city analyst; and whether he would institute proceedings against the manufacturers under the Merchandise Marks Act of 1953.—Mr. PETER THORNEYCROFT replied: If I can obtain satisfactory evidence of the offer of these goods for sale, I shall certainly consider instituting proceedings.

Dental Service in Scotland

Mr. GEORGE THOMSON asked the Secretary of State for Scotland what steps he was taking to arrest the decline in the number of dental students entering Scottish dental schools.—Commander T. G. D. GALBRAITH replied: I am afraid that the position cannot be influenced directly by any action open to the Government. The Dentists Bill, which will be reintroduced as soon as Parliamentary time permits, embodies a plan for expanding dental services for the priority classes. By giving the dental profession full self-government and thus raising its status, I hope the Bill will also stimulate recruitment to the profession. Mr. THOMSON:

Is the Minister aware that entries to the Scottish dental schools have dropped from 155 in 1946 to an estimated figure of 70 last year?

Relying to further questions, Commander GALBRAITH said that in December, 1953, there were 161 dental officers in the school dental service, the highest number ever reached. In October, 1951, the number was 100, and in June, 1948, it was 131.

The number of dental courses given under the National Health Service in Scotland to expectant and nursing mothers and those under 21 years of age since the charge for dental treatment, from which these priority classes were exempt, was introduced in June, 1952, to January, 1954, was 855,300. The number of courses for the period June, 1950, to January, 1952, was estimated at 340,000.

Medical School Scholarships

Relying to Mr. SOMERVILLE HASTINGS, Miss FLORENCE HORSBRUGH, Minister of Education, said that 380 State scholarships were taken up in 1952-53 for courses leading to a medical degree at universities in England and Wales.

Family Allowances

Relying to a question Mr. OSBERT PEAKE said that, taking as children those within the age-limits laid down by the Family Allowances Act, it was estimated that the number of married couples with only one child was about 3 million, the number with more than one child who received no family allowance for the eldest child was 3,200,000, and the total number of children including those who received family allowance was 11 million.

Mr. JOHN MCKAY: Is the Minister aware that the 3 million who have only one child are half the married couples in the country who have children; that within the first and second categories in the range of income there are 1 $\frac{1}{4}$ million families with one child who are below the income-tax level and therefore in a bad economic position? Is he further aware that there are 1 $\frac{1}{4}$ million families getting 8s., 16s., and 24s. per week who are far beyond the income-tax level? Can nothing be done to achieve a fairer share of family allowances?

Mr. PEAKE: All that seems well worthy of study and consideration.

Milk and Glandular Infection

Mr. D. T. LLEWELLYN asked the Minister of Health how many cases in Glamorgan had been drawn to his department's attention of children contracting tuberculous infection of the glands after drinking T.T. milk.—Mr. MACLEOD replied: Six children who had consumed milk from a tuberculin-tested herd came under the notice of the local health authority towards the end of last year. The one cow in the herd found to be infected was slaughtered.

In England Now

A Running Commentary by Peripatetic Correspondents

My favourite film critic, Miss Lejeune, has been hinting for a long time that British studios can, when they really set their cameras to it, turn out comedies that make Groucho Marx wipe off his moustache and take to peddling peanuts (if he doesn't happen to be occupied that way already). Indeed, it is said that Mr. Marx once raised an eyebrow during a performance by Alastair Sim, though the significance of the gesture is in doubt, for his friends whose sanity remains are confident that he was trying to attract the attention of a young lady selling 'Coca-Cola.' For my part, I have missed many of the films on which Miss Lejeune bases her opinion, so, in the absence of a less equivocal sign from Mr. Marx, I was glad to accept an invitation to find out how things really stood by seeing last week's première of *Doctor in the House*. And they stand pretty well.

Dr. Richard Gordon's novel of student life at St. Swithin's Hospital quickly established itself as one of the best jokes of the day; and it has been translated so nimbly to the screen that for once Technicolor is as glorious as print. Some of the fun at the expense of doctors and students was no doubt judged too vivid for cinemagoers who are sometimes hospitalgoers as well. So, for one thing, Sir Lancelot Spratt, surgeon to St. Swithin's, is a more genial character on the screen than in the book; and though we may readily understand why he is described in after-dinner speeches as "a surgeon of the grand old school," there is only a hint of "the less charming but equivalent epithet" which his colleagues use in private. I waited in vain for one or two memorable episodes: the Christmas dance in the Nurses' Home, for example; and there was no sight of the depressing examination candidates who "write steadily and sternly, as though they were preparing leaders for next week's *Lancet*."

But the film embellishes some of the book's other events, adds new ones of its own (a devastating interpretation of bleeding-time, for example), and urges the whole business forward at the cracking pace vital to success in this sort of enterprise. Mr. Kenneth More, as the perennial Grimsdyke, is the best of a likely bunch of students, and he is, I should judge, one of the actors on whom Miss Lejeune pins her best hopes. But they all did splendidly; and I must say there was a peanut vendor with a gangling gait in Leicester Square as I went home.

* * *

A chap came into outpatients the other day who had recently survived an operation at my hands. There are two hospitals in this group, and it happened that, when he came in, he had the choice of either. Quite by chance I asked him why he had chosen St. Crispin's for his operation. "Because in St. Swithin's the mortuary is rather damp" was his reply. And he spoke with first-hand knowledge. He is the local undertaker.

* * *

He had been sent for child guidance. He did not know who his parents had been. His daddy, he said, had been a man. He had lived in Singapore all his life, they had servants, there was a baby. Now he was tall for his age, dressed in a full cowboy outfit, with loud check trousers, American-style shirt, and a ten-gallon hat. He spoke in a grown-up manner, rather slowly and with the singsong of the Babu. He was disobedient, cheeky, and continually ran away into the streets, where he wandered aimlessly. He had not settled well at school. Now he stood in the tiny consulting-room, and answered questions while his adoptive father saw the Chief.

"The Japanese came, there were bombs, our servants ran away, and we ran too; we ran to the fields, hiding in the ditches, and then we got to the jungle. My daddy was killed first though, and my mummy, too, got a splinter. Soon she died, and then I cared for the baby, but it died, and I was alone, hiding in the jungle. My friends told me where to hide."

"How did you eat, you and your baby?"

"My friends fed me and gave me food for my baby."

"Who were your friends?"

"Children like me from the village; they were kind, they knew where to hide from the Japanese, they didn't have much to eat."

"Where did they get the food to feed you?"

"They asked their parents, and each family in turn gave me something to eat, and each family in turn gave me a place to sleep when it was needed."

"How have you come to England?"

"Uncle Jim was an English soldier. When he came to my village at the end of the war, he said to me, 'Will you come and be my boy now?' and I said 'Yes.' So we went to his camp, and they all gave me sweets and cigarettes, but now I cannot smoke, or use the words they taught me. We came here on a big ship, but I was homesick for the jungle, and here I have no friends."

The wisdom accumulated against the D.P.M. failed the four registrars. No textbook catered for this sort of difficulty. None of us had an answer ready for this child who, when he returned to his own race, found that there were no friends among them like those who had kept him alive in the jungle.

* * *

Like many other connoisseurs of Edinburgh sermons, I have been dipping into the third volume of Norman Maclean's autobiography.¹ These essays strung on the thread of the life of a minister of the Church of Scotland show the skill of a *Scotsman* leader-writer, the eloquence of a great preacher, the wit and poetry of a Gael, and the "Scottish genius for suddenly making you want to burst into tears." The matter is as varied as the manner. As an exponent of social medicine I was relieved to find that the manse at Colinton—Maclean's first charge—though placed unsalubriously in a hollow beside the Water of Leith and under the retaining wall of a crowded graveyard, was sheltered from the east wind and so provided a health-giving retreat for the young Robert Louis Stevenson and other members of the Balfour family. Indeed the Colinton doctor of those days used to send ailing children to Mrs. Balfour at the Manse saying "She kens mair aboot weans than I dae"—he was a bachelor and she the mother of thirteen children. As a doctor I was encouraged by the story of the long negotiations which led to the union of the Church of Scotland with the United Free Church to hope that the medical profession will likewise, with wise statesmanship (and under pressure of public opinion and economics), emerge from its departmental rivalries and statutory divisions to a new unity.

* * *

"Oh, to be in England now that April's there!" is a heart cry of sinister import nowadays for the exiled followers of St. Michael and St. George. The cold wars of crypto-enemies, the hot wars of the lawless, and the sell-outs to our allies have made the outposts of empire less congenial, but the home-made scientific genius of the mother country is even more disturbing to her errant lotus-eaters. It is so frightfully tiresome to have to carry a geiger-counter to the fishmonger's every week, and so awfully dreary to beachcomb in the shadow of mushroom clouds, as yet another atoll is removed around Bikini or Montebello. The Pacific now belies its name even more than when stout Cortez and all his men justifiably looked at each other in wild surmise.

And if the Pacific is a mocking name, is consolation to be found in the still-vexed Bermoothes? The Spanish Main may slumber in the noonday heat, dreaming of tourist dollars, hurricanes, and government grants-in-aid. But the shadow of Voodoo is falling again on the Antilles. Caliban rubs his hands in the undergrowth. The ghost of Blind Pew cackles hoarsely at the sight of The Black Spot. On the horizon a fore-top heralds the arrival of H.M.S. *Ben Lomond*. No export whisky for the emigrant Scot is stowed in her hold; just petri dishes, test-tubes, and guineapigs—the paraphernalia of experimental bacterial warfare.

* * *

Patient, male, weight 16 $\frac{1}{2}$ st.: "Doctor, I've got butterflies in my stomach!"
What Hieronymus Bosch!

1. The Years of Fulfilment. NORMAN MACLEAN, D.D. London: Hodder & Stoughton. 1953. Pp. 316. 20s.

Letters to the Editor

MEDICAL WITNESSES

SIR.—In view of the modern tendency towards litigation in relation to medical practice, it may perhaps not be out of place to remind medical witnesses that the principles of medical ethics are not in abeyance in Courts of Law.

Lawyers are apt to tell medical witnesses that it is improper, if not illegal, for them to discuss cases with witnesses called for the other side. Medical ethics demand, however, that any doctor asked to consider a matter which to his knowledge has been the subject of a report by a colleague should notify him of this fact and should also tell him what his personal view is. Neglect to follow this course may often mislead a judge and jury, since two expert witnesses may in all sincerity differ fundamentally merely because they are, in fact, talking about two separate matters. Two pathologists, for example, may examine a section from the same patient, but from a different part of him. Two sections from the same piece of tissue may show entirely different pictures.

It is important to recognise that medical and legal practices are at variance on this important point.

Westminster School of Medicine,
London, S.W.1. R. J. V. PULVERTAFT.

TUBERCULOSIS YARDSTICKS

SIR.—The mortality-rate has long been accepted as the most reliable measure of tuberculosis in a community, and in civilised countries it undoubtedly provides relatively accurate and comparable data. The notification-rate of new cases has also provided useful information about the incidence of new cases in this country. However, while the tuberculosis-mortality rate in England and Wales has halved during the past five years, the notification-rate of new cases has remained almost unchanged. During that time the number of cases of tuberculosis on chest-clinic registers has increased by 20%, and today more hospital beds are occupied by tuberculosis cases than for many years. It may be that just as many cases of tuberculosis are being diagnosed nowadays as 20 years ago—though, of course, earlier diagnoses are being made, and many more cases of less hazardous disease are being discovered; and patients are living longer.

It seems that the time-honoured yardsticks of mortality and notification are becoming less indicative of the amount of tuberculosis in this country. What available data, if any, would be useful in estimating more accurately the significance of the "tuberculosis problem," if, as one hopes, the mortality-rate continues to fall?

In the current issue of the *N.A.P.T. Bulletin*, Pickwick points out that it is the active cases on clinic registers which really matter. These sputum-positive cases make up the "known infector pool" of infectious persons, which, together with unknown infectious cases, constitutes virtually the whole source of fresh infection in most urban areas now that milk-borne tuberculosis is being extensively eliminated. Tuberculosis will only be controlled by persistent effort, both therapeutic and preventive, to reduce the size of this "known infector pool." It is where these pools are largest and deepest that the greatest national effort toward eradication should be directed. It would be useful if health authorities could publish the number of known active cases in their area alongside their mortality and notification rates.

The offices of the Ministry of National Insurance receive initial and final certificates for every insured person who receives sickness benefit because of tuberculosis. In the local offices of that Ministry there may be valuable data that would help chest physicians in their case-finding quest. The relapse of a case believed to be

inactive could become known to the Ministry of National Insurance although the medical officer of health and the chest physician might remain unaware of the event. According to Pickwick, approximately 20% of the total tuberculosis deaths are not statutorily notified to the medical officer of health during the patient's lifetime, and one wonders whether the Ministry of National Insurance might not be able to help us to close this gap. If medical officers of health could be advised of all newly certified cases of tuberculosis, and all final certificates received, it would enable a day-to-day sickness-rate for insured persons to be kept by each local-health authority. Now that tuberculosis control is entering a new phase, it would seem that these are the sort of yardsticks that would really indicate the significance of the disease in the community.

Bournemouth Chest Clinic.

W. H. TATTERSALL.

FEWER FARMS AND MORE BEDS

SIR.—One additional 60-bedded convalescent annexe to each mental hospital would wipe out psychiatric waiting-lists. This annexe need not be staffed at all—though, of course, it would be better if it were.

In the average mental hospital each month there are 50–80 convalescent patients awaiting discharge. Most of these could look after themselves at a pinch so far as bedding, feeding, and the like are concerned. Each of the 60 convalescent beds could be turned over 5–12 times a year.

The cost? Simple. Sell the farms attached to mental hospitals—perhaps to the Ministry of Agriculture. Millions of pounds of capital are tied up—and about a million lost in the running every year.

The money, staff, and committee work spent on the farm are miserably rewarded. Very rarely is any patient discharged from the farm working-party. No Tolstoian wisdom of the soil emerges. No skill is imparted to the patients. And nothing is a more degrading spectacle than a barrow party in single-file procession, like a chain gang.

The money put into the farm, if spent on the 20 occupational therapists, educational officers, and physical-culture instructors who could be provided instead in each mental hospital, would be reflected in even better discharge-rates and in a more effective battle against institutional intellectual deterioration.

Let the end of farm psychiatry mean more staff and more accommodation.

I. FROST.

INFESTATION WITH TRICHOCEPHALUS DISPAR

SIR.—I was much interested in Dr. MacCarthy's article (Feb. 27) on whipworm infestation in children, and especially in the possibility of using the proteolytic action of papain in treating intestinal helminths. I cannot, however, agree that her description of the clinical picture of trichuriasis is either accurate or complete.

In many tropical countries, whipworm ova are commonly found in the stools: in Southern Nigeria they were present in from 15 to 25% of specimens. The clinical picture appears to be related to the worm load, as was shown by the investigations of Jung and Beaver.¹ In brief, there may be three grades of infection: *light*, usually with no symptoms; *mild*, sometimes with allergic manifestations (urticaria) and vague abdominal pain, often in the right lower quadrant; *severe*, with prolonged diarrhoea and blood-streaked stools, abdominal pain, tenesmus (i.e., a chronic dysentery), and sometimes rectal prolapse, with whipworms easily visible to the naked eye on the mucosa of the prolapsed bowel.

As has been noted recently, however, "many authors have listed symptoms ascribed to trichuriasis, but these accounts have with few exceptions been ambiguous, inconsistent, and quite frequently far-fetched. Text-book

¹ 1. Jung, R. C., Beaver, P. C. *Pediatrics*, 1951, 8, 548.

repetitions of these lists have been vague and uncritical. . . Chronic constipation, eructation, nervous symptoms, vertigo, etc., have been reported, but the occurrence of these with trichuriasis may well be coincidental.^{1,2}

The diagnosis of trichuriasis, while usually based on stool examinations for ova, may be confirmed in some cases by sigmoidoscopy, when the helminths may be seen attached to the mucosa of the colon or rectum. The most effective treatment appears to be retention enemata of 0.2% hexylresorcinol, in water or glycerin solution, the technique of which is described elsewhere.¹

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D. B. JELLIFFE.

WATER INTOXICATION

SIR.—I should like to congratulate Dr. Wynn and Professor Rob on their very valuable paper (March 20), which should be a great help to those concerned with postoperative care and the management of fluid balance. It is clear that water intoxication must now rank with potassium loss as a new hazard to be watched for by house-surgeons and registrars, and dealt with appropriately and expeditiously.

There is one minor criticism. I have, for the good of my surgical soul and to familiarise myself with the process, developed the habit of turning mg. per 100 ml. into m.eq. per litre and back again whenever I meet them. Whereas the other m.eq. quoted in the article are correct to the nearest 10, 450 ml. of 6% NaCl are twice given, in table II and case-record 1, as containing 480 m.eq. Surely this should be 460 (actually 461) ?

Although of no great importance, this small aberration makes things even more difficult for us biochemical neophytes.

Beaconsfield.

MICHAEL REILLY.

HOSPITAL, DOCTOR, AND PATIENT

SIR.—May I, as a layman, venture to comment on the recent legal actions between hospital boards and patients ?

The National Health Service is young, and most people realise that growing pains are inevitable ; but until the relations between specialists on the one hand and general practitioners, patients, and patients' relatives on the other have regained some of the mutual trust which existed in my childhood, these actions will continue.

Thirty years ago, my brother, then a child of six, nearly died through an error of diagnosis. Our family doctor freely admitted that a mistake had been made, and did everything in his power to put the damage right. After many months the child recovered. Although this story was freely discussed by the neighbours, I doubt if a single patient left the doctor because of it. Everybody was impressed by his honesty, his devotion to duty, his genuine understanding of the family's anxiety, and by his many simple kindnesses. It would never have occurred to my family to sue this doctor. "To err is human." Had not he saved my mother's life on several occasions, brought me through a bad attack of appendicitis, and cared for the whole family during these crises ?

Recently my young son had to go into hospital for observation. It was a good hospital with modern ideas on visiting so we saw him every evening. During the twelve weeks he was in hospital, my husband and I saw the specialist twice and the house-physician once. Our anxiety was very great, and on one occasion, when we could stand the silence of the hospital no longer, my husband spoke to the ward-sister. Her reply was terse : "Oh, you intellectual parents are the worst people we have to deal with." She did not seem to realise our concern for our most cherished possession. After my son was discharged from hospital it took our doctor a fortnight and many telephone calls before he could get even a short report from the hospital on the child's condition. Four months later the clinic that we were told to attend was still waiting for a hospital report. Still, we were lucky.

2. Jung, R. C., Jelliffe, D. B. *West Afr. med. J.* 1952, 1, 11.

Tommy in the next bed had been in hospital eight months and his parents had seen the specialist once—on the night he was admitted as an emergency.

In these days when medical knowledge is put out for public consumption by radio, television, and the newspapers, as well as by the British Medical Association through *Family Doctor*, is it too much to ask that parents and relatives be given an opportunity of discussing with the doctors the patient's condition, and be given a simple explanation of what is being done for him ? Certainly, I met very few parents who would not have preferred to know—even the worst—rather than face the many weeks of anxiety and uncertainty that they were forced to go through.

Would it not be possible to build up relations between hospitals, doctors, patients, and relatives into those which exist in the best parent-teacher associations of some schools, and with the same amount of good will on both sides ? I cannot believe the doctors would lose anything of their status by this, and certainly some of the young housemen might benefit by supplementing their academic knowledge of disease by an understanding of the environment of their patients.

PARENT.

A COOLING UNIT IN CLOSED-CIRCUIT ANÆSTHESIA

SIR.—I have successfully used a closed respiratory circuit cooled down to 16°F to maintain heat-balance in therapeutic sweating, and I believe that a similar system in a closed-circuit unit for anaesthesia could lower body-temperature and metabolism during operations. The fall in circulation-rate with "artificial hibernation" decreases bleeding in the operation area and reduces the danger of surgical shock ; but anaesthetic techniques that lower the body-temperature by drugs and/or physical cooling introduce other drug hazards difficult to control.

Before the induction of anaesthesia there is usually constriction of the skin vessels, which is often followed by a cold sweat due to mental stimuli or shock. During normal anaesthesia with a closed-circuit unit with an average volume of about 2½ litres, including corrugated tubes and mask, there is a steady rise in blood-temperature because of the continuous inhalation of warm gas of high relative and absolute humidity. The temperature of the inspired gas at the face-mask averages 102°–105°F for a Waters's absorber, and 89°–91°F for a circle unit.

These temperatures relate to a breathing rate of 18 per min., a tidal volume of 500 c.c.m., and a canister of soda lime 8 cm. by 13 cm.¹ The temperature of the inspired gases in a Waters's absorber are higher than the blood-temperature, while in the closed-circuit unit they are only 8·4–7·4°F lower than blood-temperature ; but both their absolute and relative humidities are high. Thus the gases in the Waters's absorber, instead of cooling the lung vascular bed, warm it. In the circle unit there is a slight tendency to cool the blood, but the cooling effect on the lung bed cannot compare with that produced by the inhalation of gas at normal atmospheric temperatures and low absolute and relative humidities.

The steady rise in temperature turns the cold sweat into a hot sweat and the skin vessels are dilated. The soda-lime container also adds its quota of heat and water to the inspired gases, for each gramme-molecule of CO₂ produces 310 calories and water. Under normal conditions only a small proportion of the heat produced is used in warming the inspired air.

These considerations suggest that we might regulate the temperature of the inspired gases by means of a cooling system before attempting to lower the body-temperature by drugs and physical cooling. A cooling system in the return circuit to the face-mask could bring down the temperature of the inspired gases to 32°F.

1. Adrian, J. *Chemistry of Anesthesia*. Springfield, 1946.

which would make induction of anaesthesia more pleasant; and it would stop hot sweating, reduce the pulse-rate, and lessen bleeding.

Tunbridge Wells.

E. F. ST. JOHN LYBURN.

ANTIBIOTIC ENTEROCOLITIS

SIR.—Your excellent editorial of Dec. 12 encourages me to add some observations about the side-effects of broad-spectrum antibiotics.

Using aureomycin and oxytetracycline (terramycin) for different diseases, and especially for urogenital tract infections and amoebiasis, I was surprised to find that patients of Greek or Balkan origin did not suffer side-effects; they were much less liable to the gastro-intestinal symptoms—nausea, diarrhoea, burning in the anorectal region, &c.—to which Anglo-Saxon patients were prone. I found that the main cause of this was the difference in their eating habits, and especially the use of yogurt, which most of the Balkan patients eat daily, especially when they are on a diet. I then started prescribing the antibiotics with yogurt, and the results were excellent.

Yogurt is a true culture of *Lactobacillus bulgaricus* plus the lactic acid produced by the fermentation of lactose. By adding 3 or 4 cups daily to the diet, it may be possible to avoid the multiplication of other resistant organisms. Whatever the explanation, I recommend yogurt as a means of preventing these side-effects. The same results can be achieved for patients who dislike yogurt by the use of preparations of lactic acid bacilli.

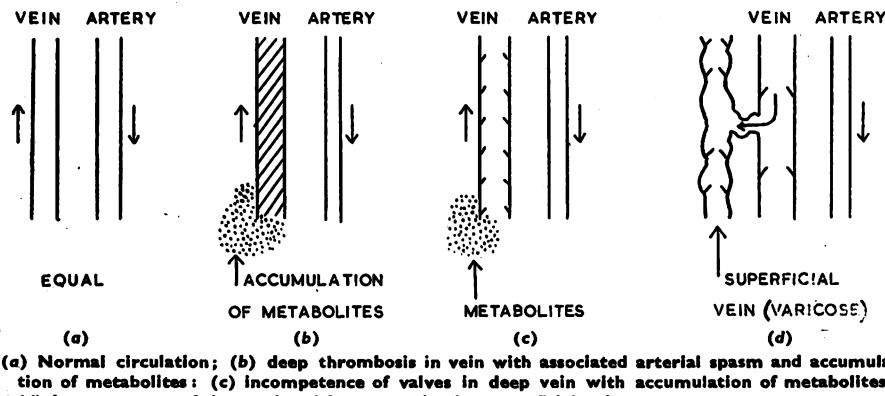
Toronto, Ontario.

LEONIDAS G. POLYMERAKOS.

TREATMENT OF VARICOSE ULCERS

SIR.—A multitude of treatments have been advised for varicose ulcers, and a maze of medicaments and bandages have been applied. Firm support by bandaging remains the basis of all treatments¹; but not all ulcers will heal by this means alone, and something more must be done to break down the vicious circle in the lower limb.^{2,3}

In most cases varicose veins cannot by themselves account for ulceration. Varicosities generally occur in the superficial veins, and the ulcers associated with them are often small and usually heal promptly after



(a) Normal circulation; (b) deep thrombosis in vein with associated arterial spasm and accumulation of metabolites; (c) incompetence of valves in deep vein with accumulation of metabolites; (d) incompetence of deep vein with communicating superficial vein.

the veins have been treated by injection or ligation. More often, ulcerated legs are the aftermath of a deep thrombosis. Instead of calling them varicose, or gravitational, it would be better to call them post-thrombotic ulcers.

The accompanying figures illustrate the changes that lead to ulceration.

Fig. a represents the normal state of the circulation in the lower limb: the arterial inflow equals the venous outflow and the circulation is in a state of equilibrium.

In fig. b a deep venous thrombosis has upset the equilibrium between inflow and outflow, which is further affected by the arterial spasm that always accompanies a deep thrombosis. Because of the deep thrombosis, metabolites accumulate, causing poor nutrition of the tissues and eventually ulceration. A slight injury may start the ulceration, or eczema may be the beginning of the trouble.

The same situation develops when the deep veins are incompetent, as in fig. c. Here the incompetence has followed a deep thrombosis, but although the thrombosed vein has been recanalised the valves remain incompetent. Hence the venous return is hampered, waste products accumulate, and ulceration follows, as in deep thrombosis.

Sometimes the deep incompetence shows itself as distension and incompetence of the superficial veins, by means of communicating venous channels, as in fig. d. It is then very easy to assume that the ulceration is due to incompetence of the superficial veins. If these veins are then injected or ligated the deep venous incompetence is not affected at all and the underlying condition is unchanged. Even the ligation of this communicating vein (in the "ankle blow-out syndrome"⁴) does not have any effect on the ulceration.

A condition indicating deep venous trouble is induration of the lower half of the leg, with the firm skin tethered down to the underlying structures. This type of leg, which I have described as the "inverted Guinness-bottle leg," is pathognomonic of deep thrombophlebitis or incompetence of the deep veins. It results from the slow inflammatory reaction set up in the tissues by the accumulation of metabolites, and it impedes the return flow still further.

The basis of all forms of treatment is compression by bandages, whether 'Elastoplast,' 'Diachylon,' 'Ceraban,' or any other of the many now on the market. The type of bandage which will prove most satisfactory depends on the tolerance of the patient's skin; for bandages can, by themselves, set up a trail of symptoms which further tries the patient and the doctor. The aim of repeated firm compression is to get rid of the accumulated exudates and so permit healing. But not all metabolites can be dispersed in this way: it depends on how much they are fixed locally. Occasionally, the only way to promote healing is to put the patient to bed and so counteract the effects of gravity.

My purpose in this letter is to describe two other forms of treatment which I believe will also promote healing.

First, the arterial blood-supply of the leg can be increased by means of vasodilators such as tolazoline ('Priscol') or papaverine, injected into the femoral artery in the groin. Tolazoline (50 mg.) may be given once a week through a fine needle. The injection is carried out as an outpatient operation, and there is no need for the patient to rest in bed. The limb immediately becomes flushed from above downwards and its temperature rises a few degrees.

I have always thought that, in the treatment of varicose ulcers, it was wrong to ignore the arterial side of the circulation,⁵ and this method attacks the condition from the arterial side. A lumbar sympathectomy will do the same as the intra-arterial injections of tolazoline, and it will be more permanent in its effect. But patients are seldom keen on this operation, for it means a long time in bed, and they regard it as too drastic. Moreover, in these patients, who are often fat and flabby, sympathectomy is not without its risks.

Secondly, the venous return can be encouraged by using hyaluronidase ionisation to disperse the accumula-

1. Dickson Wright, A. *Brit. med. J.* 1940, i, 699.
2. Lee, M. *Brit. J. Derm.* 1953, 65, 131.
3. Lee, M. *Practitioner*, 1953, 170, 288.

4. Cookett, F. B., Elgan Jones, D. E. *Lancet*, 1953, i, 17.
5. Anning, S. T. *Brit. med. J.* 1949, ii, 458.

tion of metabolites. For this treatment, the patient must attend a physiotherapy department regularly. There is no doubt that it has an effect: in very many cases the tissues become softer, and in some the pain is relieved. This form of treatment is most useful in the post-thrombotic leg before ulceration takes place—a condition in which pain is often intense when the patient is up and about. I have noticed that the pain becomes less as soon as ulceration occurs, probably because there is then an outlet for the accumulated metabolites.

Thus, by a combination of compression bandages, tolazoline injections for the arterial side, and hyaluronidase ionisation for the venous side, one hopes to interrupt the vicious circle and restore the circulation to normal, or as near normal as possible. Probably the Bisgaard treatment, for which such success is claimed, has the same effect as hyaluronidase treatment in dispersing the metabolites.

The various operations described for excision of the ulcer and for skin-grafting seem to me to be based on false premises, and the successes attained with them are perhaps due to the patient having to remain in bed. Again, a skin-graft applied to such an unhealthy site as an ulcerated leg is likely to break down when the patient gets about again, and this in fact happens time after time. Such operations as ligation of the communicating veins do not attack the underlying condition.

Princo of Wales's Hospital,
London, N.15.

MAURICE LEE.

CONTROL OF CANCER MORTALITY

SIR.—With reference to Professor Smithers's letter of Feb. 13, it seems necessary to point out again that the appraisal (through vital statistics) of the value of treatment, early or otherwise, in preventing death from breast cancer was based on those rates which showed good evidence of reliability. Firstly, there was the consistent maintenance of level trends in the recorded age-specific breast-cancer mortality (except that in old age), in spite of vastly different circumstances from which the rates were derived—differences in time, in place, in provision and availability of diagnostic and treatment services, in utilisation of specialist services and hospital accommodation, in acceptance of extensive investigation and treatment, in economic situation, in "cancer education" of the public and of the profession, in the speeding-up of treatment, in publicity and propaganda, and with the book-keeping done under the same and under different auspices. The only reasonable explanation of that stability and uniformity in the trends is that the recorded rates are highly indicative of reality and practically insusceptible to the influence of artificial factors.

Further, any contention that the rates deriving from such different and changing conditions were maintained at their respective levels by similar changes in diagnosis (*at death*) or in certification asks too much of credulity. Secondly, if any material proportion—say, even 10%—of the mortality charged to breast cancer were actually due to other causes, the declines in mortality from causes other than cancer in women under 60 years of age in the past 25 or 30 years should have yielded an appreciable concomitant decline in the recorded breast-cancer mortality of those age-groups. The lack of decline is substantial evidence that the mortality charged to breast cancer in those age-groups did not contain any appreciable proportion that was not caused by breast cancer. Thirdly, when the selection of cause of death was made the responsibility of the physician—in 1939 in England, in 1949 in the U.S.A., and in 1950 in Canada—changes in the rates resulting from that change in selection were almost entirely confined to the rates in the older age-groups. The paucity of the change, if any, in the rates in other age-groups—on which the comparisons were based—is further consistent evidence of the reasonable reliability of those rates. Thus, the trends do not show

any of the characteristics that they should show if Professor Smithers's contention that the mortality charged to breast cancer included any material proportion not caused by breast cancer were valid. On the other hand, they show very substantial internal evidence of their reliability.

Professor Smithers contends that the very early spread as shown by the various analyses provides a sound reason for still earlier treatment. This contention would be timely if there were some means of detecting breast cancer before the appearance of a tumour or discharge or any other sign or symptom. The attack on the very early and on so-called "precancerous" conditions, as in Saskatchewan, Ontario, and Massachusetts, has failed to effect any assured reduction in mortality. Thus, without means of earlier detection of cancer the contention is hardly pertinent.

I am sorry that my writings have given Professor Smithers "an uncomfortable feeling" that I will misconstrue or otherwise evade any evidence of progress that may come in the future. I do not know the basis for his "horrible imaginings," but let me assure him that I will neither misconstrue nor evade any sound evidence. As he well knows, however, neither feelings nor opinions nor impressions nor beliefs nor even the most favourable interpretations of ambiguous data constitute sound evidence.

I have never inferred, much less implied, that all the efforts towards earlier diagnosis and better treatment have been "entirely a waste of time." One has only to recall John Brown's *Rab and His Friends* to be acutely conscious of the progress that has been made in the past century. And the fact that breast-cancer mortality showed no change coincident with the introduction and use of effectual chemotherapy for infection indicates clearly that the earlier risks of infection in treatment had been well met by the surgeons before the advent of the sulphonamides and antibiotics. Although I am concerned only with evidence and not with what anyone, myself included, says or opines, perhaps it is fair to say that I have stated repeatedly and I fully concur that treatment of all cancer and all pathological conditions is fully justified, even when it gives only mental or physical relief as in the case of cancers that kill by remote metastases (e.g., most breast cancers), or definitely postpones death as in the case of cancers that kill by local extension before metastases cause trouble (e.g., many bowel and pelvic cancers), or gives complete cure as in the case of non-metastasising cancers (e.g., the vast majority of skin cancers or what are called skin cancers). One would surely be queer who did not admit and admire the improvements in and the results of treatment of laryngeal cancers as well as others, including breast cancer, but, gratifying as they are, they should not lead us to claims beyond our capacity or blind us to our present limitations. Even in lethal breast cancer there may be, as Sir James Paget pointed out a century ago,¹ an occasional case in which "by happy chance" the lesion can be removed before remote spread occurs. But the number of such cases, if any, must be too small in relation to the whole of breast cancer to make any decisive impression on the mortality-rates; no more precise measurement of that number is available today. And no-one, surely, doubts that a healed lesion is infinitely preferable to an ulcerated, infected, sloughing mass. I hope this clears up any misconceptions which either Professor Smithers's or my words may have left.

Reference can now be made to the further consistent evidence of the early remote lethal spread from the primary cancer, provided by Williams, Murley, and Curwen.² Different methods of treatment—radical

1. Quoted by Lane-Claypon, J. *Rep. Minist. Hlh, Lond.* 1934, no. 28, p. 8.

2. Williams, I. G., Murley, R. S., Curwen, M. P. *Brit. med. J.* 1953, ii, 787.

mastectomy, simple mastectomy, irradiation, &c.—were equally effective, as measured by survival-rates, in spite of the fact that regional recurrences were less frequent in cases treated by radical mastectomy. The authors point out "that all methods of treatment may have been equally ineffective in prolonging life."

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N. E. MCKINNON.

SENSITIVITY TO ISOPRENALEINE

SIR,—I think it is worth while placing on record the case of a man of 54, with chronic asthma, who has become sensitive to isoprenaline. I started him on isoprenaline for his asthma in September, 1953, which gave him considerable relief. On Nov. 18, however, he sought advice because of a persistent sore mouth with redness and vesiculation, particularly in the soft palate but involving also the whole buccal mucosa. It was established by repeated trial that this was undoubtedly due to tablets of isoprenaline sulphate, and he has been free from this trouble since stopping the tablets.

Workington.

R. N. R. GRANT.

TRAINING OF NURSES

SIR,—I agree with Dr. Findlay (Feb. 6) that there is need for radical changes in the nursing syllabus if we are to maintain an efficient and effective service in the future.

Three main types of nursing staff are needed :

(a) Highly intelligent, academic, and technically minded girls who will form the teams for specialist units—e.g., thoracic, neurological, and general operating in all types of hospitals.

(b) Equally gifted but more socially minded women for ward sisters, suited to become the educators of families and patients, and able to coöperate with lay social workers. These nurses should become the key workers in every hospital and public-health department.

(c) Semi-skilled attendants forming perhaps 60% of the service. It used to be the practice—a wholly sound and sensible one, I think—to give these people only the simplest theoretical training. Many of them are still giving devoted service, but they are a dwindling band ; the truth is we are not replacing them, and, with an ageing population and the introduction of shorter duty hours, recruits are urgently needed.

Can it be expected that any one syllabus would do for these three groups, any more than one would expect an industrial concern to train scientists, engineers, and factory hands as one group ?

At present there are two main curricula : the basic general training with S.R.N. qualification ; and the assistant nurse course with S.E.A.N. status. The final result is that the academically minded girls who stay the course get into the specialist teams, but far too many of them are lost, because valuable specialised training is being given to too many people, most of whom are frankly bored with it, while the keen ones get side-tracked into taking more certificates, just to keep their wits sharpened. The second group are being offered many new incentives as industrial nurses and social workers, but most of them remain to form the solid core of the nursing service. The third group should, I think, have the opportunity to go straight on to the wards for the first six months of their training and then receive very simple instruction with a strictly practical bias, lectures and written work being reduced to a minimum.

When I advertise for staff I always get replies from *trainee* assistant nurses ; and I always make a point of seeing them to find out why they will risk leaving the security of a hospital. Invariably, they say they are tired of the theoretical side of the work ; and many are the wrong type, but have been taken on because they have a pair of hands. In one hospital near my home, the assistant nurse trainees draw just a little over £7 monthly after all deductions ; this hospital has a costly training scheme, a permanent advertisement in the nursing press,

and a chronic shortage of staff. Maybe this is an exception, but I doubt it.

This whole question of nursing recruitment, selection, and training, is urgent. It would be a help if some simple psychological test could be applied to weed out the immature and the frankly hysterical, who because of their lack of staying power are costly, and who, if they do stay the course, do so at tremendous cost to themselves and their patients. As for an overhaul of the whole syllabus, it would be interesting to know if Dr. Findlay has any definite scheme in mind. Would he have a basic training for all nurses, or two schemes with many modifications, as at present ?

Lancashire.

MATRON.

POLIOMYELITIS IN CHILDREN'S WARDS

SIR,—Dr. Ferguson (March 27) draws timely attention to the "increasing awareness of the connection between paralytic poliomyelitis and injections of all kinds." The interest and concern occasioned by evidence of association between immunising injections and paralytic poliomyelitis have perhaps lessened the attention which would otherwise have been paid to paralysis occurring in conjunction with other kinds of injection.

Dr. Stanley Banks (Feb. 27) inculpates parenteral penicillin, and there is reason to believe that other injections may be fraught with comparable hazard. In 1952, an adult woman had facial palsy due to poliomyelitis ; a very short time before she became ill, she had had dental treatment involving injections on the same side. In 1953 Dr. J. K. Grant, medical officer of health for Great Yarmouth, informed me of a resident from this area, in whom poliomyelitis presented with a unilateral palatal palsy, shortly after dental treatment involving a maxillary injection on the same side.

One is compelled to the conclusion that when poliomyelitis is prevalent in an area, it may be wise, particularly in dealing with children, to reserve injections for those conditions which are urgent, if there is no acceptable alternative to the intramuscular route for administering the therapeutic agent of choice.

J. STEVENSON LOGAN
Medical Officer of Health.

Southend-on-Sea.

PATHOLOGISTS AND PNEUMOCONIOSIS

SIR,—My letter of March 20 was not meant as a personal attack on Dr. Triger, but as a protest against all those who, without proof, assume greater accuracy and validity for one method of diagnosis than for another. Dr. Triger last week accuses me of the very assumption against which I was protesting. I did not claim that "clinical and radiological diagnosis of industrial dust disease is more reliable than post-mortem diagnosis," but only that the errors and validity of the former have been studied and that until pathologists have done the same they cannot play the rôle of assessors.

It is interesting that while Professor Browne and Dr. Triger agree that the radiograph is a mere "shadow," they disagree as to the "substance" of the problem. The one (a clinician) holds to disability, the other (a pathologist-clinician) to the post-mortem diagnosis. I certainly consider the function of the lungs in life more important than their appearance after death. We need to know much more about the effects of dust inhalation upon pulmonary function before we can really assess the incidence of "pulmonary dust disease"—a term that may have much wider implications than the present legal definition of pneumoconiosis. Meanwhile, we know that, in many cases, the "shadow" in the radiograph today may portend the "substance" of disability tomorrow, so it should not be ignored.

Among many sources of sampling error in post-mortem statistics, the most important is the very one that Dr. Triger mentions in seeking to deny them ! Post-mortem

examinations are, as he says, selectively carried out on cases where pneumoconiosis is suspected as a cause of death. Those in which the suspicion does not arise tend to be excluded whether they have pneumoconiosis or not.

Richmond Green,
Surrey.

C. M. FLETCHER.

ORDINARY YOUTHS

SIR.—To my religious bias revealed by Dr. Malleson (Feb. 27) and now my emotional bias discovered by Dr. Logan and Miss Goldberg, let me add a third, an intellectual bias; for clarity as against obscurity. It has been sorely tried by the letter from the last-named correspondents in your issue of March 27. Parts of it are as incomprehensible to me as were parts of the original article.¹

But Dr. Logan and Miss Goldberg made it quite clear that they accused me of irresponsibility in attributing 'implications and interpretations to their writing which were not true. This is a serious allegation, and one, if proved, deserving of the strongest possible censure.

But what are the facts? On Feb. 13 I commented astringently on your leader of Jan. 23, based on the article by Dr. Logan and Miss Goldberg. In my letter I gave a long quotation from their article: there was not the slightest wish or attempt to distort the meaning of the extract; enough only was given (as I thought) to exclude any suggestion that I was taking it from its context. (What more could the authors want? They already had had 1½ pages in your leader.)

In the quotation, all 74 youths under survey had indicated their approval of premarital sexual intercourse with a "steady" girl friend. At the end of my letter, I wondered what precisely were the implications of the last sentence in the quotation: that "there does seem to be evidence, however, that these young people were reaching towards a freer and less guilt-ridden expression of heterosexual relationship, and that this may become an important factor in mental health."

Since there then followed complete silence on the authors' part, I indicated in my reply to Dr. Malleson on March 6 what this sentence meant to me: "that there was evidence that uninhibited premarital sexual intercourse would be beneficial to the mental health of young people."

Meantime, however, I had done some literary research; small, but significant.

I submitted the quotation given in my letter to 12 senior members of the staff of this University, including 7 professors; a mixed bag from the faculties of art, medicine, science, and divinity (1 only, for religious bias!). Such men are more than usually alive to the dangers of quotation out of context, and more than usually precise in the use and understanding of words. With one exception (and he did not allege the quotation was unfair to the context), they all agreed with the implication I put on the sentence. In the face of such evidence, it is difficult to accept the authors' excuse for not replying to my first letter—that they believed my wrong emphasis would be obvious to everyone.

Before leaving your readers to judge where the "irresponsibility" in the use of words properly rests, I should like to advert to the corollary from this literary investigation.

We have it on the authority of Dr. Morris (Feb. 27), of the Medical Research Council, that the research on these 74 youths was no hurried collection of facts and opinions for some ad-hoc purpose; the report on it was 4½ years in gestation. If the authors, after such a period for reflection and choice of words, on a matter of such vital importance to everyone interested in the health and education of young people, could be so obscure and ambiguous that a group of highly intelligent men understood them to mean what they, the authors, now so violently repudiate as their intention, what con-

ceivably was the state of confusion in the minds of the 74 rising eighteen-year-olds, confronted with questions from the same authors, ranging from the virginity of their sisters to that of their wives-to-be; and what kind of answers and stories could be expected of them? Hans Andersen?

Most people will learn with relief that Dr. Logan and Miss Goldberg repudiate the advocacy of that sexual behaviour for the young, which so many of us believed, however mistakenly, their article to imply. But the fault lay in their obscurity, not in our understanding.

A. STEWART HENDERSON
Medical Officer to Student Health Service,
University of Glasgow.

Obituary

ERNEST HENRY MARCUS MILLIGAN M.D. Belf., D.P.H.

Dr. E. H. M. Milligan, for many years medical officer of health for Glossop, died on March 22 at the age of 75.

He was born in Belfast, the son of Seaton Forest Milligan, M.R.I.A., and he was educated at the Methodist College and at Queen's College, Belfast. After studying law he turned to medicine and graduated as M.B. in the old Royal University in 1906. After holding a resident appointment at Purdysburn Fever Hospital in Belfast he proceeded to his M.D. degree in 1910. The following year he took the D.P.H. and became M.O.H. for Long Eaton in Derbyshire. In 1917 he was appointed school medical officer for Bath, but in 1920 he returned to Derbyshire as M.O.H. for Glossop, a post he held with distinction for twenty-five years. His chief interest was nutrition, and with officers of the Ministry of Health and of the Medical Research Council he shared in dietary, dental, and clinical surveys, in trials of the nutritive values of dried yeast, and in emergency feeding preparations. But he also found time for work of his own, including therapeutic trials with vitamin preparations. In 1946 he retired but he soon joined the staff of the Ministry of Health to conduct nutrition inquiries. For the next four years he was happy in this work, and he did not spare himself, but was always ready with fresh schemes for inquiry and research. Most of his clinical work for the Ministry was published in progress reports in the *Monthly Bulletin*; during the last year or so he made extensive surveys of haemoglobin levels in women during and after pregnancy.

H. E. M. writes: "I first met Milligan in 1934 when he wrote to the Board of Education for advice about the nutrition of the children in his borough.

"In those days Glossop was a distressful place; some 60% of its working population were idle with no prospect of employment. In such conditions, complacency or discouragement might have been excused, but escapism of this sort was foreign to his nature. To him the situation was a challenge, and he faced it with an enthusiasm which carried him beyond his immediate goal into the field of research.

"Probably the official interest in his problems encouraged him to launch the nutritional activities which were to remain his absorbing interest. The first practical outcome was the 'health sandwich' in 1934, based on the same principles as the Oslo breakfast, which it anticipated by some two years. The presumption was that the home diets of the children were deficient in constructive and protective nutrients; dietary surveys later made this abundantly clear. It was, therefore, common sense that the school supplement should make good these defects. Later, when school meals were introduced Milligan's logical mind was uneasy because the composition of the proposed meals did not conform as closely to these principles as his own carefully designed sandwich. His protests were not in vain, and the constitution of the meals was in due course modified.

"The classification of children into the four nutritional categories recommended by the Board of Education—excellent, normal, slightly subnormal, and bad—was not good enough for Milligan; it savoured too much of the art and too little of the science of medicine; there must be some objective measurements of physiological efficiency to support such assessments, for the nutritional state is a physiological

1. *Brit. J. Sociol.* Dec. 31, 1953, p. 323.

concept. He seized eagerly on the dynamometer as a means of providing such data, and later developed his test of endurance. But his irrepressible enthusiasm would not let it rest there. He had to see how these measurements were related to a wide variety of anthropometric data, sitting height, chest expansion, and so on, and later to the haemoglobin and phosphatase of the blood. The masses of data which he collected provided him with a new field of endeavour in mathematics and statistics; how many of his working hours were spent in exploring the many hypotheses conceived by his fertile brain, only his family can tell.

"Despite eccentricities he drew people towards him and suspicion eventually gave way to affection. His fund of ideas and schemes of research—all of a practical bent—seemed inexhaustible. His reading of medical and scientific literature was wide and profitable; the extent of his knowledge of physiology as well as of public health and clinical medicine was remarkable. Though frail in physique he was tough. He had a perfectly clear vision of his purpose which, I am convinced, was to do his utmost for the good of his fellow men, particularly those placed in his charge. He was not deterred by obstacles and pursued his purpose unselfishly to the end of his life. Only a few months before his death he wrote several articles to the Manchester papers explaining the nutritional significance of the reintroduction of white flour.

"He had many literary affiliations; his sister, Alice Milligan, who died last year, was the well-known Irish poetess. He was an active member of the Irish Literary Society and he had written short plays for the radio and some poetry. He also had a good knowledge of Gaelic literature. Had he been able to discipline his bright intelligence he would doubtless have risen high in science or medicine, perhaps even in literature—but he would have been very different. As it is, many friends in England and Ireland will mourn a courageous and determined seeker after truth who was tolerant of most things except injustice or hypocrisy."

Dr. Milligan was extremely happy in his family life, and two years ago he returned from the Midlands to Glossop to be near his grandchildren. He leaves a widow and three daughters, one of whom is a doctor.

FRANCIS BRETT YOUNG

M.B., D.Litt. Birm.

In some of his best novels Francis Brett Young acted as an informed and sympathetic interpreter of his own profession. And whatever he wrote about he wrote as a doctor. "There is nothing in the world," he once said, "which so fits a man of letters to wrestle with the mind of man as an intimate acquaintance with his body. Literally and figuratively the doctor sees thousands of men and women naked: he sees the spring of curious motives, he shares strange secrets. A man or woman will tell lies or feign emotion to the pastor or lawyer. With the physician they know that only the truth will help them." Brett Young's training as a doctor served well his talent as a writer, and much of the strength of his work lay in his capacity for impartial, shrewd, yet sympathetic observation.

The son and grandson of a doctor, he was born in 1884 at Halesowen in Worcestershire. From Epsom College he went to the University of Birmingham, where he graduated as M.B. in 1906. Even before he qualified he had decided that he would rather be a writer than a doctor, and after a voyage to Japan as ship's surgeon he settled in a country practice in Devon which left him leisure to write lyric poetry and settings for the poems of A. E. Housman and Robert Bridges. Before this way of life was interrupted by war in 1914, he had already written three novels.

With a commission in the R.A.M.C. he served during the war as R.M.O. in the Rhodesian Regiment under Field-Marshal Smuts, and he has described these years in *Marching on Tanganyika*. Invalided home with malaria, he lived for the next four years at Anacapri, writing steadily. *The Young Physician*, a partly autobiographical novel, centred on the Birmingham Medical School, was published in 1918. In 1927 the *Portrait of Clare* brought him the James Tait Black prize and established his reputation. Though it is not a description of medical life, in the octogenarian Dr. Weir it contains a memorable portrait of a country doctor. *My Brother Jonathan*, perhaps the most famous of the medical novels, which appeared in

1928, was the story of the daily round of a slum practice, lacking in glamour but full of humanity.

For many years, besides his house at Anacapri, Mr. Young also had a fruit farm in Pershore, and he continued to cherish his associations with country life and with the Midlands. But after the late war he settled in South Africa, and he died in Cape Town on March 28.

HAROLD GEORGE WILLIAMS

M.R.C.S., D.P.H., D.P.M.

Dr. Harold Williams, a psychiatrist to the London County Council, died at his home in Hampstead on March 21 at the age of 51.

He studied as an engineer before qualifying in medicine from St. Thomas's Hospital in 1931, and he always took great pleasure in the skill of his hands, which he showed particularly in his drawing and painting. After a period of ill health he decided to leave general practice, and, during the war, he took the diplomas of public health and psychological medicine. He worked for a time as medical director of the child-guidance clinic in Canterbury before he joined the central staff of the L.C.C. in 1949 as a whole-time (what he called "odd job") psychiatrist.

D. P. writes: "During these last five years Dr. Williams held an unusual position, and he has been an important influence in the development of the work of his colleagues both medical and lay, and in the changes that have taken place in the care of children not only in the L.C.C. public-health department but also in the education and children's departments. He was closely concerned with the education of maladjusted children, the child-guidance service, and the beginnings of preventive mental health work, as well as with the care of his child patients. It may have taken some time for those who worked with him to appreciate the Freudian philosophy that underlay his recommendations, but all soon learned to rely on his integrity, which he maintained in what were sometimes difficult conditions."

Dr. Williams leaves a widow, Dr. Miriam Williams, and a young son.

Appointments

LITTLE, B. R., M.R.C.S., F.F.A. R.C.S., D.A.: consultant anaesthetist, Bristol clinical area (Weston-super-Mare).

MCCARTHY, DENIS, M.D., N.U.I., M.R.C.P.I.: resident medical superintendent, St. Kevin's Institution, Dublin.

MOLONY, CONOR, L.R.C.S.I.: resident medical superintendent, City Home and Hospital, Limerick.

ROWLANDS, IRENE P., F.R.F.P.S., M.R.C.P.: geriatrician (S.H.M.O.), North Gloucestershire clinical area.

STANTON, J. B., M.B. Camb., M.R.C.P., D.P.M.: asst. neurologist, Northern General Hospital, Edinburgh.

VAUTIER, C. K. J., M.B. N.Z., M.R.C.P., D.M.R.D., D.C.H.: consultant radiologist, Merthyr and Aberdare H.M.C.

WALTON, H. C. M., M.B. Camb.: consultant pathologist, Swansea.

East Anglian Regional Hospital Board:

LOPERT, HEATHER J., M.B.: anaesthetic registrar, Peterborough Memorial Hospital.

SALMON, J. M., M.B. N.U.I.: asst. chest physician, Great Yarmouth and Lowestoft chest clinic area.

WELSH, R. I. H., M.B. Witwatersrand, F.R.C.S.: surgical registrar, Peterborough Memorial Hospital.

South Eastern Regional Hospital Board, Scotland:

MACGREGOR, T. N., M.D. Edin., F.R.C.S.E., F.R.C.O.G.: consultant obstetrician and gynaecologist, Western General Hospital, Edinburgh.

MCLEOD, H. M., M.B. Edin., M.R.C.P.E.: asst. tuberculosis physician (S.H.M.O.), East Fortune Hospital, North Berwick.

TURNBULL, F. W. A., M.B. Edin., M.R.C.P.E.: tuberculosis physician (S.H.M.O.), Royal Victoria group of hospitals, Edinburgh.

South Western Regional Hospital Board:

BURROWS, W. L., M.D. Belf., M.R.C.P.L.: clinical asst. in general medicine, Royal United Hospital, Bath.

COLLINS, J. R., M.B.: general-practitioner anaesthetist, Newquay and District Hospital.

DORAN, H. J., M.B. Belf., D.L.O.: clinical asst. E.N.T. surgery, Exeter clinical area.

REES, D. I., B.M. Oxf., D.L.O.: general-practitioner anaesthetist, Stroud General Hospital, Glos.

The Hospital for Sick Children, Great Ormond Street, London:

KIRKMAN, DAPHNE M., M.B. Lond.: house-physician.

MONTGOMERY, J. N., M.D. Belf., M.R.C.P., D.C.H.: resident asst. physician.

PARKINSON, T. J., M.B. St. And., B.Sc., M.R.C.P., D.C.H.: house-physician.

PENRY, B. J., M.R.C.S.: house-surgeon.

SILBERSTEIN, E. P., M.B., B.Sc.: house-physician to the neurological and neurosurgical department.

THOMSON, MARY F., M.R. Glasg.: resident M.O., Tadworth Court.

Notes and News

EHRLICH CENTENARY EXHIBITION

To mark the centenary of the birth of Paul Ehrlich, "father of chemotherapy," the Wellcome Historical Medical Museum has prepared an exhibition at the Wellcome Foundation, Euston Road, London, N.W.1. It was opened on March 25 by Sir Henry Dale, O.M., F.R.S., chairman of the Wellcome Trustees. Among those at the ceremony were Miss Martha Marquardt, Ehrlich's secretary from 1902 to 1915, and Dr. E. Ashworth Underwood, director of the Wellcome Historical Medical Museum. Mr. M. W. Perrin, chairman of the Wellcome Foundation, presided.

Sir Henry announced that the Wellcome Trustees had agreed to publish a collected edition of Ehrlich's works; and it is hoped that this will appear later in the year. It will contain all his published and a large number of his unpublished papers, each being reproduced in the original language (thus, Ehrlich's Haber lectures will be in English). They have been collected by Sir Henry, Miss Marquardt, and Dr. Himmelweit. Sir Henry told how some of the exhibits had been rescued from Ehrlich's ruined institute at Frankfurt after the war, and how others were in a chest of documents which his widow had taken with her when she was driven out of Germany. Now, with the help of his grandsons, these papers had been made available to the Wellcome Museum on indefinite loan. Sir Henry suggested that the future would come to regard Ehrlich's contributions in medical treatment as ranking with those of Lister in surgery, though Ehrlich was at heart an inorganic chemist and a biochemist.

Sir Howard Florey, F.R.S., contrasted the orderly methods of Ehrlich with what he described as the hit-or-miss-waiting-for-something-to-turn-up approach which was prevalent in the search for new remedies in chemotherapy today.

The exhibition includes photographs of Ehrlich at work in his study: "in spite of the apparent chaos Ehrlich could find any paper that was required," the caption says. Beside two yellow cards or "blocks" containing instructions by Ehrlich, the comment is: "The writing and brief note form frequently gave the assistants some difficulty in interpreting the instructions." Examples of the work of those associated with him include a paper in THE LANCET in 1907 by Prof. Carl Browning, F.R.S., entitled Experimental Chemotherapy on Trypanosomes Infections: it was Ehrlich who coined the term "chemotherapy." Around the diploma of the Nobel prize awarded to Ehrlich in 1908 for his work on immunology are grouped some of the other honours that he won. Admission to the exhibition is free.

ALMONERS AT DINNER

By the end of last year the Institute of Almoners had a subscribing membership of 1579, including 1174 in active work; and the annual meeting held in London last Saturday was again impressive. Prof. A. L. Banks, F.R.C.P., of Cambridge, gave the principal address, entitled Clients and Patients.

At the annual dinner Miss Enid Warren presided and the toast of The Institute was proposed by Sir Arthur Howard, chairman of the board of governors of St. Thomas's Hospital. In these days, he said, when so many fine titles, such as *sedile*, *manciple*, and *seneschal*, have disappeared, it was encouraging that that of almoner persists. A working definition of it would be "one who with sympathy and skill does good by stealth"; and Sir Arthur emphasised the necessity for both sympathy and (with strong support from Florence Nightingale) skill. The power of doctors and nurses to help their patients had been immensely increased by the work of almoners in relieving those patients' anxieties both before they came into hospital and after they left it. At St. Thomas's, where "almoners" had been appointed in 1557 to look after the day-to-day affairs of the hospital, the proposal some fifty years ago to have a lady almoner caused no small perturbation, and the post was projected as that of "lady inquiry officer." Nevertheless Miss Annie Cummins was appointed lady almoner in 1905: and, though she always wore a hat (to show that she did not regard her status as permanent), she started a great tradition, directly inherited and enhanced by Miss Morris. Responding, Miss E. C. Morris looked back over forty years but found the present more exciting. The main problem was numbers, for "matrimony winnows our ranks"; but the profession was now recruiting men. (Not that this was new: she recalled, in the

old days, a little bearded gentleman—an assiduous attender of committees—who was always known as "the lady almoner of the Metropolitan.") Miss Morris rejoiced in the two-way traffic between the United States and the United Kingdom, and in the splendid profession that has grown up in Australia. As for the effects of praise on herself and her colleagues, she recalled the remark of Mr. Adlai Stevenson when a friend said: "Will all these things go to your head? Will you be a less good person?" "No, it's quite all right," said Mr. Stevenson, "provided one doesn't inhale."

After Miss M. J. Roxburgh had dealt with The Guests informatively but gaily, Dr. Albertine Winner described almoners as professional colleagues in the highest sense of the word: "It is," she said, "your professionalism that endears you to all of us." If she were to choose one epithet for the profession it would be a *grown-up*—and she could think of no higher compliment. Moreover she was proud that the calling of almoner was almost entirely the creation of women, and she hoped that when men enter it (bringing their own intellectual contribution) they will not destroy the feminine touch—the feeling of understanding and tolerance of what is essentially a maternal profession.

SEX AND SOCIETY

THE April issue of the *Practitioner*¹ contains a symposium on Sex and its Problems. The first article, by the Bishop of Rochester, gives a clear summary of the attitude of the church to sexual life, marriage, promiscuity, divorce, contraception, artificial insemination, and homosexuality. Four articles are devoted to homosexuality. The first, by Dr. C. G. Learoyd, sorely lacks objectivity; the medical aspect is well dealt with by Dr. W. Lindesay Neustatter, endocrinology by Dr. G. I. M. Swyer, and the criminal law by Mr. John Maude, q.c. Dr. Joan Malleson describes the sexual problems of the woman in early marriage who suffers coital discomfort, and gives advice on simple treatment. Dr. David Stafford-Clark discusses the aetiology and treatment of impotence in a paper which should enable the practitioners to help many of these patients. Other articles are devoted to prostitution, the celibate male, premarital chastity, and sex problems at adolescence, in the unmarried women, at the climacteric, and in old age. The article on sex problems in the Services is rather sketchy; the question of the immaturity of the National Serviceman is hardly touched on, though surely this is the point about which the doctor is likely to be approached by anxious parents. The concluding article, on criminal aspects of sexual abnormalities, written by the Chief Constable of Nottingham, offers little but punishment.

A PHYSIOLOGIST HONOURED

Prof. Alexander Lipschutz is known for his early discoveries in the field of endocrinology. Outstanding among these were the conditions for successful gonadal grafting; the reactions of an ovarian fragment after removal of the rest of the ovarian tissue from the body, which led him to formulate the "law of follicular constancy"; the disturbance of quantitative relations between pituitary and ovary when a fragment of the ovary remained, resulting in failure of the fragment to check hypophyseal function; and much fruitful work with his associates on the tumorigenic and opposing actions of certain steroid hormones.² Associates and friends from all over the world have contributed to honour the occasion of Professor Lipschutz's 70th birthday in *Acta Physiologica Latino-Americana*.³

In his introduction to the dedicatory issue of this journal, Prof. B. A. Houssay, for. mem. r.s., refers briefly to the life and work of Professor Lipschutz in Europe and America. Of the thirty-one papers in three languages several confirm and extend Professor Lipschutz's own observations. Prof. S. Zuckerman, F.R.S., reports experiments which conform with a main presupposition of the law of follicular constancy, in so far as they indicate that oogenesis ceases before puberty in the rat, rabbit, and monkey. He reminds us, too, that as long ago as 1929 and 1930 Professor Lipschutz found that desiccated ovarian tissue that had lost 50% of its original weight would still "take" when grafted. No "takes" were obtained from this tissue when kept at 0°C. A. S.

1. Published at 5, Bentinck Street, London W.1. 7s. 6d.

2. Lipschutz, A. Steroid Hormones and Tumours. Baltimore, 1950.

3. *Acta physiol. Latino-Amer.* 1953, 3, 49.

Parkes, F.R.S., summarises some of his own and his colleagues' experiments on the conservation of gonadal tissue for transplantation, thus drawing attention to the remarkable property of glycerol in protecting living cells against the effect of low temperature. Nakahara⁴ may have been the first to make use of this preservative property of glycerol for dried and frozen mammalian cells.

Among many other unrelated but no less interesting subjects, there is a delightful historical research by G. W. Corner into the discovery of smooth muscle, and an elegant demonstration by W. Buño of the direct action of cortisone in degranulating mast-cells.

University of London

The title of professor of cytogenetics has been conferred on Mr. P. C. Koller, D.Sc., in respect of the post held by him at the Institute of Cancer Research, Royal Cancer Hospital.

University of Manchester

At recent examinations the following were successful :
D.P.M. (part II).—D. L. Fox, Kenneth Rawnsley.

University of Sheffield

The bequests, of about £50,000, made to the university by Sir George Franklin, pro-chancellor from 1905 to 1916, and by Miss Daisy Franklin are to be used to endow a full-time chair of medicine to be known as the Sir George Franklin chair.

Royal College of Obstetricians and Gynaecologists

At a meeting of the council held on March 27, with Mr. A. A. Gemmell, the president, in the chair, Edward Solomons was admitted to the fellowship.

Association of Surgeons of Great Britain and Ireland

This association is holding its annual meeting in Leeds from May 13 to 15. Prof. Alfred Blalock (Johns Hopkins Hospital, Baltimore) will deliver the Moynihan lecture on the Expanding Scope of Cardiovascular Surgery. The programme also includes discussions on Hiatus Hernia; Ulcerative Colitis; Exophthalmos; and Duodenal Diverticula.

Nutrition Society

On Saturday, May 8, at 11 A.M., in the department of biochemistry of the University of Glasgow, the Scottish group of this society is to hold a symposium on Nutrition and the Liver. Prof. J. N. Davidson will be in the chair, and the speakers will include Dr. H. N. Munro, Dr. J. M. Naftalin, Dr. E. Kodicek, Dr. J. Waterlow, and Dr. A. L. Latner. Further particulars may be had from the secretary of the group, Rowett Research Institute, Bucksburn, Aberdeenshire.

Study Leave

Regional hospital boards and boards of governors have hitherto been allocated each year fixed sums to provide study leave for their staffs. The Minister of Health has reconsidered this arrangement and has decided that in future no annual maxima are to be laid down (HM[54]28). He proposes to review the arrangement after two years, and asks that meanwhile boards record the sums authorised.

Southend-on-Sea Hospital

Sir Francis Walshe, F.R.S., will deliver the first Sydney Body lecture on Wednesday, April 14, at the General Hospital, Rochford, at 8 P.M. He will speak on the Changing and the Unchanging Face of Medicine. After the lecture the first Sydney Body gold medal will be presented to Dr. William Evans for his work in cardiology.

British Council for Rehabilitation

The council is holding a residential course from April 12 to 14, in Liverpool, with the help of the extramural department of the University of Liverpool, on the Disabled—their Capacity for Work. The programme will include discussions on the Gastric Problem (speakers, Prof. C. F. W. Illingworth and Dr. J. N. Macdonald); Rehabilitation of Chest Conditions (Dr. A. Thelwall Jones and Dr. Peter Edwards); and the Cutaneously and Orthopaedically Disabled Worker (Dr. F. Glyn-Hughes and Mr. H. G. Almond). Further particulars may be had from the secretary of the council, Tavistock House (South), Tavistock Square, London, W.C.1.

Institution of Sanitary Engineers

On Tuesday, April 6, at 6 P.M., at Caxton Hall, Westminster, Dr. R. F. Guymer will address this institution on the Roles of the Doctor and the Engineer in Public Health.

Design of Animal Houses

The Laboratory Animals Bureau will hold a symposium on this subject at 1, Wimpole Street, London, W.1, at 10.45 A.M., on Thursday, May 6, under the chairmanship of Dr. H. J. Parish.

National Society of Children's Nurseries

This society is holding a conference on May 8 at County Hall, Westminster, London, S.E.1, on the Needs of the Family in a Changing Society. Further particulars may be had from the secretary of the society, 45, Russell Square, W.C.1.

Hospital Laundries

Mr. S. J. Whitaker has been appointed as a laundry engineer to the staff of the Ministry of Health, to advise on the efficiency, economical operation, and design of laundries and laundry plant in hospitals. He will also advise hospital authorities which may be considering reorganisation of their laundry services.

Dr. Ludwig Guttmann has left London for Pakistan, where he is to advise the government on a rehabilitation programme for disabled ex-Servicemen.

Diary of the Week

APRIL 4 TO 10

Monday, 5th

INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1

5 P.M. Dr. Bronson Crothers (U.S.A.): Extrapyramidal Disorders Due to Erythroblastosis.

Tuesday, 6th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1

5 P.M. Prof. D. M. Dunlop: Complications of Diabetes. (First of two Lumleian lectures.)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1

8 P.M. Section of Pathology. Dr. P. A. Gorler, Mr. R. E. Billingham, D.P.Hil., Mr. W. J. Dempster, Prof. P. B. Medawar, F.R.S.: Immunological Problems of Tissue Grafting.

Wednesday, 7th

ROYAL SOCIETY OF MEDICINE

5.15 P.M. Section of History of Medicine. Dr. M. H. Draper: Sir Michael Foster. Sir Arthur MacNalty: Sir John Burdon Sanderson.

8 P.M. Section of Surgery. Prof. Ian Aird, Dr. T. Counihan, Prof. W. J. Hamilton, Mr. Norman Veall: Surgery of Conjoined Twins.

MANCHESTER MEDICAL SOCIETY

4.30 P.M. (Medical School, University of Manchester.) Section of Medicine. Dr. W. Brockbank: Treatment of Asthma with Cortisone.

YORKSHIRE SOCIETY OF ANAESTHETISTS

8 P.M. (General Infirmary, Leeds.) Prof. R. R. Macintosh: Experiences Abroad.

Thursday, 8th

ROYAL COLLEGE OF PHYSICIANS

5 P.M. Professor Dunlop: Complications of Diabetes. (Second of two Lumleian lectures.)

ALFRED ADLER MEDICAL SOCIETY

8 P.M. (11, Chandos Street, W.1.) Prof. W. C. W. Nixon, Mr. Norman Morris: Psychosomatic Reactions in Obstetrics and Gynaecology.

MEDICAL SOCIETY FOR THE CARE OF THE ELDERLY

10 A.M. (Queen's Hospital, Croydon, Surrey.) Dr. A. D. Thomson. Dr. Francis Bach: Rheumatic Disease.

2 P.M. Dr. Trevor Howell: Problems of a Geriatric Unit.

SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION

7.30 P.M. (Long Grove Hospital, Epsom, Surrey.) Dr. D. J. Adderley: Cardiazol Treatment. Dr. A. B. Monro: Assessment of Psychiatric Cases.

ASSOCIATION OF CLINICAL PATHOLOGISTS

3 P.M. (Old Swan Hotel, Harrogate.) Opening of three-day meeting.

Friday, 9th

ROYAL SOCIETY OF MEDICINE

8.30 P.M. Dr. M. G. Candau: Role of W.H.O. in International Health Work.

BIOCHEMICAL SOCIETY

11 A.M. (Department of Biochemistry, University New Buildings, Edinburgh.) Scientific papers.

Saturday, 10th

SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY

10.30 A.M. (County Hall, Maidstone, Kent.) Dr. E. R. Jones, Dr. Lynne Reid: In Circulation and Out.

4. Nakahara, W. *Gann*, 1926, 20, 13.

THE SECRETIONS OF THE BRAIN*
**RELATION OF HYPOTHALAMUS TO PITUITARY
 GLAND**

S. ZUCKERMAN

C.B., M.A. Oxf., M.D. Birm., D.Sc. Lond., F.R.S.
 PROFESSOR OF ANATOMY, UNIVERSITY OF BIRMINGHAM

The name of Thomas Addison, whom we commemorate in this lecture, separates the history of endocrinology into a past which his achievement left in deep shadow—so deep, indeed, that he is sometimes regarded as a symbol marking the beginning of the subject—and a present that goes on radiating the promise which the most significant of his studies revealed. His genius, which lay in an acute, accurate, and persistent power of observation, reached its fulfilment in the realisation that the symptoms and signs of the illness which bears his name are associated with disease of the adrenal glands. Most big discoveries in biological and medical science begin at the descriptive level, at the level of accurate observation, of discerning classification, and of useful correlation. It was in itself an achievement to generalise as a single syndrome the various signs and symptoms manifested by eleven different individuals. It required even more insight to suggest that the disease could be causally related to destruction of the suprarenal glands. From the point of view of modern science, however, the essential act of genius lay in the realisation that if this were so, something of the kind we now designate as a hormonal mechanism was at play. For there must have been some such idea in Addison's mind, even if his brief writings on the subject are anything but explicit on this point.

Emergence of the Concept of Hormonal Action

We need to remind ourselves that in 1849, when Addison first reported his observations, and in 1855 when he published his now classical monograph, there was no clearly stated concept of hormonal action. That emerged slowly during the latter half of the 19th century, as a result of the experimental studies of men such as Claude Bernard, E. Brown-Séquard, George Oliver, and Edward Schafer (later Sharpey-Schafer), and of the clinical observations of such physicians as Hilton Fagge, William Gull, and Addison himself. And it did not take the specific shape which it has today until 1904, when Bayliss and Starling elaborated the idea that the different tissues and functions of the body are coördinated by chemical messengers "speeding from cell to cell along the blood stream." "These chemical messengers or 'hormones,'" as Starling (1905) called them, "have to be carried from the organ where they are produced to the organ which they affect by means of the blood stream and the continually recurring physiological needs of the organism must determine their repeated production and circulation through the body."

Yet though this conception did not crystallise until the turn of the century, the epoch in which Addison was pondering the significance of his observations was far from devoid of ideas of some such mechanism. It may well be that he was unfamiliar with any of the 17th and 18th century writings which seemed to suggest—however vaguely—that there were such things as hormones. It may also be—in fact, it is almost certain—that he was unaware that in the very year in which he first reported his observations and his suspicion that the adrenal glands "may be either directly or indirectly concerned in sanguification" and with "the proper elaboration of the body generally, or of the red particles more especially," a young experimentalist of Göttingen, A. A.

Berthold (1849) had published a short paper in which he had not only reported that the transplantation of the testes of the cock to another part of the body prevented the normal changes of castration, but also correctly concluded that male secondary sexual characters and behaviour depend on some substance secreted by the testes into the blood. But even if he knew none of this, Addison must have known that his colleague T. Wilkinson King (1836) believed that the thyroid gland stored some material which, passing into the general circulation, exercised "important subsequent functions in the course of the circulation."¹ He also must have known about the experimental thyroidectomies and studies of the chemical nature of thyroid fluid made by his other colleague, Astley Cooper (1836). He could hardly have been surprised, therefore, that a year after the appearance of his own monograph, Brown-Séquard (1856a and b) showed that pigs, dogs, cats, rabbits, and mice died very rapidly when their adrenal glands were removed, and from this drew the conclusion that the adrenals elaborated some principle which was essential for life. He could not have been surprised, for the simple reason that although his discoveries were made before the dawn of the hormonal theory, as we know it today, they belonged to a period which had certainly not freed itself from the influences of an older theory of internal secretions. Wilkinson King thought in terms of such an hypothesis, as Brown-Séquard was still doing when, at the turn of the century, he sought to generalise his views on hormonal action, and in doing so merely restated the hypothesis which de Bordeu had put forward in 1775 (Brown-Séquard and D'Arsonval 1891; see also Rolleston 1936). Another whose mind flowed in similar channels was Jonathan Hutchinson (1856), surgeon of the London Hospital, who was among the few who set out to confirm and corroborate Addison's clinical analysis of adrenal insufficiency. In his little book on constitutional medicine Hutchinson (1884) clearly reveals that many of the conventional physiological conceptions of the 19th century took their origin from the old theory of the humours. Clearly these were still in the air when Addison pondered over the strange symptoms and signs of the patients whose adrenal glands had been destroyed by disease.

To say this in no way disparages Addison's share in the development of modern endocrinological concepts. Nor does it mean that there is no real distinction between the old and the new humoral theories. The old theory was formulated in a way which did not call for experimental verification. The new is a predictive or causal type of modern scientific hypothesis. The general proposition that it states demands test; and at the same time it reveals an endless vista of research which cannot but be fruitful both from the point of view of the content of pure knowledge, and from that of the aims of clinical practice. Yet there are parallels between the two kinds of theory. They reveal themselves clearly when we compare the difficulties into which 17th and 18th century physicians got themselves when they tried to explain how the presumed secretions of the brain pass to the pituitary with those which now beset us in our understanding of the functional relations of the latter organ to the hypothalamus.

1. "All living organs receive supplies of the circulating fluids, calculated to maintain their growth or secreting functions; and, in particular cases, other additional ingredients form essential parts of the materials on which the organs are destined to operate. Now, we find that the circulating fluids, with or without these superadded ingredients, are submitted to the actions of various organs, and to as many different modes of operation, each for its peculiar results" (King 1836). In 1840 George Gulliver suggested that the adrenal glands poured into the blood "a peculiar matter which has doubtless a special use."

*The seventh Addison Memorial Lecture, delivered at Guy's Hospital, London, on Dec. 16, 1953.

The Old View of the Secretions of the Brain

THE FOUR HUMOURS

Let us begin by recalling some of the central features of the old theory of the humours (e.g., see Singer 1925, Meyer 1937, Singer and Rabin 1946, Singer 1952). It derives from the Aristotelian concept that every material thing is made up of different proportions of the four common elements—earth, water, air, and fire—of which any one or two are dominant in every object. Each of these four fundamental essences or existences represented the union of two of four primary and opposite qualities (hot, cold, wet, and dry), and corresponding to them were the four fundamental humours—blood, phlegm (or pituita), yellow bile, and black bile (melancholia). When the four humours were in proper balance, the body was healthy.

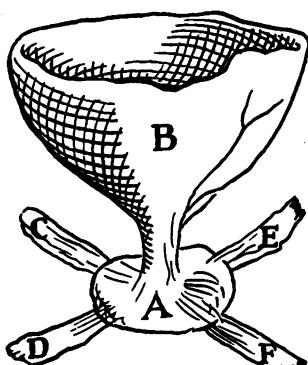


Fig. 1.—Vesalius's conception of the funnel (infundibulum) (B) through which the phlegm from the brain trickled into the pituitary gland (A). The four imaginary ducts C, D, E, F, carried the phlegm from the gland.

There was also the idea that while the four humours pervaded the body, and determined its state of health and the temperament or "complexion" (literally "weaving together") of the individual, each had its principal organ. Yellow bile or choler came from the gall-bladder, and black bile or melancholy from the spleen. Blood arose from the liver, and the brain was responsible for the phlegm or pituita, which escaped by way of the infundibulum of the third ventricle into the pituitary body, and thence along the olfactory nerves through the cribriform plate of the ethmoid into the nose.² Over and above all this, the Ancients realised that some tissues (e.g., the testes) endowed the body with particular humours or particular qualities.

PRODUCTION OF CEREBRAL HUMOUR

One of the more useful discussions regarding the cerebral humour is provided by Swedenborg in a posthumous monograph published³ for the first time in 1882, 140 years after his death.

"For the purpose of preparing the blood," Swedenborg wrote, "the soul has established in the cerebrum an illustrious chymical laboratory, which it has arranged into members and organs and by the ministry of these it distils and elaborates a lymph animated by the animal spirit, whereby it imbues the blood with its own inmost essence, nature, and life."

Two spirits were produced: one, "the animal spirit or the nervous force," which is elaborated in the glandules of the grey substance" (i.e., in the Pacchionian bodies), and contained within the individual nerve-fibres of the

2. Vesalius (see Singer 1952) did not accept this view. He believed that channels passed on each side from the pituitary to the superior orbital fissure and foramen lacerum. (See fig. 1.)

3. Together with numerous annotations by R. L. Tafel, the editor of this posthumous work.

cortex; and the second, a nervous juice which exuded from the capillaries and circulated between the nerve-fibres.

PASSAGE OF CEREBRAL HUMOUR TO THE PITUITARY

Like others before him, Swedenborg was exercised about the way in which the essential spirit so formed, or pituita, left the brain. Thomas Willis (1664) had argued that "the position and structure" of the infundibulum indicate that

"some humour out of the ventricles of the cerebrum is carried into the pituitary gland. For that part is so constituted, that a discharge of humours is effected into its aperture from every angle and recess of the interior cerebrum, and its appendage; and while in the various animals the shape and the situation of the ventricles differ, nevertheless in every one of them all the ventricles, of whatever kind they be, have apertures opening in the direction of the infundibulum."

Willis felt that

"there was no room for doubting, that serous liquids descend by this way from the cerebrum into the pituitary gland. . . . If any one takes but a cursory view of the parts which are situated around the ventricles, and if he examines their structure but lightly, he will easily agree with the Ancients, that the excrements of the cerebrum are discharged partly through the infundibulum into the palate underneath, or that in an anterior direction they are cast out through the olfactory bulbs into the nares."⁴

Tied to the idea that there had to be some connection of this kind, Swedenborg also had no doubt about it, in fact, existed.

"The infundibulum," he wrote, "is not only a *vas deferens* or an excretory duct, but it is also a *vas secerens* or a secretory vessel; for those things which in the ventricles have become mixed up, thickened, and in a certain extent amalgamated, the infundibulum separates and filters; . . . [one part] it instils by a fibrous channel immediately into the substance of the gland; the latter it relegates around the gland, between the sides of the sella turcica."

He realised that the "highly liquid and refined alcohol of animal nature" about which he spoke was "utterly beyond the ken of the senses," but at the same time he felt certain that not only did the "enclosed moisture" of the infundibulum get into the pituitary, as described, but that the infundibulum also transmitted to the pituitary gland "a genuine and fresh spirit of its own."⁵

The invisible opening from the infundibulum into the pituitary, about which Swedenborg had no doubts, disturbed others, and one or two tried to find out experimentally whether, in fact, it existed—as theory demanded that it should. So it was that Vieussens (1685) injected a coloured alcohol into the third ventricle. He found that the fluid passed through the infundibulum and stained the upper and lateral parts of the gland, but that it did not dye its interior. Dismayed though he no doubt was by the lack of a canal or "sensible perforation" in the lower part of the infundibulum, he nevertheless had to

4. Willis's own text has been consulted, but the translation is that of Tafel, Swedenborg's editor. Richard Lower (1631–1690), Willis's pupil, rejected this teaching, and believed that "whatever serum is separated into the ventricles of the brain and tissues out of them through the infundibulum to the glandula pituitaria distills not upon the palate but is poured again into the blood and mixed with it" (see Rolleston 1936).

5. ". . . a copious fibre descends into this organ [the pituitary gland] from the fornix and the centrum ovale—it enters into the pituitary gland itself, and infuses into it the spirit it derives from its origins, that is, from the cortical substances, and thereby it restores and vivifies the older spirit, or that which arrives in the passages between the fibres." After further speculation about the interaction of the two types of fluid or humour which enter the pituitary, Swedenborg continues: "This chymical operation which is accomplished in the infundibulum and finally in the pituitary gland, may be called not only a secretion and purification, but also a rectification and alcoholisation."

conclude that the latter was probably "furnished with loose pores and to consist of a substance which is highly fitted for the reception of a certain aqueous humour and for excreting the same again."

A few students appear to have followed a different path in their researches into this question. One was Lieutaud, professor of medicine in the University at Aix, and a foreign member of the Royal Society of London.⁶ His observations about the pituita are no more than a historical curiosity; but those he made about what we now know as the hypothalamo-hypophyseal connection are extremely interesting. For it so happens that in the course of his studies he stumbled on what is called today the pituitary-portal system of veins.

VESSELS OF THE PITUITARY STALK

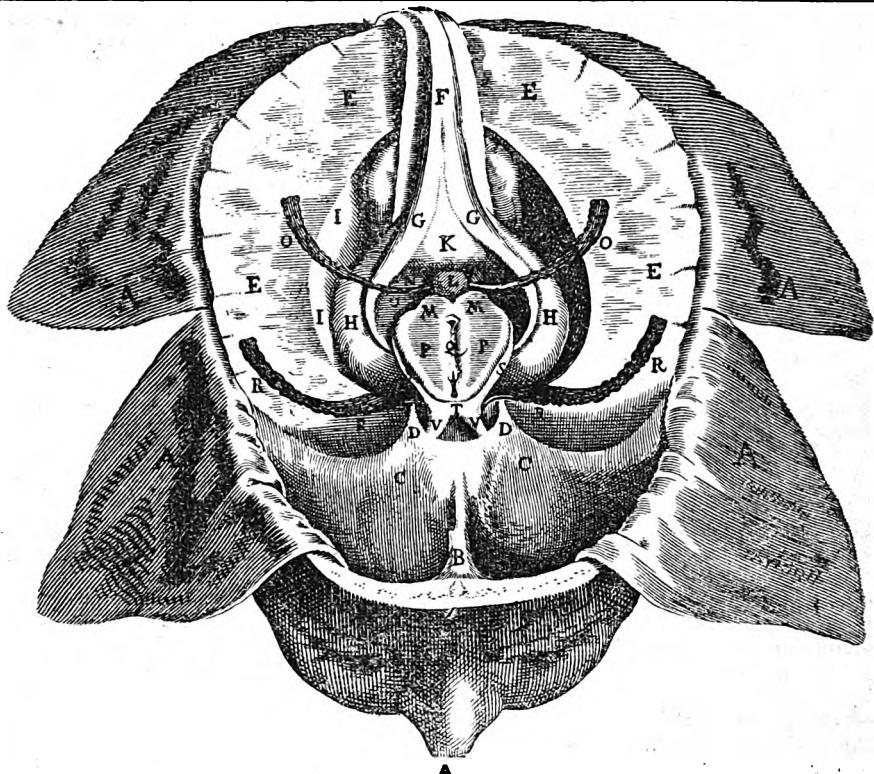
The record of this discovery is in a volume that was published in 1742 under the title *Essais Anatomique*—essentially a general textbook of anatomy. Its fifth section deals with the central and peripheral nervous system, and in his description of the third ventricle of the brain Lieutaud drew attention to a deep fossa anteriorly whose aperture gradually narrows as it approaches the base of the pituitary stalk. According to Lieutaud, the stalk, contrary to usual belief, is not canalised, but instead is a kind of cylinder "two to three lines" thick, formed of a grey substance, and covered by pia mater. On the other hand, running along it are very small longitudinal vessels which communicate with those of the pituitary gland below.⁷

Hardly ten years had passed before this observation, as well as Lieutaud's general views about the functions and secretions of the brain, were attacked by Théophile de Bordeu, the physician to whom we owe the first fairly clear conception of humoral action.⁸ For Lieutaud the

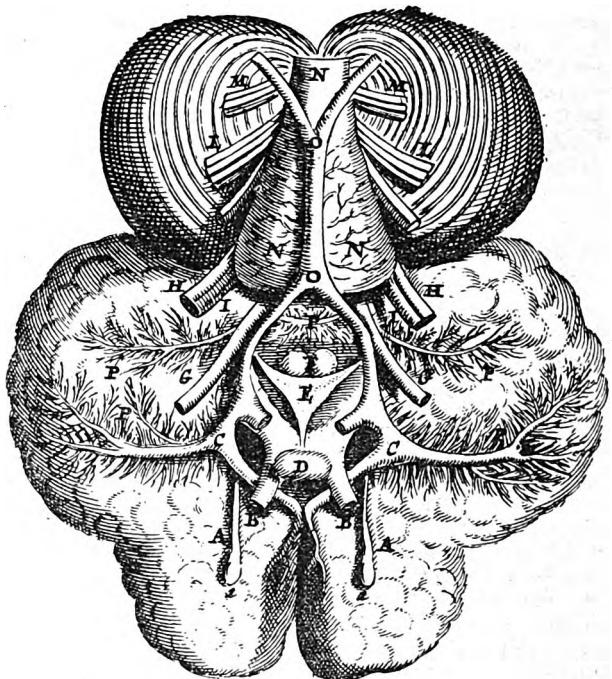
6. He was elected in 1739, the same year as his more renowned fellow-countryman, Buffon.

7. "La tige, qui s'élève de la glande pituitaire, répond véritablement à la partie la plus profonde de cette fosse : mais elle n'a point de cavité, comme on le prétend ; c'est une espèce de cylindre de deux ou trois lignes de hauteur, formé par la substance cendrée, et recouvert de la pie-mère. On remarque de très-petits vaisseaux qui marchent dans son axe, communiquant avec ceux de la glande qui reçoit cette colonne ou qui la soutient. J'ai donné à cette partie le nom de *tige pituitaire*, parce que j'ai cru que celui d'entonnoir ne sauroit lui convenir. Il n'est point difficile de montrer la solidité de la tige pituitaire, j'en donnerai la manière dans l'administration"—which he does in the chapter which follows.

8. The concept is outlined in the sixth part, entitled "Analayse Médicinale du Sang" of his volume *Recherches sur des Maladies chroniques*, first published in 1775. de Bordeu held that the different organs were related to each other through the spongy cellular tissues of the body, and that in this way the "humours" of one organ were able to influence the functions of another. de Bordeu particularly emphasised the effect of testicular and ovarian secretions; and the fact that the gonads in some way control the development of secondary sexual characters and behaviour. While one should not deny de Bordeu the distinction of having provided an indication of hormonal action, it would be an exaggeration to say that his writings reveal the precise formulation of hormonal action as understood today.



A



B

Fig. 2.—Riolan's diagrams showing the pathway of the pituita from the third ventricle to the pituitary.

(A) View, from above, of horizontal section of brain.

P, ? Thalamus. M, ? Superior quadrigeminal body. L, Pineal gland. {T, Optic chiasma. V, Optic nerves. Q, "The bottom of the third ventricle in which behind is the hole likened to the fundament; it tends to the beginning of the marrow of the back; before it is the hole compared to the womb, and is carried to the funnel." (Culpepper's translation of Riolan's legend.)

(B) The base of the brain.

B, The optic nerves. D, Pituitary gland. E, Infundibulum or funnel. F, "The protuberances of the brain, set before the passage which carries the phlegm to the funnel"—i.e., the mammillary bodies. N, Brain-stem.

problem of the brain was simple. In designing it Nature had three purposes, and three only : (1) to provide, as it were, a scaffolding for the blood-vessels of the brain ; (2) to provide a structure in which the life spirit could be separated out ; and (3) to provide an adequate reservoir for this spirit. Would not, he asks, a porous, palpable, or simple spongy mass of moderate density satisfy these requirements ? Why, he asks, search further in order to understand the nature of the brain, a secretory organ whose main function is to separate the extremely fine molecules of the ethereal liquid which is the animal spirit ? And as for the cerebral nerves, are they not the channels by which this spirit courses from the brain to all parts of the body ?

de Bordeu delivered his criticism in 1751. His main theme was that the glands of the body release their emanations as a result of some intrinsic action, in certain circumstances augmented by local irritation or shaking of the body, and not as a result of compression by neighbouring muscles or organs. He devoted a large part of his discussion to the widely held belief that the brain is a glandular organ, and that some vital spirit is directed along the nerves. In the course of his statement, in which he indicates quite clearly that he was no supporter of these views, de Bordeu points out that the three functions which Lieutaud attributed to the brain as a glandular organ could just as well have been applied to almost any organ or tissue of the body. The vital spirit, he remarks, is always shaped by the particular fantasy of the person writing about it ; and the arguments of those who are convinced that the brain distils such spirits, or that the nerves, and particularly the olfactory nerves, are a channel for the passage of some cerebral distillation, are no more probable than the opinions of those who deny them.

de Bordeu was equally unimpressed with Lieutaud's view that the solidity of the pituitary stalk can be easily demonstrated by cutting it in successive sections. The stalk, he found, is too delicate, and is only crushed and torn by such treatment. He admits, however, the existence of axial vessels along the stalk, and in doing so leaves the impression that in describing them Lieutaud had implied that they were a channel for the humours of the brain to the pituitary. de Bordeu also states that Riolan⁹ had long before noted the same vessels, and that he, too, had regarded them as a pathway for the pituita (see fig. 2).¹⁰ Finally, he was unconvinced by Lieutaud's assumption that the axial-stalk vessels communicate with those of the pituitary gland. The ventricular injections which he made to determine the nature of the connection between the base of the brain and the pituitary being indecisive, he ended by emphasising the urgent need for new researches to find out whether the infundibulum was indeed the excretory canal of the brain.

As we now know, Lieutaud and de Bordeu were both right and wrong. de Bordeu was wrong and Lieutaud right in suggesting that the axial-stalk vessels communicate with those of the pituitary below ; while de Bordeu was well justified in attacking Lieutaud's conception of the structure and function of the brain, and in doubting that a vital fluid flows from the base of the brain to the pituitary.

ECLIPSE OF THE HUMORAL THEORY

The point is that while he was one of the architects of the modern theory of hormones, de Bordeu was a never-tiring opponent of the old humoralism (see Cumston

1926). His controversy with Lieutaud was inspired less by any fundamental disagreement with the latter's anatomy (which, for its period, was far from bad) than by opposition to his attempt to interpret anatomical observations in terms of an outworn dogma. Those who believed in the old humours had to find a route by which the pituita escaped from the brain—whether through the stalk which connected the infundibulum and the pituitary, or by way of vessels along the stalk. Those who did not were suspicious of the whole idea that something passed from the brain to the pituitary. The eclipse of the old humoral theory—the end to which de Bordeu had turned so many of his energies—was finally due to the increasing use of experiment in medicine during the 17th century (following Harvey's great discovery of the circulation), and to the emergence of the cellular theory of bodily processes and disease in the 19th century. Morgagni, whose labours all but filled the 18th century, showed that diseases could be classified according to the parts of the body in which their symptoms occurred, and that it was reasonable to explain them by reference to the associated anatomical changes. His underlying theme was that disease is due to pathological change in specific organs, and not to an imbalance of humours which affect the whole body. From organs it was a relatively short step to the cells and tissues by which they are constituted. In the end it was the cellular theory, the triumph of which we owe to Virchow, and the bacterial theory as developed by Pasteur, Koch, and Lister, which displaced the older humoral theory of disease.

As the old humours disappeared, so too did the need to establish a specific pathway between the pituitary and the third ventricle. And thus it was that the axial-stalk vessels of Lieutaud dropped from view. But the question of a tubular connection between the infundibulum and pituitary continued to exercise successive generations of anatomists. Vieussens's experimental injection of a dye into the third ventricle, which had been repeated by de Bordeu in 1751, was tried again by the brothers Wenzel (1812). During the period 1796–1800 they performed twelve experiments on the human brain, and concluded that when any suitable liquid is injected into the third ventricle nothing passes into the infundibulum, and further that the latter is more closely joined to the posterior than to the anterior lobe of the hypophysis.

This last observation foreshadows what we know today—that whatever the connection between the hypothalamus and the pituitary, it is much more intimate in the case of the posterior than of the anterior component of the gland. Wenzel also observed vessels, connecting the pituitary with the infundibulum, which may well have been the same channels as are now called the pituitary-portal system of veins, and which Lieutaud originally described. So, too, did Luschka, who in 1860 described what we might now recognise as the primary capillary loops of the pituitary-portal vessels.

"Here and there," he writes, "the vessels bulge out, and in the form of loops which are arranged in various ways, they make their way into the interior of the infundibulum, and sometimes their number is so great, that they alone constitute a loose, red substance in the interior . . . By these vascular loops and the productions which result thence, not only the cavity of the infundibulum is obstructed, but also the proper substance of this organ is crowded out and broken up."¹¹

He also speaks of "blood vessels which run in a longitudinal direction, and which not infrequently are enlarged in the fashion of aneurisms."

Luschka, it should be noted, was quite certain that as a rule "the infundibulum has an aperture only in its upper extremity and in that portion which communicates with the tuberculum cinereum . . . Only in exceptional cases the cavity of the infundibulum can really be traced into the pituitary gland." He also appears to have had a remark-

9. Jean Riolan the younger (1577–1657).

10. The passage in question occurs in Riolan's *Enchiridium Anatomicum et Pathologicum*, first published in Paris in 1648, and translated into English in 1657. The reference is, however, hardly precise ; all that Riolan says is that there are four minute channels on the infundibulum through which some "serum" is distilled on to the palate and fauces.

11. The translation is that of Tafel.

ably clear understanding of the anatomical relationship of the tuber cinereum, the infundibulum, and the posterior lobe of the gland. They were, he realised, parts of the same anatomical complex, possessing fundamentally the same finer structure.¹² Even more striking was his observation that "fine nerve tubes" passed from the infundibulum into the posterior lobe, where they became varicose and broke up. This achieves a particular significance in the light of new discoveries, to which I shall shortly refer, over the past few years, which resurrect, to mystify us once again, the problem of how the brain controls the functions of the pituitary.

(To be concluded)

VARICOSE VEINS

COMPARISON OF THE STRIPPING OPERATION WITH OTHER METHODS OF TREATMENT

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THERE have been many recent reports on the treatment of varicose veins, but few in which the results have been assessed after an adequate follow-up (Hodge and Grimson 1945, Mahorner and Ochsner 1938, Mathiesen 1953).

In 1949 an attempt was made to follow up all the cases of varicose veins that had been operated on in the surgical unit at University College Hospital between 1942 and 1948. Owing to the war, there were only 81 cases; of these, 48 were traced and reviewed. 15 were males, and 6 of these had recurrence necessitating further treatment; of the 33 females, 11 required further operative treatment and 16 required further injections. The patients had been treated originally by interruption of the saphenous vein and its tributaries at the saphenofemoral junction with, in some cases, further interruptions lower down the course of the vein and retrograde injections of ethamoline olate or sodium morrhuate. None had been adequately followed up after operation.

In view of these findings it was decided to organise a follow-up clinic and attempt to compare the results of various forms of treatment. The choice of treatment of each case was left to the surgeon who did the operation; some surgeons did not approve of the more drastic procedures of stripping and excision. All the cases, however and by whomsoever they were treated, have for the last three years been followed up, at regular intervals, by one person. In this way assessment of the various forms of treatment in an unselected group of cases has been possible.

Classification

In order to compare results, the cases have been divided into three groups according to the severity of the condition:

Group I : uncomplicated varicose veins.—In this group the symptoms consisted in no more than aching and slight swelling of the ankles, and the signs of no more than demonstrable superficial varicosities, with or without oedema after long standing but with no evidence of skin changes.

12. "The fundamental substance of the infundibulum is really a soft, reddish grey mass which on the one hand is continued into the tuber cinereum, and on the other into the posterior lobe of the gland . . . But it must be well observed that the nervous substance properly constitutes neither the infundibulum nor the posterior lobe of the gland, to any great extent; and that the substance of said lobe consists essentially of a growth of connective-tissue ingredients and of epithelial elements. These ingredients gain the upper hand more and more, and the nervous elements grow less and less, the nearer the infundibulum approaches the pituitary gland." (Translation taken from Tafel.)

Group II : complicated varicose veins.—In this group were included all those with a past history or present signs of ulceration, eczema, or superficial phlebitis, but without a history or evidence of deep venous thrombosis.

Group III : varicose veins secondary to deep venous thrombosis.—In this group were included all cases in which there was a past history of deep venous thrombosis or in which investigation showed incompetence of the deep venous system.

The various forms of treatment were as follows:

Injection alone.—In the majority of cases ethamoline olate was used, but a very few were treated with sodium morrhuate. Those cases in which there was no evidence of retrograde flow were treated in this manner.

Groin tie alone.—"Groin tie" implies interruption of the long saphenous vein and all its tributaries at the saphenofemoral junction.

Groin tie and injection.—All the cases treated by groin tie (with or without ties lower in the course of the vein) together with injection of sclerosant fluid by retrograde catheterisation or needle at the time of operation are placed under this heading.

Stripping and excision.—This operation included interruption of the saphenous vein and all its tributaries at the saphenofemoral junction, stripping out of the saphenous veins with interruption of the communicating vein between the long and short systems, and excision of those veins in the calf which were too tortuous to permit the passage of the stripper: in short, ablation of all visible and palpable superficial varicosities.

Short saphenous tie alone.—Interruption of the short saphenous vein in the popliteal fossa.

Lower tie or ties.—Interruption of superficial varicosities, without interruption of the long saphenous vein at the saphenofemoral junction. This operation was occasionally done under local anaesthesia in patients whose general condition or age did not warrant more major procedures.

Physiotherapy.—All patients with ulceration were given massage, surging faradism, and Bisgaard (1948) type bandages; and they wore elastic stockings afterwards until the skin was soundly healed and oedema controlled. All patients with a past history of deep thrombosis with skin changes or oedema were similarly treated.

Grafting.—Cases with ulceration in which healing was unduly slow, despite physiotherapy and bed rest, were treated by split-skin grafting.

Assessment of Results

Although the follow-up period has been no more than three years, this seems enough for a first assessment; and it is hoped that these cases will again be assessed after a further five years. The assessment has been made by dividing the results into five classes as follows:

1st class.—No symptoms or signs of varicosities in the limb, no injections required.

2nd class.—No symptoms, but an injection required at not less than six-monthly intervals for minimal recurrences.

3rd class.—No symptoms, but injections required at two-monthly or three-monthly intervals to keep the recurrences in check.

4th class.—Recurrent or remaining symptoms, and requiring repeated injections.

5th class.—Recurrent ulceration, eczema, or incompetent varicosities requiring further treatment other than injection.

GROUP I : UNCOMPLICATED VARICOSE VEINS

This group comprised 124 patients (55 males, 69 females); 68 had bilateral varicosities, making a total of 192 limbs for therapy. 22 of the patients had had previous treatment as shown in table I.

TABLE I.—PREVIOUS TREATMENT ELSEWHERE OF 22 PATIENTS IN GROUP I

Type of treatment	No. of patients
Unilateral groin tie	7
Bilateral groin tie	5
Local tie and injection	3
Injection	6
Elastic stockings	1

TABLE II—GROUP I (UNCOMPLICATED VARICOSE VEINS): TREATMENT AND RESULTS

Type of treatment	No. of limbs	Assessment of result (class)						No. assess- ment
		1st	2nd	3rd	4th	5th		
Stripping and excision ..	110	50	21	7	1	3	28	
Groin tie and injection ..	52	2	13	12	14	2	9	
Groin tie alone ..	17	1	5	4	0	4	3	
Injection alone ..	8	0	0	2	4	2	0	
Lower tie or ties ..	4	1	1	1	0	1	0	
Short saphenous tie alone ..	1	1	0	0	0	0	0	

86 patients complained of aching in the legs, and 16 of oedema of the ankles, at the end of the day: 9 sought operation for cosmetic reasons; while 29 had no symptoms.

Of the 124 patients treated, 68 are still attending the follow-up clinic, 52 have defaulted, and 4 have not once attended. The average length of follow-up of those still attending is thirty-two months. The average length of follow-up of those defaulters who have been assessed is twenty-two months. No assessment was made on 40 limbs since the patients had not attended for long enough to warrant this. The types of treatment and assessment of results are shown in table II.

Complications

Associated with operation.—All the patients who were treated by the stripping procedure had a postoperative course of penicillin for five days and were made to walk about on the day after operation. There were no serious complications of operation. 1 patient developed a haematoma in the groin on the day after operation; this was evacuated. 1 patient had the right saphenous nerve damaged in the calf by a stripping operation; a patch of anaesthesia, the size of half a crown, developed just below the medial malleolus, and this took nine months to recover.

During follow-up.—In 1 patient spontaneous superficial phlebitis developed. In another patient popliteal thrombosis developed the day after an injection of 1.5 ml. of ethamoline oleate in the calf; this was treated by

TABLE III—PREVIOUS TREATMENT ELSEWHERE OF 15 PATIENTS IN GROUP II

Type of treatment	No. of patients
Unilateral groin tie ..	5
Bilateral groin tie ..	4
Bilateral groin tie and injection ..	4
Unilateral groin tie, ulcer excision, and graft ..	1
Injection ..	1

physiotherapy and a supportive bandage. There was 1 case of severe ethamoline sensitivity with glottic oedema.

GROUP II: COMPLICATED VARICOSE VEINS

There were 66 patients in this group (26 males, 40 females); 47 had bilateral varicosities, making a total of 113 limbs for therapy. 15 of the patients had had previous treatment as shown in table III.

The numerous symptoms and signs in this group are shown in table IV. 8 of the patients in this group were investigated by phlebography (5 descending, 3 ascending). 2 were investigated by measurement of the venous pressures (Longland and Walker 1950). These investigations were undertaken to prove the competence of the deep venous system.

Of the 66 patients in this group, 43 are still attending the follow-up clinic, 20 have defaulted, and 3 have never been seen since discharge from hospital. The average length of follow-up of those still attending is thirty-five months. The average length of attendance of those defaulters who have been assessed is twenty-six months.

No assessment was made on 24 limbs, as the patients had not attended long enough to warrant this. The types of treatment and assessment of results are shown in table V. The results of physiotherapy and grafting have not been assessed, as in nearly all cases they were combined with other forms of therapy.

Complications

Associated with operation.—1 patient had a small area of anaesthesia owing to damage to the long saphenous nerve; this took two years to recover. There was 1 case of postoperative haematoma in the groin; and 1 patient developed multiple stitch abscesses eight weeks after discharge from hospital. 1 patient treated by groin tie alone had transient but definite postoperative oedema of the leg which was considered to be due to deep thrombosis; this was rapidly relieved by physiotherapy.

During follow-up.—There were 2 cases of popliteal thrombosis following injections of 1.5 ml. of ethamoline in the back of the calf; there was 1 injection ulcer due to extravasated ethamoline, which took a long time to heal. 1 patient was intolerant to both ethamoline oleate and sodium morrhuate (pain in the back and vomiting).

TABLE IV—SYMPTOMS AND SIGNS IN GROUP-II CASES

Symptoms and signs	No. of patients
Past unilateral ulceration ..	20
Past bilateral ulceration ..	6
Present unilateral ulceration ..	14
Present bilateral ulceration ..	2
Unilateral eczema ..	21
Bilateral eczema ..	2
Unilateral superficial phlebitis ..	14
Bilateral superficial phlebitis ..	4
Oedema of ankles ..	16

There were 2 recurrent ulcers, 3 cases of recurrent eczema, 2 cases of recurrent superficial phlebitis, and 1 case of spontaneous popliteal thrombosis in a labourer, apparently after climbing a ladder. Of the 3 cases treated by stripping and excision and assessed in the 5th class, 2 had recurrent eczema, and the 3rd a very ugly redilation in the popliteal fossa, where the short saphenous vein had been inadequately stripped. There were no cases of recurrent ulceration following stripping.

GROUP III: VARICOSE VEINS SECONDARY TO DEEP THROMBOSIS

There were only 17 cases in this group (3 males, 14 females); in 4 there was a history of bilateral thrombosis, and there were thus 21 limbs for therapy. Previous treatment had been as follows: 1 patient had had a superficial femoral ligation and graft, followed by lumbar sympathectomy and further graft; another had had the groin explored and the veins tied twice and been grafted twice; and a 3rd had had a course of injections.

Phlebography was done in 8 of the cases (descending 5, ascending 3). The venous pressures were measured in 2 other cases.

The symptoms and signs of the cases in this group are shown in table VI, the types of treatment and the assess-

TABLE V—GROUP II (COMPLICATED VARICOSE VEINS): TREATMENT AND RESULTS

Type of treatment	No. of limbs	Assessment of result (class)					
		1st	2nd	3rd	4th	5th	
Stripping and excision ..	59	10	24	3	2	3	17
Groin tie and injection ..	26	1	8	7	5	3	2
Groin tie alone ..	15	0	3	4	2	6	0
Injection alone ..	9	0	0	1	0	3	5
Physiotherapy ..	18
Grafting ..	2

TABLE VI—SYMPTOMS AND SIGNS IN GROUP-III CASES

Symptoms and signs	No. of patients
Unilateral superficial varicosities	11
Bilateral superficial varicosities	3
No apparent superficial varicosities	3
Oedema of lower leg	12
Past ulceration	8
Present ulceration	5
Eczema	3
Superficial phlebitis	3
Bursting pain	2

ment of the results in table VII. 15 of the patients have continued to attend the follow-up clinic, while 1 has defaulted and 1 has never been seen since leaving hospital. Assessment of results of therapy has been made on 12 limbs, the average length of follow-up of these being thirty months.

All the patients with oedema or skin changes had a course of physiotherapy, and all were advised to wear supportive stockings until the oedema had been controlled completely for six months; several were advised to wear them permanently. In 1 case, associated with severe bursting pain, the pain was relieved by a superficial femoral tie, but the oedema of the leg rapidly returns if he gives up wearing an elastic stocking. Another patient was given a course of heparin for severe bilateral superficial phlebitis.

Complications

The only complication of operation was 1 groin hematoma. There have been 4 cases of recurrent ulceration, seen at follow-up: in 2 of the cases treatment had been by physiotherapy alone, and in the other 2 by injection and physiotherapy.

Discussion

Comparison of the various forms of treatment in groups I and II (table VIII) shows that the stripping and excision has been the most effective method. Of 82 limbs with uncomplicated varicose veins treated by stripping and excision, 50 (61%) have remained free from any sign of recurrence for a follow-up period

TABLE VII—GROUP III (VARICOSE VEINS SECONDARY TO DEEP THROMBOSIS): TREATMENT AND RESULTS

Type of treatment	No. of limbs	Assessment of result (class)					
		1st	2nd	3rd	4th	5th	No assessment
Stripping and excision	6	1	2	0	0	0	3
Groin tie alone	2	0	0	2	0	0	0
Groin tie and injection	1	0	0	1	0	0	0
Injection alone	5	0	0	2	1	2	0
Short saphenous tie alone	1	0	1	0	0	0	0
Physiotherapy	17	No assessment					
Superficial femoral tie	1						
Heparin	1						

averaging twenty-seven months, and these have not required a single postoperative injection.

175 limbs have been treated by stripping and excision, with no serious postoperative complications such as thrombosis, infarction, or sepsis. In the past it was said that this procedure, owing to the associated mortality and morbidity, was not justified, and that the less drastic procedures, if not quite as effective, were safer. This criticism is without foundation under present-day conditions, provided that sepsis is prevented by the routine administration of an antibiotic, early ambulation is instituted, and the operating time is not unduly long. In bilateral cases the operating time can be considerably shortened by two surgeons working at the same time.

In this series the complications from the injection of sclerosants in the follow-up clinic have been more serious

than the immediate postoperative complications. 3 patients have suffered a popliteal thrombosis after an injection of 1.5 ml. of ethamoline oleate into varicosities in the back of the calf, despite the application of a tourniquet to the back of the knee; in 1 patient an indolent ulcer developed after an extravenous injection of sclerosant; there have been 2 unpleasant cases of allergy. In the same group of cases only one serious complication of operation was seen—a deep thrombosis following a groin tie. The results in all three groups (see tables II, V, and VII) confirm that injection treatment is disappointing and reocanalisation soon ensues. Kinmonth (1948) has demonstrated that any valves present at the site where sclerosant is injected are destroyed, and, if the vein is later recanalised, incompetence is bound to be present at the site of recanalisation and also in the communicating veins in the immediate neighbourhood. The potential dangers of retrograde injection of sclerosing solutions by

TABLE VIII—COMPARISON OF RESULTS OF TREATMENT

Method of treatment	No. assessed	% in 1st class	% in 2nd class
<i>Group I :</i>			
Stripping and excision	82	61	25.6
Groin tie and injection	43	4.6	30
Groin tie alone	14	7	36
<i>Group II :</i>			
Stripping and excision	42	25	57
Groin tie and injection	24	4	33
Groin tie alone	15	0	20

catheter are well known (Atlas 1943, Boyd and Robertson 1947). In this series it has been shown that a thorough stripping operation by ablating the veins reduces the rate of recurrence, and thus also reduces the necessity for postoperative injection of sclerosants.

Of 207 patients whose names were originally entered in this follow-up, 81 have defaulted and failed to attend when written for and given a further appointment—this despite the fact that all were warned that their varicosities would recur if they did not attend regularly for a check. With a condition such as varicose veins, in which the symptoms are usually trivial until complications arise, there will always be some defaulters; it is therefore reasonable to apply initially that form of therapy which is least likely to be followed by recurrence.

This follow-up has shown that stripping and excision, or ablation, of varicose veins is a safe procedure; 175 limbs have been treated in this way without serious morbidity. The disappointing and sometimes dangerous results of the injection of sclerosants have been demonstrated. Ablation has reduced the necessity for such injections and has, in this series, given better results than other methods of treatment.

Summary

The results of various methods of treatment of varicose veins have been assessed in 207 patients followed up for approximately three years.

Complete ablation of the veins by stripping and excision was done on 175 limbs without any serious complications.

This method was the most effective of those studied.

I wish to thank Prof. R. S. Pilcher for his advice in the preparation of this paper.

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TWO-GENERATION PYLORIC STENOSIS

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Rammstedt described his operation for congenital pyloric stenosis in 1912. It was first used at The Hospital for Sick Children, Great Ormond Street, in 1917 and an increasing number of successful operations were done there from 1918 onwards. The figures for 1918-25 are shown in table I.

Before then relatively few children were admitted to the hospital with this condition, and most of these died

TABLE I—TREATMENT AND NUMBER OF SURVIVORS OF CHILDREN WITH PYLORIC STENOSIS 1918-25

Years	Rammstedt's operation		Medical treatment		Total	
	Survivors	Dead	Survivors	Dead	Survivors	Dead
1918-19	6	14	1	6	7	20
1920-21	25	26	4	14	29	40
1922-23	55	18	0	6	55	24
1924-25	72	15	0	1	72	16

in hospital. It is natural therefore that, until recently, it has been most unusual to find children with pyloric stenosis one of whose parents also had well-documented pyloric stenosis. Caulfield in 1926 reported a mother and 2 children affected. But operation on both parent and child was first reported by Ashton (1929), the child having had Rammstedt's operation and the mother a gastro-enterostomy—though in the mother's case it was not recorded whether a tumour was found. Even in a very large series such examples have been rare (McKeown et al. 1951). Similarly there were no examples of proved pyloric stenosis among the parents of the 480 children treated between 1943 and 1947 at The Hospital for Sick Children, though Carter and Savage (1951) found that on two occasions a father was reputed to have had the illness. Since then it has been found that the mother of 1 child in the series described by Carter and Savage had the disease and was medically treated in The Hospital for Sick Children from the age of 8 to 20 weeks in 1912. The contemporary notes show that the diagnosis was not in doubt, a tumour being distinctly felt. The infant made a good recovery and has since had by her first husband 1 child with pyloric stenosis, confirmed at operation at another hospital, and by her second husband 2 children with pyloric stenosis confirmed at operation at The Hospital for Sick Children (fig. 1).

Another most interesting family, comprising a father, two sons, and a nephew, all proved affected, has been reported by Fenwick (1953). The father's condition was confirmed at operation at the age of 39, after 10 years of dyspepsia; as far as could be discovered this man had had no symptoms of the condition in infancy.

Since 1947, however, among the hundred or so children treated each year by Rammstedt's operation at The Hospital for Sick Children there have, except in 1949, always been one or two with a parent who also had pyloric stenosis confirmed at operation. There were 2 such children in 1948, none in 1949, 2 in 1950, 1 in 1951, 1 in 1952, and 3 in 1953 up till August (figs. 2-10). Of

these parents 5 underwent operation at The Hospital for Sick Children (figs. 2-4, 8, 10) and 1 at St. Thomas's Hospital (fig. 6); and their contemporary records are available. The other 3 were, according to the family, treated by members of the staff of The Hospital for Sick Children at London nursing-homes. The contemporary records are not now available, but all 3 have a characteristic abdominal scar.

Obviously in the parents of index cases the proportion affected is likely to increase steadily as more and more successfully treated children grow up. But in the children of index cases the proportion affected is likely to alter less. An estimate of this proportion is of greater value in fixing the mode of inheritance, as well as being a practical aid to diagnosis. In order to get a first approximate estimate of this proportion we attempted to trace from their original addresses all the 358 (299 male and 59 female) individuals who survived operations between the years 1920 and 1929 at The Hospital for Sick Children and St. Thomas's Hospital. In this way 85 (73 male and 12 female) were traced, of whom 28 (22 men and 6 women) had married and started their families and 9 were dead. None of the remaining 273 (226 male and 47 female) were traced from their original address, although 2 were known because they had already brought an affected child to hospital and 4 more because they brought an affected child to the hospital after the attempt to trace them had failed.

This gives two independent estimates of the proportion of children affected—one from the men and women traced from their original addresses, the other from those not so traced. The "traced" series is small, but the exact number and state of the children are known. The "untraced" series is larger, but the total number of children born to these men and women is not known and their affected children are known only if the child was brought to The Hospital for Sick Children or to St. Thomas's Hospital.

Data on the families of the 28 "traced" individuals who have children are summarised in table II, and the two families with an affected child are shown in figs. 11 and 12.

In these twenty-eight families it will be seen that of the 25 boys, 3 have had pyloric stenosis and Rammstedt's operation. These three operations took place at London hospitals, but not at The Hospital for Sick Children or

TABLE II—CHILDREN OF "TRACED" INDEX CASES WITH PYLORIC STENOSIS CONFIRMED AT RAMMSTEDT'S OPERATION IN 1920-29

Sex	No.	Index case		Sons		Daughters	
		Affected	Normal	Affected	Normal	Affected	Normal
Men	22	2	19	0	18		
Women	6	1	3	0	3		
Total	28	3	22	0	21		

St. Thomas's Hospital, and contemporary notes were available for all 3. Of the 21 girls none had pyloric stenosis treated by operation. This "traced" series is small, but it leaves little doubt that the proportion of sons of index cases with definite pyloric stenosis is well above the proportion affected in the general population. In addition to the children with proved pyloric stenosis 1 girl had projectile vomiting and some failure to gain weight and was successfully treated by the general practitioner with atropine methonitrate ('Eumydrin'); 1 boy and 1 girl had the same symptoms but required no treatment; 1 girl had projectile vomiting but no failure to gain weight and required no treatment. This association between suggestive symptoms and confirmed pyloric stenosis in the parent-child relationship is seen too in

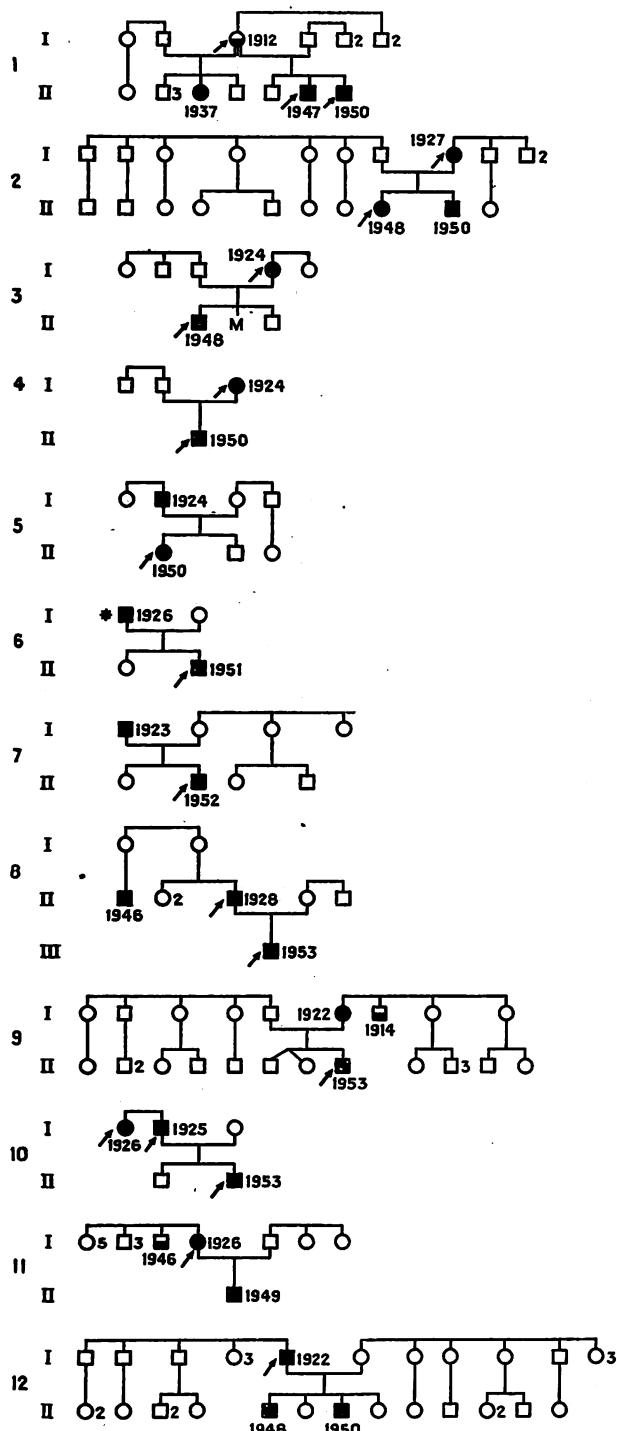
other family relationships—for example, in the family reported by Cockayne (1938). It is natural to suggest, as Cockayne did, that "pylorospasm" represents a milder manifestation of the genetic factors predisposing to

pyloric stenosis, but it is not yet possible to be certain that this is so.

From the second series—the 273 men and women who were not traced from their original address—there is good confirmation of the view that the children of index cases have an increased risk of developing pyloric stenosis. The number of children they have had is, of course not known, but from the 1951 1% sample census (Census 1952) it may be estimated that the number will by now be roughly 150, more or less equally divided between sons and daughters.

From table I.1. of this report it is possible to estimate the proportion of men and women in Britain in each year of age who have been married for a given number of years. From table x.5. it is possible to estimate the average fertility of women in Britain by age and duration of marriage. No fertility figures are given for men, and so it is assumed in this estimate that they have married wives 2 years younger than themselves and the fertility of these wives estimated.

From a comparison, according to year of operation, with those traced the estimated number would be 170. The two estimates are compatible, but the first is probably the more reliable. It is, however, known (v.s.) that of



Figs. I-12—Pyloric stenosis in two generations.

- Pyloric stenosis confirmed at Rammstedt's operation.
- Pyloric stenosis, diagnosis certain but medically treated.
- Two brothers and two sisters, normal and without children. Birth order accurately shown in sibship of affected child in generation II but not in generation I.
- M Miscarriage.
- ↗ Treated at The Hospital for Sick Children.
- * Treated at St. Thomas's Hospital.

TABLE III—CHILDREN KNOWN TO BE Affected AND ESTIMATED TOTAL NUMBER OF CHILDREN BORN TO 273 "UNTRACED" CASES OF PYLORIC STENOSIS CONFIRMED AT OPERATION IN 1920-29

Sex	No.	Index case		Sons		Daughters	
		Known affected	Estimated total	Known affected	Estimated total	Known affected	Estimated total
Men	..	226	3	58	0	58	58
Women	..	47	3	17	1	17	17
Total	..	273	6	75	1	75	75

these children at least 5 sons and at least 1 daughter (families 3, 4, 6, 8, 10 and the daughter of family 2) have had pyloric stenosis confirmed at Rammstedt's operation at The Hospital for Sick Children and 1 son had pyloric stenosis similarly confirmed at another hospital (the son in family 2). The children known to be affected and the estimated total of children born to these untraced men and women is shown in table III. The number of children known to be affected gives of course only a minimum estimate; further children may well have been affected but treated at other hospitals.

It is difficult to guess how many affected children of the "untraced" series will have been treated elsewhere; but a rough preliminary estimate, giving weight to both the "traced" and the "untraced" series and keeping the usual ratio of boys to girls affected, is that 1 son in 10 and 1 daughter in 50 have pyloric stenosis sufficient to require Rammstedt's operation. Larger and more complete series are needed to discover whether the risks of having affected children vary from family to family, whether the risks are the same for the children of male as of female survivors, whether the risk is increased after one affected child has been born, or whether one of the surviving parent's brothers or sisters was also affected.

Discussion

The proportion of sons affected is sufficiently high to make it worth watching these children in the early weeks for symptoms and signs of early pyloric stenosis. In several instances the grandmother, who was the mother of the affected parent, was sure of the diagnosis some time before the family doctor was convinced that the child had pyloric stenosis. Later when the risk is precisely known it may even be worth attempting some prophylactic treatment from birth in these families.

The aetiology of pyloric stenosis remains a mystery, but the finding that sons are unduly often affected increases the probability that genetic factors are important. It has long been known that brothers and sisters are often affected. Caulfield (1926) notes that a family with 3 affected girls was reported in the 18th century. The risk is about 1 in 10 for brothers and 1 in 50 for sisters (Cockayne and Penrose 1943, McKeown et al. 1951). This might be due to a shared environment, but it is more difficult to imagine an environmental factor which is common to two generations of a family. On the other hand McKeown et al. (1951) found no increased risk for first cousins.

It may well be that several different genes predispose to the development of pyloric stenosis, but it is worth considering the simplest unitary hypothesis that would fit the findings so far. These findings are that about 1 in 10 of brothers and 1 in 50 of sisters are affected and that the proportions of sons and daughters affected is of the same order, though less accurately known. A dominant gene producing full clinical manifestation in 1 in 5 of the boys and 1 in 25 of the girls who possess the gene would fit the findings well. The hypothesis of a recessive gene producing full clinical manifestations in 2 in 5 of the boys and 1 in $12\frac{1}{2}$ of the girls who are homozygous fits the findings in brothers and sisters well. It is compatible with the findings in children, but one would expect in larger series that the proportions affected would be less and come close to 1 in 20 sons and 1 in 100 daughters. The dominant-gene hypothesis fits better at the moment, though neither explains the finding from Birmingham (McKeown et al. 1951) that there is no increased risk to first cousins. Other reasons for the dominant-gene hypothesis are that step-sibs are not uncommonly affected and that it is rare to find a relation on both the father and the mother's side of the family affected; but the strength of the arguments cannot yet be assessed statistically.

Genetic predisposition is, however, only one aspect of aetiology. Whether one assumes that a single dominant or recessive gene is mainly concerned, it is clear that only a minority of children with the gene develop symptoms of pyloric stenosis and a palpable pyloric tumour. Again the one definite conclusion from the small series of twins hitherto reported (Ford et al. 1941, Powell and Carter 1951, Metrakos 1953) is that sometimes only one

TABLE IV—BIRTH ORDER BY AGE OF ONSET OF SYMPTOMS OF PYLORIC STENOSIS, JANUARY, 1946, TO AUGUST, 1953
(Excluding 14 children whose records did not give birth order)

Birth order	Day of onset					Total
	0-6	7-13	14-20	21-27	28	
First-born	22	35	66	75	131	329
Later born	32	37	76	72	135	352
% First-born*	41	49	46	51	49	48

* First-born accounted for 46% of the 268 cases with onset at 0-20 days, and for 50% of the 413 cases with onset at 21-28 days.

of a pair of identical twins is affected, and so the penetrance of the gene or genes concerned cannot be complete. McKeown et al. (1952) have recently made two interesting observations which have some bearing on the environmental factors responsible. One is that children born in hospital develop symptoms later, on the average, than those born at home. The other is that the effect of birth order is much reduced or absent in those in whom symptoms start early. Birth order now has relatively little influence among children with pyloric stenosis confirmed at operation at The Hospital for Sick Children. The proportion of first-born is only some 5% greater than the proportion among all children

born in Greater London or London and South-East England. But an analysis of birth order by week of onset of symptoms supports the observation of McKeown and his colleagues. This analysis is shown in table IV. The proportion of all children first-born in the same area in the years 1946-51 varied from 46 to 40%. Here, as in a Liverpool sample quoted by McKeown et al. (1952), the excess of first-born becomes remarkable only when the onset is later than the third week and not, as in Birmingham, the second week. It is possible, however, that the small birth-order effect and the later onset where children are born in hospital may be due merely to more skilled baby-feeding by experienced mothers or hospital nurses.

Another line of approach to the environmental factors is suggested by the rarity of pyloric stenosis in some areas today with reasonably good medical services—for example, Malaya (Field 1951). Kellett (1933) has put forward suggestive, if not conclusive, grounds for believing that the condition was rare in Europe two or three hundred years ago. Only fifty years ago Cautley (1899) was writing that the condition was rare "though not so extremely rare as has been supposed." Now pyloric stenosis is one of the commonest disorders of childhood, with a frequency of 2-4 per 1000. It is difficult to believe that this is due merely to more complete diagnosis.

Summary

An attempt was made to trace from their original addresses 358 men and women who had pyloric stenosis confirmed at Rammstedt's operation at The Hospital for Sick Children and St. Thomas's Hospital between 1920 and 1929.

The 85 individuals traced in this way had had so far 25 sons and 21 daughters. Of these children 3 sons, but no daughters, had had pyloric stenosis confirmed at Rammstedt's operation.

The number of children born to the 273 men and women who were not traced from their original addresses is unknown but roughly estimated to be about 75 sons and 75 daughters. It is known, however, that 6 of these boys and 1 of these girls had pyloric stenosis confirmed at Rammstedt's operation because their parents (though not traced from their original address) brought them to The Hospital for Sick Children for treatment.

The children of individuals with pyloric stenosis have a risk of being affected of the same order as brothers and sisters. This strengthens the hypothesis that genetic factors are important in the causation of pyloric stenosis, though environmental factors must also play a part.

We are grateful to the members of the staff of The Hospital for Sick Children and of the Children's Department of St. Thomas's Hospital, for access to the patients under their care; and we are indebted to Dr. J. A. F. Roberts and Dr. Martin Bodian for reading this paper and making valuable suggestions.

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TREATMENT OF THYROTOXICOSIS WITH POTASSIUM PERCHLORATE

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PERCHLORATE prevents the accumulation of inorganic iodide in the rat's thyroid (Wyngaarden et al. 1952); and in man 100 mg. of potassium perchlorate has inhibited the uptake of radio-iodine for about six hours (Stanbury and Wyngaarden 1952).

Godley and Stanbury (1954) have now used potassium perchlorate successfully in the treatment of 24 cases of thyrotoxicosis. Symptoms were relieved, and the basal metabolic rate and plasma protein-bound iodine fell to normal levels. Their observations encouraged us to undertake a clinical trial of potassium perchlorate in the hope that it might prove effective in controlling thyrotoxicosis, without exposing the patient to the risk of the toxic side-effects sometimes seen with the thiouracil drugs.

Perchlorate acts only on the iodide-concentrating mechanism of the thyroid. Thiouracil, on the other hand, leaves this mechanism unaffected but prevents the oxidation of iodide and its subsequent incorporation into protein molecules to form thyroglobulin. Thiouracil is therefore effective whatever the concentration of iodide in the blood; but perchlorate would become ineffective with blood-iodide levels sufficiently high to raise the concentration within the thyroid to the level normally attained by the gland's iodide-concentrating mechanism. In such circumstances the concentrating mechanism would become redundant and drugs which act only on it could have no effect on hormone synthesis. Hence a patient whose thyrotoxicosis is controlled by perchlorate would be liable to relapse if his blood-iodide level were suddenly raised, for example, by the administration of an iodide-containing cough medicine. This is a theoretical difficulty which might arise during perchlorate therapy, but so far we have not observed it. It might also be expected that, if a thyrotoxic patient is prepared for operation with perchlorate, similar difficulties would arise when iodide is added during the final stages to reduce the vascularity of the goitre. Godley and Stanbury (1954) found that patients prepared in this way tended to relapse in the expected manner when given iodides. For this reason we have not attempted to use perchlorate for preoperative preparation but have reserved it for patients whose thyrotoxicosis is to be treated by drugs alone.

Since perchlorate has a simple and relatively non-reactive molecule, it seemed reasonable to hope that it would not provoke hypersensitivity reactions (drug fevers, rashes, agranulocytosis, and so on), such as are observed from time to time in patients treated with any of the drugs related to thiouracil. On the other hand, it might have other unexpected properties. Godley and Stanbury (1954), treating 24 cases of thyrotoxicosis, twice observed gastro-intestinal symptoms which might have been due to the perchlorate. In one patient perforation of a duodenal ulcer was thought to have taken place; but, since the patient was treated medically, the diagnosis cannot be considered proved, and these workers were uncertain whether the event was related to perchlorate therapy or not.

The object of the present trial was to find out whether potassium perchlorate is effective, safe, and suitable for routine use in the medical treatment of thyrotoxicosis. Its effect on untreated cases has been compared with

that of methyl thiouracil and methimazole because these are the two drugs of which we have most experience. In addition potassium perchlorate has been substituted for methyl thiouracil in a group of patients already under treatment.

Methods

Potassium perchlorate was made up in tablets containing either 50 mg. or 200 mg. These were administered either once or twice daily.

The patients were usually seen at monthly intervals, when body-weight and resting pulse-rate were recorded. In previously untreated cases the plasma-cholesterol level was estimated initially and again after three or four weeks' treatment. In some cases, both untreated and those already receiving methyl thiouracil or methimazole, a white-cell count was made before starting perchlorate and repeated a month later. In some patients the efficiency of the perchlorate dosage was tested by measuring radio-iodine uptake; this was expressed either as % uptake at twenty-four hours or as the ratio of neck counts to thigh counts (neck-thigh ratio) an hour after the radio-iodine had been given.

25 patients had had no previous treatment for their thyrotoxicosis; 10 had previously completed a course of methyl thiouracil but had subsequently relapsed; 64 were receiving methyl thiouracil up to the time when perchlorate was started; and 9 were receiving methimazole. The diagnosis was based on the clinical findings but had been confirmed in all the cases either by measurement of radio-iodine uptake or by a known response to methyl thiouracil or methimazole.

Results

EFFECTIVENESS

Clinical improvement was observed in all the cases of previously untreated thyrotoxicosis. An example of

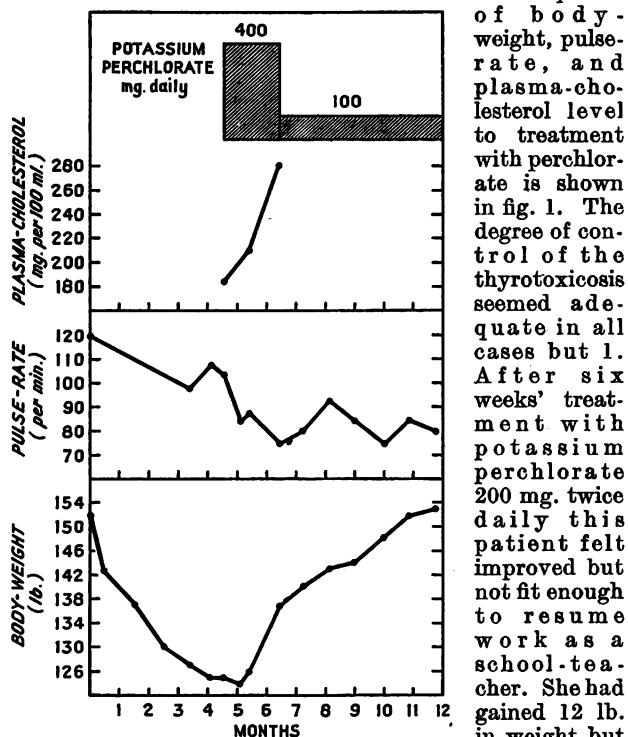


Fig. 1.—Changes in plasma-cholesterol, pulse-rate, and body-weight in a patient with thyrotoxicosis before and after treatment with perchlorate. She had been under observation for loss of weight before thyrotoxicosis was diagnosed and confirmed by radio-iodine test.

* In receipt of a grant from the Sir Halley Stewart Trust.

EFFECT OF TREATMENT FOR 3-4 WEEKS ON BODY-WEIGHT AND PLASMA-CHESTEROL LEVEL IN PREVIOUSLY UNTREATED PATIENTS WITH THYROTOXICOSIS

Drug	Dosage (mg. daily)	No. of cases	Body-weight (lb.)		Plasma-cholesterol level (mg. per 100 ml.)	
			Initial (mean and s.e.)	Increase (mean and s.e.)	Initial (mean and s.e.)	Increase (mean and s.e.)
Methyl thiouracil	200	25	117 ± 3.4	3.4 ± 0.9	142 ± 7.2	57 ± 6.8
Methimazole	20	14	125 ± 3.6	3.8 ± 1.1	144 ± 10.4	43 ± 8.2
Potassium perchlorate	400	16	123 ± 3.1	2.9 ± 0.9	142 ± 7.5	31 ± 7.5

The mean increase of plasma-cholesterol level is less in patients treated with potassium perchlorate than in those treated with methyl thiouracil ($P < 0.01$). Other differences are not significant.

hours was 15% of a tracer dose. She was then changed to a combination of 200 mg. of potassium perchlorate plus 10 mg. of methyl thiouracil twice daily. After four weeks on this régime she gained a further 5 lb. in weight and resumed work without symptoms.

Although it proved possible to control thyrotoxicosis in all the other fresh cases, we gained the impression that the rate of response was less than in patients taking 200 mg. of methyl thiouracil daily. This impression is supported by the data shown in the accompanying table. The rise in plasma-cholesterol level in the patients treated with potassium perchlorate is significantly less than in those treated with methyl thiouracil.

The effect on body-weight and pulse-rate of changing from methyl thiouracil to potassium perchlorate is shown in fig. 2. A small decrease in mean body-weight and an increase in mean pulse-rate occurred in the first two months after the change-over. Both functions

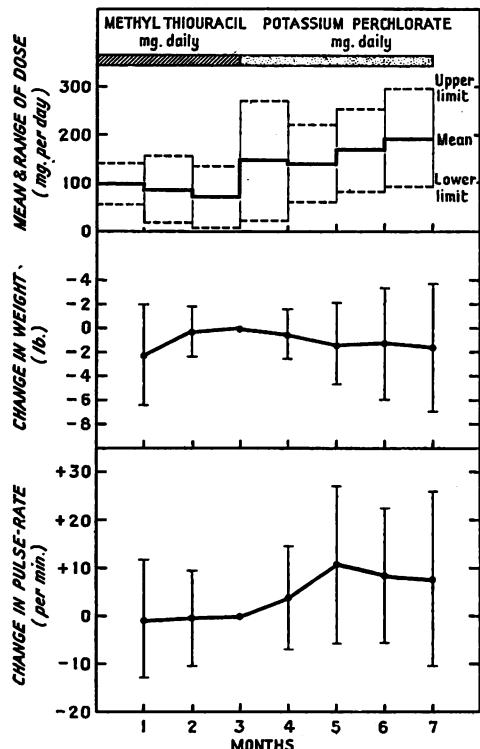


Fig. 2—Changes in mean body-weight and pulse-rate in 64 patients with thyrotoxicosis who had been treated with methyl thiouracil, which was changed to what were thought to be equivalent dosages of potassium perchlorate. The limits shown are 1 standard deviation from the mean.

appeared to become stabilised after a further increase in dosage. Comparison of the dosages of the two drugs needed for control is complicated by the fact that the dosage of methyl thiouracil was decreasing at the time of the change-over. The change-over was made during the months of August, September, and October; this is a time of year when the dose necessary for control is believed to decrease (Morgans and Trotter 1949). Obviously only a crude comparison of the two drugs can be made, but it seems safe to say that the effective dosage of potassium perchlorate is from two to four times that of methyl thiouracil.

The decrease in weight and the increase in pulse-rate seen in the mean figures are mainly derived from 2 exceptional cases. One case in particular is notable in that the patient had been well controlled with moderate doses of methyl thiouracil but became severely thyrotoxic when changed to potassium perchlorate. The behaviour of her weight and pulse-rate is shown in fig. 3. It seems likely that in her case effective control will be achieved

by the combined use of small doses of the two drugs. While she was taking 400 mg. of potassium perchlorate twice daily, her uptake of radioiodine at twenty-four hours amounted to 10% of a tracer dose. In 9 other patients whose symptoms were controlled with 200 mg. twice daily, radioiodine uptakes at twenty-four hours were 10-19%; where only the neck-thigh ratios were measured at one hour the values were low normal or subnormal. In 1 exceptional case, a man

with thyrotoxicosis only partly controlled with 200 mg. of perchlorate twice daily, the uptake at twenty-four hours was 40%. His dosage has now been increased to 400 mg. twice daily; if this proves insufficient, he will be treated with a combination of perchlorate and methyl thiouracil. These are the only 2 cases in which the control of thyrotoxicosis with perchlorate has been unsatisfactory compared with the control attained with methyl thiouracil or with methimazole.

Among 108 patients treated with potassium perchlorate signs suggesting myxoedema have only once been observed; and enlargement of the goitre has been inconspicuous. These observations are compatible with the impression that perchlorate in the dosages we have used is a somewhat less potent anti-thyroid agent than methyl thiouracil.

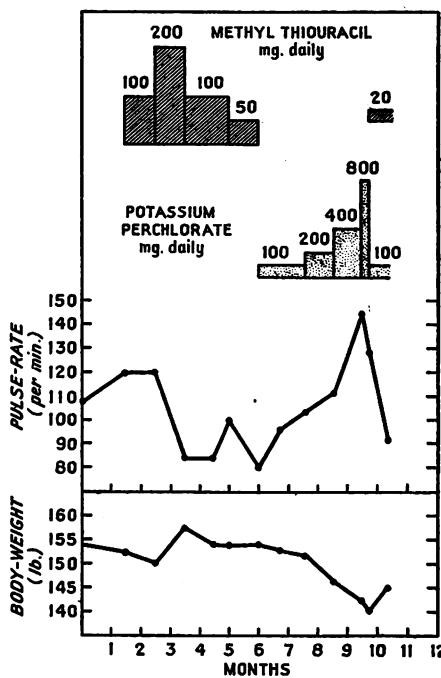


Fig. 3—Changes in pulse-rate and body-weight in a patient with thyrotoxicosis who had relapsed after a remission following a previous course of anti-thyroid treatment. Her thyrotoxicosis was controlled with methyl thiouracil but relapsed when potassium perchlorate was substituted. Since an increasing dosage of perchlorate did not control her thyrotoxicosis, she is being treated with a small combined dosage of methyl thiouracil and potassium perchlorate.

TOXIC EFFECTS

Among 358 cases of thyrotoxicosis treated by us with methyl thiouracil toxic effects have been noted in 9%; in two-thirds of these the methyl thiouracil had to be discontinued. The incidence of toxic effects among 23 cases treated with propyl thiouracil and 45 cases treated with methimazole was not significantly different. The reactions observed include drug fever, rashes, leucopenia, polyarthritis, and peripheral neuritis. Agranulocytosis was seen in 1 patient treated with propyl thiouracil and in 2 out of 53 cases treated with thiouracil.

None of these toxic effects has been seen among 108 cases treated with potassium perchlorate for from one to ten months. Leucopenia was not found in any of the 84 patients in whom white-cell counts were made before and after a month's treatment with perchlorate.

In view of Godley and Stanbury's (1954) experience a careful watch has been kept for indications that perchlorate might be a gastro-intestinal irritant. 2 patients have had gastric symptoms while taking perchlorate:

(1) A woman, aged 56, had had indigestion intermittently for the previous five years. This had been troublesome two years previously when thyrotoxicosis was first diagnosed. Under treatment with methimazole, and later methyl thiouracil, her gastric symptoms disappeared. They returned on changing from methyl thiouracil 50 mg. daily to potassium perchlorate 50 mg. twice daily. Epigastric pain came on half an hour after food, and there was occasional vomiting. Perchlorate was stopped after a month, and methyl thiouracil was substituted. The dyspeptic symptoms disappeared, but they reappeared when perchlorate was tried again a month later. Treatment with methyl thiouracil was therefore resumed. A barium swallow and meal showed a fair-sized sliding diaphragmatic hernia. During treatment with perchlorate there were no signs of thyrotoxicosis, and the patient's weight was steadily increasing at a slow rate.

(2) Another woman, aged 61, had had epigastric pain after meals intermittently for the previous three years. About three years previously she had had melena. This was shortly before thyrotoxicosis had been diagnosed. The dyspepsia had not been troublesome during treatment with methyl thiouracil, but the patient had never been wholly free from it. On changing from methyl thiouracil 50 mg. daily to potassium perchlorate 50 mg. twice daily she did not notice any increase in dyspepsia. A month after the change-over she did not complain of gastric symptoms but had lost 3 lb. in weight. The dosage of potassium perchlorate was increased to 200 mg. once daily. She did not notice any increase in her dyspepsia, but a month later she was admitted to another hospital with a severe haematemesis. Laparotomy was done on the day of admission, but no ulcer was found. Two weeks later gastroscopy showed a small healing superficial ulcer on the lesser curve of the stomach. Two months after the haematemesis (no perchlorate having been taken in the interval) she was still getting some epigastric pain, with occasional vomiting. She is now being treated with methyl thiouracil, although it seems unlikely that the perchlorate was the cause of her haematemesis.

2 other patients who are known to have had peptic ulcers in the past had no gastric symptoms while taking perchlorate.

Discussion

Thyrotoxic patients, treated with potassium perchlorate 400 mg. daily, have on the whole responded satisfactorily. We think that the average rate of response has been somewhat slower than is usually seen after treatment with methyl thiouracil 200 mg. daily. This was only important in 1 of 25 fresh cases treated; this patient's ability to resume work was delayed, and she was therefore given a small dosage of methyl thiouracil (20 mg. daily) in addition to perchlorate. The rapid abolition of thyrotoxicosis is not always necessary or

even desirable, but in a situation where speed of recovery is important (as in thyrotoxicosis complicated by cardiac failure) it might be unwise to rely on perchlorate alone. Changing over another series of patients from methyl thiouracil to potassium perchlorate has shown that the equivalent dosage of potassium perchlorate is from two to four times as great as that of methyl thiouracil. But even on this dosage occasional patients (2 out of 64 in our series) were not so well controlled with perchlorate as they had been with methyl thiouracil. The general conclusion from our experience is that potassium perchlorate is perfectly satisfactory for controlling thyrotoxicosis in most cases, but in a few it is not completely effective. The possibility of using a combination of small dosages of perchlorate and methyl thiouracil in such cases seems worth exploring; since the two drugs act at quite different points in hormone synthesis they might well have a synergistic action.

Toxic effects from potassium perchlorate have been inconspicuous. Hypersensitivity reactions were not observed among our 108 cases, and are not to be expected on theoretical grounds. It is possible, but not yet proved, that potassium perchlorate can act as a gastric irritant in some people.

Potassium perchlorate has the advantage of being cheap. Enough tablets to treat a patient at a dosage of 400 mg. daily for a month cost 2d. This is from a tenth to a three-hundredth of the cost of equivalent doses of other anti-thyroid drugs in common use.

Our experience with potassium perchlorate has encouraged us to continue using it and to recommend it as worthy of further trial. The only reservations we wish to make are that it is unsuitable for use in combination with iodides for preoperative preparation; that in a few cases it has proved relatively ineffective; and that the possibility that it is a gastric irritant for some people has not yet been excluded.

Summary

Potassium perchlorate inhibits thyroid function, but its action is quite different from that of thiouracil. Perchlorate prevents the thyroid from concentrating iodide, whereas thiouracil and related substances prevent the synthesis of thyroglobulin.

When tested clinically, potassium perchlorate in a dosage of 400 mg. daily was effective in controlling thyrotoxicosis in most patients. The rate of response appeared to be somewhat slower than with methyl thiouracil, and 1 out of 25 previously untreated cases was not completely controlled.

When patients on maintenance doses of methyl thiouracil were changed over to potassium perchlorate, effective control of the thyrotoxicosis was maintained in all but 2 of 64 cases. The average dosage necessary was from two to four times as great as that of methyl thiouracil.

No toxic effects were seen in 108 patients treated with potassium perchlorate, except for possible signs of gastric irritation in 2 patients, both of whom had a previous history of dyspepsia.

We are very grateful to Dr. A. F. Godley and Dr. J. B. Stanbury for letting us see a copy of their paper in advance of publication, and to Dr. Stanbury for a very helpful discussion on perchlorate therapy. We also wish to thank Mr. W. H. Bruce, of the dispensary staff, for making the potassium perchlorate tablets, and for ascertaining the price of various anti-thyroid drugs. Messrs. Ward, Blenkinsop & Co. Ltd., supplied the methimazole.

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CEREBRAL SALT WASTING

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LECTURE IN PHYSIOLOGY IN THE UNIVERSITY OF
BIRMINGHAM

EXCESSIVE renal loss of sodium is usually studied with primary reference to either adrenal or pituitary insufficiency or renal disease. Welt et al. (1952) call attention to the possibility, first recognised by Claude Bernard (1858), of a more direct relationship between the central nervous system and the renal excretion of osmotically active solutes. These workers reported six cases of widely varying forms of cerebral disease (trauma, neoplasm, and infection) all of which exhibited an extreme degree of clinical dehydration, low serum-sodium levels, a negative balance of sodium of renal origin, and a lack of associated potassium retention. The patients responded only to the administration of sodium chloride, deoxycortone not reversing the renal loss of sodium; and their eosinophil-counts were distinctly lower after the administration of adrenaline. This evidence, together with their excretion of electrolytes, led Welt et al. to conclude that neither pituitary nor adrenal insufficiency played any part in the syndrome, and to postulate an interference with direct neural control of renal tubular reabsorption of sodium. In view of the work of Kaplan and Rapaport (1951) on dogs they suggested that the cause might be a failure of proximal tubular reabsorption, leading to an "osmotic" diuresis in the distal tubule. The work reported here consists of balance studies in a case resembling those reported by Welt et al.

Case-history

A housewife, aged 43, was admitted to hospital with eight weeks' history of generalised headaches and blurring of vision, and three weeks' history of generalised abdominal pain and vomiting, without either comatose or ataxic episodes.

On admission the only abnormal findings were papilloedema, restlessness, and transient periods of disorientation. Soon after admission the patient experienced two grand-mal convulsions. Ventriculography revealed a mass in the region of the right posterior thalamus and hypothalamus shifting the third ventricle to the left and closing off the entrance to the aqueduct, with resulting hydrocephalus.

Progress.—The patient began to show signs of clinical dehydration, with a serum-sodium level of 128 m.e.q. per litre (294 mg. per 100 ml.), and a serum-potassium level of 4.8 m.e.q. per litre (18.7 mg. per 100 ml.). Simultaneously she became semicomatose, being capable of verbal response only to the simplest shouted questions, and developed ophthalmoplegia. In an attempt to correct both the dehydration and the hyponatraemia, her salt intake was gradually increased over several days, until it was about 15 g. a day, without the desired effect. By this time she was incontinent and required feeding by stomach-tube. To study her condition more fully and to determine accurate values for replacement therapy, she was put on to a constant daily intake of less than 2.5 m.e.q. of sodium (with the use of 'Casilan') for two electrolyte-balance studies, one lasting three and the other nine days. Twenty-four-hour collections of urine were made under paraffin and toluene through an indwelling catheter, and she was treated with chloramphenicol to prevent urinary infection. No faeces were passed during any of the balance periods, presumably owing to the purified fluid diet.

Investigations.—Samples of blood were taken daily for the estimation of chloride, sodium, and potassium levels in the serum. The urine was examined for its specific gravity and the estimation of its content of chloride, sodium, potassium, creatinine, 17-ketosteroids, 17-hydroxysteroids, and gonadotrophin. The nine-day balance study was made as follows: first three days no treatment; fourth, fifth, and sixth days corticotrophin 30 mg. six-hourly; seventh, eighth, and ninth days deoxycortone acetate 5 mg. a day. On the tenth day she was put back on to an intake of 15 g. of sodium chloride.

Eosinophil-counts were made after the administration of intramuscular corticotrophin and after that of subcutaneous adrenaline before any hormone therapy.

Outcome.—The patient died three and a half weeks after the balance studies in gross dehydration, hypotension, and circulatory failure with terminal shock.

Necropsy Findings

The suprarenal glands weighed 24 g. and appeared normal; the pituitary gland also appeared normal. There was a small right parietal subdural abscess under the burr hole, but there were no signs of increased pressure, and the convolutions of the brain were clearly visible.

Histologically the liver showed acute fatty infiltration, with focal necrosis, predominantly centrilobular. The kidneys showed well-marked arteriosclerotic change (without evidence of arterial obstruction), congested medulla, and little vascular filling of the cortex. The pituitary stain showed patchy areas of fibrosis and scarring of the anterior lobe, but adequate normal cellular patterns; the posterior lobe was intact. The lungs showed suppurative bronchiectasis at the right base, with fibrosis and bronchopneumonia. Thigh muscle showed diffuse atrophy. The suprarenal glands showed focal nodular hyperplasia, with lipid depletion in the zona fasciculata ("stress" change of Selye). In the brain, there was a pleomorphic glioma (predominantly astrocytoma) in the posterior part of the right thalamus, extending down to distort, but not directly to involve, the right posterior part of the hypothalamus. Its gross position is shown in fig. 1. A mid-brain section (fig. 2) shows an area of demyelination in the region of the right thalamo-olivary tract, involving the fibres adjacent to this tract and including the medial longitudinal fasciculus and the surrounding reticular substance carrying the descending fibres from the hypothalamus (Clark 1947). The area of demyelination ended at the rostral border of the medulla, and there were no signs of degeneration below that. No other abnormalities were found.

Results of Electrolytic-balance Studies

All the calculations are based on the chloride space assumptions set out by Gamble (1951). Table I shows the results of the nine-day balance study.

Cumulative balances.—On withdrawal from a sodium chloride intake of 15 g. a day, the patient was in negative balance of 100 m.e.q. of Na, and 70.2 m.e.q. of K for the first twenty-four hours. Thereafter she settled down to a steady loss of 60–70 m.e.q. of Na and 30–50 m.e.q. of K a day, and this urinary excretion was unaffected by either corticotrophin or deoxycortone. McCance's (1936) study of Na deprivation in normal man has shown that in eleven days on a Na intake of 1.5–2.5 m.e.q. a day the subjects came into balance by the fifth day and were in positive balance from the sixth to the eleventh day.

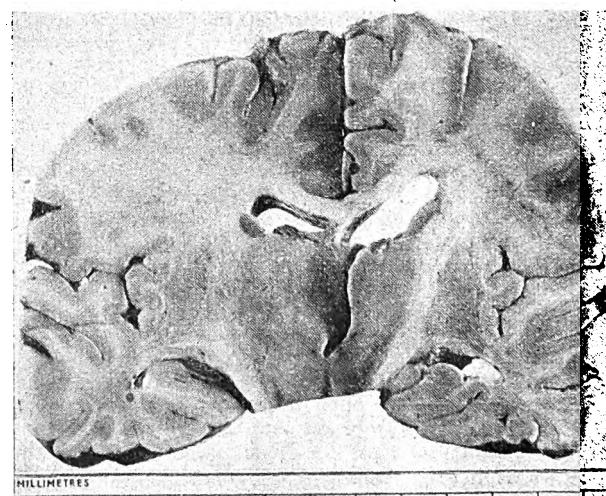


Fig. 1.—Section of brain, showing tumour in right side of thalamus and encroaching on third ventricle.



Fig. 2.—Section of mid-brain just anterior to the pons, showing large area of demyelination (unstained area in silver preparation) in region of right thalamo-olivary tract. Descending hypothalamic fibres are supposed to run in reticular substance just medial and superior to obvious demyelination, ventral to the aqueduct.

Serum levels.—The serum-sodium level fell from 128.3 to 108.6 m.eq. per litre and the serum-potassium level from 4.8 to 3.4 m.eq. per litre during the period of Na deprivation. Both values were restored towards normal by the administration of 15 g. of sodium chloride on the tenth day.

Extracellular fluid shifts.—The calculated amounts of extracellular cation changed in the case of Na from a positive balance of 79 m.eq. on the first day to 15 m.eq. on the ninth day. The "intracellular" balance of K remained negative throughout at 23.63 m.eq. a day. The possible significance of these calculations is discussed below.

"Intracellular fluid" shifts.—The calculated amounts of intracellular cation changed in the case of Na from a positive balance of 79 m.eq. on the first day to 15 m.eq. on the ninth day. The "intracellular" balance of K remained negative throughout at 23.63 m.eq. a day. The possible significance of these calculations is discussed below.

Chloride space is calculated from serum-chloride levels and the external chloride balance expressed as an absolute volume of extracellular fluid lost or gained. The patient showed a decreasing loss of volume of extracellular fluid from 1.4 litres on the first day to 690 ml. on the ninth day. After the addition of sodium chloride to the diet on the tenth day there was a calculated gain of about 1 litre of extracellular fluid.

Volume and specific gravity of urine were within normal ranges and showed no significant changes throughout the period of sodium deprivation. There was no polyuria or other evidence of faulty reabsorption of water. The urine was at all times free from protein, cells, casts, and bacteria on microscopy.

Creatinine excretion decreased progressively from 1.0 g. a day to 0.7 g. a day over the balance period and rose again to the initial value following the addition of sodium chloride to the diet.

Blood-pressure.—Both systolic and diastolic pressures showed a slight tendency to fall during the balance period but not to any significant extent.

Other urinary excretion.—The excretion of 17-ketosteroids was 8 mg. a day. The normal for a woman aged 40-50 is 4-10 mg. a day (Hamburger 1948). The excretion of 17-hydroxysteroids was 7.7 mg. a day, which is within the normal range. Gonadotrophins: equivalent as glycine, 60 mg. an hour (normal 25-200

TABLE II.—EOSINOPHIL-COUNTS

Time	No. of eosinophils per c.mm. in relation to injection of			
	Corticotrophin		Adrenaline	
	Before	After	Before	After
10 A.M.	..	98	..	65
2 P.M.	..	30	..	51

μg. an hour); equivalent as glucose, 300 μg. an hour (within normal range).

Eosinophil-counts are shown in table II.

Discussion

The defect that has been to some degree measured in this patient involves a serious renal loss of electrolyte, particularly sodium, and a concomitant loss of extracellular fluid, the latter effect being further complicated by failure to maintain extracellular osmotic pressure. As may be expected with a loss of circulating extracellular fluid, the glomerular filtration-rate, assessed from the total excretion of creatinine, seems to have fallen by 30% during the depletion of extracellular fluid

TABLE I.—RESULTS OF ELECTROLYTE-BALANCE STUDY

Day	Serum Na (m.eq. per litre)	External Na balance (m.eq. daily)	Serum K (m.eq. per litre)	External K balance (m.eq. daily)	Chloride space (litre)	E.C.F. Na balance (m.eq. daily)	E.C.F. K balance (m.eq. daily)	"I.C.F." Na balance (m.eq. daily)	"I.C.F." K balance (m.eq. daily)	Urine vol. (litres)	Urine sp. gr.	Creatinine excreted (g. daily)	Blood-pressure (mm. Hg)	Treatment
1	128.3	-100	4.8	-70.2	-1.4	-179.8	-6.7	+79.8	-63.5	1.94	1.021	1.0	145/80	None
2	120.4	-84	4.7	-55	-1.2	-110	-4.3	+48.0	-23.7	1.68	1.038	0.76	138/78	
3	120.4	-62	4.7	-28	-0.91	-110	-4.3	+48.0	-23.7	2.23	1.018	0.78	130/65	
4	117.8	-61	3.8	-34	-0.91	-98.9	-3.2	+30.9	-25.8	1.48	1.041	0.76	128/74	
5	117.8	-68	3.8	-29	-0.84	-98.9	-3.2	+30.9	-25.8	1.51	1.039	0.74	126/72	Corticotrophin
6	117.8	-67	3.8	-46	-0.74	1.58	1.038	0.72	124/68	
7	109.5	-66	3.6	-57	-0.70	-76.7	-2.5	+10.7	-54.5	1.91	1.021	0.70	132/68	
8	109.5	-58	3.6	-38	-0.71	-75.0	-2.4	+15.0	-29.6	1.82	1.027	0.72	128/69	Deoxycortone
9	108.6	-60	3.4	-32	-0.69	-75.0	-2.4	+15.0	-29.6	1.80	1.029	0.72	138/74	
10	118.3	..	5.6	..	+1.1	+131	+6.2	1.18	..	Sodium chloride

E.C.F., extracellular fluid.

"I.C.F.", intracellular fluid (external balance minus E.C.F. balance). -

(Cort 1952). One would expect that a falling glomerular filtration-rate would, if anything, have decreased the excretion of sodium (Warren and Stead 1944) and, far from explaining the renal loss of sodium, would tend to ameliorate this loss. The blood-pressure might be expected to fall with a decreasing volume of extracellular fluid, and indeed a slight tendency in this direction was noted. The increase in intracranial pressure, produced by the tumour, might have tended to counteract this particular change.

The absence of any signs of renal disease other than electrolyte wasting during the electrolyte-balance study before the development of terminal shock seems to indicate that the salt loss was probably due to some external influence on renal function. A lack of retention of potassium, associated with the loss of sodium and with the high normal excretions of 17-ketosteroids and 17-hydroxysteroids and gonadotrophins, would further the argument in suggesting that this extrarenal influence was not of adrenal or pituitary origin. This suggestion is further supported by the lack of response to corticotrophin and to deoxycortone.

The interpretation of the eosinophil-counts is difficult. The base-line counts were rather low, an unusual finding in pituitary or adrenal insufficiency, and there was a significant response to corticotrophin, further evidence against adrenal disease. The response to adrenaline, though a decrease, was not significant, which might suggest an interruption in some hypothalamic-anterior pituitary relationship. However, Thorn et al. (1951) cast doubt on the interpretation of eosinophil-counts by showing significant decreases in the numbers of circulating cells after the administration of adrenaline to two known addisonian patients. Moreover, the subcutaneous administration of adrenaline involves local vasoconstriction and therefore a variable rate of absorption into the circulation from the peripheral site. If the true significance of the test could be established, perhaps it would be better to give the test dose of adrenaline intravenously, provided there were no contra-indications for such a procedure. With the exception of the adrenaline test, the entire body of data does not seem to agree with any of the known manifestations of adrenal insufficiency. Despite the areas of fibrosis in the anterior lobe of the pituitary gland there was adequate functional tissue by histological criteria.

Until recently Gamble (1951), using chloride-space assumptions, advocated equating the difference between the external and the extracellular fluid balances with the balance of intracellular fluid. If this were true, on the first day of the balance study, for example, 79 m.eq. of Na moved into cells, while only 63 m.eq. of K moved out. On the basis of the recent work by Cooke et al. (1952), suggesting that K can exchange with either Na or H at the cell membrane, the cellular exchange could be brought into balance by postulating a movement of 16 m. eq. of hydrogen ion out of cells, leaving the patient with an intracellular alkalosis and an extracellular acidosis. However, the recent demonstration that 20% of bone Na can leave bone in Na depletion (Bergstrom 1952), and the unknown quantitative nature of this exchange, make the derivation of intracellular fluid composition from balances alone very hazardous. Muscle biopsy is needed to obtain accurate data on intracellular composition of the largest cellular mass in the body.

Welt et al. (1952) suggested that the most probable explanation of the mechanism of Na loss in the kidney was decreased proximal tubular reabsorption. Since the proximal tubules usually reabsorb 85% of the electrolyte delivered to it (Walker et al. 1941), a small decrease in efficiency would present the distal tubule with a large amount of osmotic material, and might lead to an "osmotic" distal tubular diuresis. The importance of tubular locus in this discussion lies in the differentiation between hormonal and nervous mechanisms of control

of tubular function. The action of adrenal cortical steroids seems to be in the distal tubule (Smith 1951), and Kaplan and Rapaport (1947) have argued that the salt-losing syndrome produced in dehydrated dogs with denervated kidneys is due to a proximal tubular defect. No pertinent data can be presented in the present case to assist this differentiation of tubular locus. A hypertonic glucose diuresis was produced to measure the effect of such a procedure on Na excretion; but, until more data are collected from normal people and similar cases under exactly comparable conditions, little can be said of the results.

The necropsy findings in this case have been more helpful than any in the series of Welt et al. (1952), since the lesion was small enough to permit of some localisation. Both the tumour and the area of demyelination in the mid-brain were in a position to interrupt the descending fibres of both the anterior and the posterior parts of the hypothalamus. The limitation of the lesion to one side is interesting in view of Bernard's (1858) original observation that a unilateral lesion in the reticular substance at the floor of the fourth ventricle produced a diuresis of Cl without a diuresis of glucose, and that a bilateral lesion merely intensified the effect. Bernard reproduced this syndrome by renal denervation. There may be, then, a nervous connection between the hypothalamus and the proximal tubule of the kidney which influences electrolyte reabsorption. This possibility is now being actively investigated in experiments on animals.

Summary

A patient with a right posterior thalamic tumour and extreme clinical dehydration was studied by the technique of electrolyte balances, and was found to be in negative balance of both sodium and potassium. Tests of adrenal and pituitary function were normal, and the administration of corticotrophin and of deoxycortone did not affect the syndrome. The condition might be due to an interruption in hypothalamic-renal pathways affecting electrolyte reabsorption.

I wish to thank Mr. E. A. Turner, F.R.C.S., of the department of neurosurgery at the Queen Elizabeth Hospital, Birmingham, for his interest in the case, and for his permission both to study the patient and to publish the results; Dr. W. T. Smith, of the department of pathology at the hospital, for help with the histological examinations; and Miss Pamela Dawson for the biochemical determinations.

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" . . . The time has not yet come when there is a couch under every patient, nor a psychiatrist by every bed, but . . . the time has come when we must accurately determine whether the incidence of mental illness in minor and major forms is truly great enough, as the psychiatrists claim, to justify their demands for more and more teaching hours in the medical curriculum and ever expanding facilities and personnel. If such as they claim be so, then we must do all in our power to facilitate their emergence from behind their mahogany desks and tape recorders and get them out into the homes and sickrooms where they can do the most good!" —J. W. REID, *Canad. med. Ass. J.*, March, 1954, p. 337.

JUVENILE SPRING ERUPTION

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ON April 4, 1953, 150 children arrived at a holiday camp at Ewhurst in Surrey. Of these children 81 were boys and 69 girls. Their ages ranged between 8 and 11 years.

The children came from three schools in the London districts of Lambeth, Dulwich, and North Kensington. On arrival none of them showed any gross skin abnormalities, but on April 7 bullous lesions were noticed on the ears of some of the boys. This outbreak was reported by the sister in charge to the visiting medical officer (E. I. B. H.).

By April 12 the outbreak had spread through the camp, and 96% of the boys and 76% of the girls were affected.

DISTRIBUTION AND CLINICAL FEATURES OF JUVENILE SPRING ERYTHEMA IN CHILDREN

School	Dulwich	Lambeth	North Kensington
Sex	Girls	Girls	Boys
No. of children	27	42	39
No. affected	23 (85%)	30 (72.5%)	37 (95%)
Classification of ear lesions:			
Severe (bullous)	0%	0%	3%
Moderate (papules and vesicles)	35%	47%	73%
Mild (papules and erythema)	26%	0%	24%
Slight (erythema and scaling)	38%	53%	0%
Lesions on hand	1

(see table). The lesions appeared on the girls' ears about a week later than on those of the boys.

On April 14 2 of the boys were sent to St. John's Hospital for Diseases of the Skin for diagnosis, and on this occasion investigations were made to exclude any infective element. Before the investigations were completed the matter was reported to the L.C.C. medical authority, who advised that the camp should be dispersed because it was considered by them that this might be an unusual virus infection, possibly herpes simplex. The children returned to their homes on April 18. Some of the children had residual lesions on their ears; these healed, however, within a few days.

Clinical Features

The initial lesion was erythema of the helix. In a few patients this was followed by scaling only. The more characteristic clinical picture was of erythema followed within twelve to twenty-four hours by the appearance of oedematous papules or macule papules. These were deep red and in some instances showed concentric rings.

There were also smaller papules, sometimes of only pinhead size. The larger papules were sometimes surrounded by a small vesicle (fig. 1) or, less frequently, became bullous. These bullæ were complicated by secondary infection, and crusting followed. As the eruption subsided, the ears showed scaling and crusting (fig. 2), but no atrophy.

In 89 of 90 patients the lesions were limited to the ears, and in most of them only the helix and lobule were involved. In some children only one ear was affected. In the more severe cases the antihelix and the tragus were involved, and in 1 patient there were lesions on the back of the hands and the dorsa of the fingers (fig. 3). The appearance of lesions on the hands and the fingers were those of erythema multiforme; and indeed the aural lesions described above may also be considered as a localised form of this disease.

In addition to the skin lesions some of the children had enlarged cervical glands, the greater glandular enlargement being found in those children who had bullous lesions on the ears. At first it was thought that the glandular enlargement was associated with throat infection, because several of the children had enlarged tonsils or inflammation of the fauces; but this was later found to be coincidental.

Investigations

Virus studies were made on vesicle fluid obtained from the patients seen at St. John's Hospital for Diseases of the Skin, and the cytology of the base of the vesicle was examined.

Cytology revealed no evidence of virus infection. There was no evidence of herpes simplex virus in animals inoculated with vesicle fluid.

Historical

The older literature concerning this dermatosis is rather confused, and it seems that little distinction was made between herpes simplex activated by sunlight and this eruption, both of them being described under the heading of *l'herpès des Alpinistes*. Koehler (1938) suggested that the disease was first described by Von Gaal (1858), who described an epidemic in a group of prisoners in Bosnia.

Thibierge and Rabut (1921) described a dermatosis similar to our juvenile spring erythema under the name *une éruption papuleuse et prurigineuse développant*

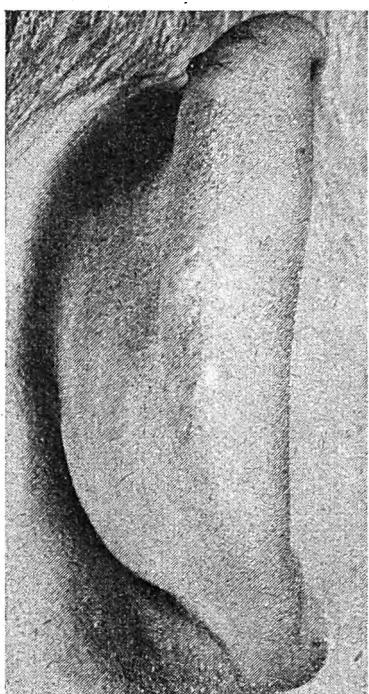


Fig. 1—Papular and maculopapular lesions on ear, showing early vesiculation.

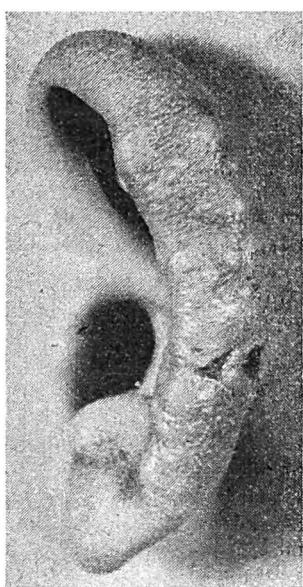


Fig. 2—Bullous lesions on ear, showing crusting.

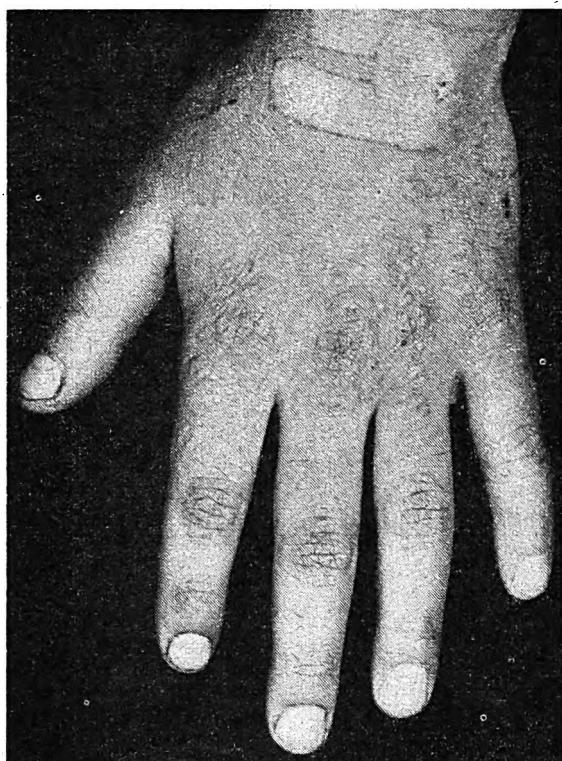


Fig. 3.—Lesions resembling erythema multiforme on hand.

au printemps sur les mains des jeunes sujets. Although in 9 patients the lesions were limited to the backs of the hands and fingers, in 2 of them lesions appeared on the face as well. The patients were aged 5 $\frac{1}{2}$ -12 years, and the eruption lasted from eight days to three weeks. Various plants were suspected as actinological agents causing photosensitivity. These workers mention that in thirty years they had seen one or two instances of this disorder yearly in April and May. It was apparently then known as *prurit vernal des jeunes sujets*.

Jausion and Pagés (1933) mention a somewhat similar disorder in 9 soldiers engaged in gardening. This disease was named *photodermite dysidrosiforme des acrocyano-tiques*.

Koehler (1938) described an outbreak of this dermatosis as an epidemic of erythema exudativum multiforme. He observed 186 men from a German labour camp, some of whom had lesions on the ears and on the backs of the hands. The photographs accompanying Koehler's paper are very like ours. The epidemic was extensively investigated, and a record of meteorological findings in the camp is given for the time of the onset of the epidemic :

Meteorological Findings (evening forecast at 9.25 p.m.)—Wind strength zero. Humidity : rel. 82%, absolute 3.9. Air-temperature 0.3°C. Ground-temperature at 10 cm. depth 6.8°C, at 20 cm. depth 7.5°C.

General Weather Forecast.—Variable cloud and snow several times during the day on higher ground, clear in the evening.

Koehler thought cold was an important factor and did not discuss the influence of sunlight.

Keining (1940) described the same condition under the name "spring perniosis." He believed that its peculiar distribution was to be explained by the fact that the ears and hands are perniotic areas. In particular he describes "capillary stasis" in these areas. Koehler (1938) mentioned that Kaposi (1900) believed that the distribution

of erythema multiforme was according to where capillary stasis developed.

Burckhardt (1942) described the condition as an actinic dermatosis affecting the ears during the spring. In the spring of 1941 and 1942, during a spell of unusually fine weather, he observed the dermatosis among high-school children in Zürich. In a class of 50 boys 44 had papules and crusts and 1 had crusting only of the ears. Among 50 girls, most of whom had their hair over their ears, only 1 had crusts on the ears. A biopsy specimen from 1 patient showed the histological picture of erythema multiforme. Burckhardt believed that the eruption was an actinic reaction, but he could not reproduce the lesions with a Kromayer lamp. Therapeutically he had the impression that nicotinamide produced some relief of the disorder. The idea of using nicotinamide probably derived from the report of Keining and Oldach (1941), who used nicotinamide in the treatment of erythema multiforme.

Discussion

The aetiology of this disorder is still unsettled. The published reports and our own observations seem to show that it is predominantly an actinic reaction.

Among our patients there were more boys than girls, and the boys had a more severe form of the eruption. This is probably because the girls' hair covered their ears, protecting these somewhat from the sunlight.

In this outbreak, as in others, the children had come from city homes, where exposure to direct sunlight was less common than in the country, where they were playing out of doors most of the day.

We were unable to support the idea that the so-called epidemic was due to an infection. In most years sporadic cases of this dermatosis are seen by dermatologists and general practitioners, and the large numbers of cases recorded from this camp were probably due to the fact that all these children were exposed to particular climatic conditions.

Climatic data obtained from the Air Ministry meteorological office for April 4-18, 1953, taken at two stations about twelve miles from the Ewhurst camp, indicate that this was a particularly fine period. On seven of the fourteen days the number of hours of sunshine daily was more than 6.0, and on April 7, when the eruption was first noticed, there were 9.1 hours of sunshine. The wind was mild to moderate on most days. It was rather cold.

From these figures and those of Keining (1940) it is suggested that the combination of sunlight and cold is important.

Hitherto we have been unable to determine whether any particular wave-lengths of light are responsible; nor have we attempted to reproduce the eruption artificially.

Summary

An unusual outbreak of dermatosis mainly affecting the ears occurred in April, 1953, among London schoolchildren sent to a holiday camp in Surrey.

The eruption is thought to have been an actinic reaction precipitated by exposure to sunlight and cold.

We are indebted to Dr. J. A. Dudgeon for the virus investigations.

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WHITE NAILS IN HEPATIC CIRRHOSIS

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PALLOR of the finger-nails is commonly seen in anaemia and with vasoconstriction of the nail bed. The nails themselves become whitened and opaque in leuconychia totalis, which, according to Pardo-Costello (1936), is extremely rare: although it is not associated with any particular disorder, he has seen it in leprosy, trophic disturbances of the extremities, and chronic arsenical poisoning. Other references to leuconychia are similar and also indicate that the opacity is in the nail rather than the nail bed (Howard et al. 1917, Weiss 1918, Pernet 1919, Studenbord and Studenbord 1935, O'Donovan 1938). The present report is concerned with opacity of the nail bed causing *apparent* whiteness of the finger-nails, and its occurrence in cirrhosis of the liver and some other conditions.

Appearance of White Nails

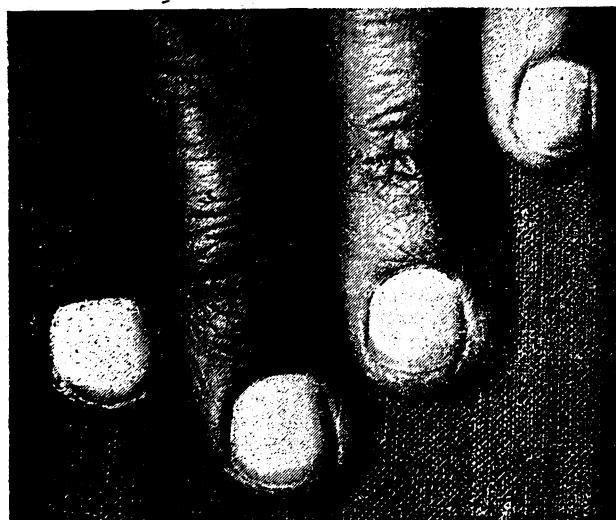
Fully developed white nails exhibit a ground-glass-like opacity of almost the entire nail bed. It extends from the base of the nail, where the lunula is indistinguishable, to within one or two millimetres of the distal border of the nail bed, leaving a distal zone of normal pink. The condition is bilaterally symmetrical, with a tendency to be more marked in the thumb and forefinger. In less "classical" examples the opacity varies widely in degree and distribution (see accompanying figure).

Demonstration of Opacity

Any vasoconstriction of the nail bed is overcome by grasping the penultimate phalanx of the patient's finger or thumb and squeezing blood into the terminal phalanx, while the patient flexes the terminal joint. The normal nail bed becomes congested and, except for the lunula, attains a uniform pink colour varying in intensity with the level of haemoglobin. Any whiteness of the nail bed is unaffected by the congestion and indeed is accentuated by contrast with the congested distal pink zone.

Characteristics of White Nails in Cirrhosis

Prevalence.—White nails were found in 82 of 100 consecutive patients with cirrhosis. The aetiology of the



Finger-nails of case 1 showing well-developed white nails and distal pink zones.

cirrhosis was alcoholic in 91, postnecrotic in 7, and cholangiolitic in 2. The 18 patients without white nails were all among the alcoholic group.

Nails Affected.—In nearly all the cases where white nails were present all the nails in both hands were affected.

Density of Opacity.—The opacity or whiteness of the nails was graded as gross in 6 patients, severe in 23, moderate in 42, and slight in 11. (In this grading gross= lunula indistinguishable, severe=lunula just visible, moderate=lunula easily visible, and slight=opacity just apparent.)

Gradation of Opacity in Same Hand.—All the nails were equally white in 29 patients, but in the remainder there was usually some gradation. Thus the opacity decreased regularly from the thumb to the little finger in 34 and increased regularly in 6. Regular gradations from other fingers were present in 10, and there was complete irregularity in only 3 patients. Whatever the gradation, it was always the same in both hands.

Distal Pink Zone.—The white opacity covered the whole nail bed of all the fingers in some cases, but more usually it stopped short of the finger-tip in one or more nails, leaving a distal pink zone of normal nail bed.

Irregularity of Distal Pink Zone.—The distal border of the opacity was usually well defined and ran across the nail parallel to the end of the nail bed, leaving a regular distal pink zone. In 29 instances, however, the border was uneven in some of the nails, producing an irregular distal pink zone.

Symmetry.—The density of the opacity was often strikingly similar in corresponding fingers in the two hands, and was identical in all five corresponding fingers in 24 patients. Whether the opacity extended to the end of the nail bed or stopped short of it, the corresponding fingers in each hand were usually affected alike. Symmetrical distribution of the opacity was present in all five fingers in 47 patients. Irregular pink zones were present in corresponding fingers in 16 patients. In many instances the irregular distal borders of the opacity in corresponding nails were mirror images of one another.

Other Changes.—Severe longitudinal ridging of the nails was common, as was some thickening. Flattening of the nails, however, was only seen in 2 instances, in contrast to the experience of Kleeborg (1951), who reported its frequent occurrence in cirrhosis.

Correlation.—Of patients with *spider naevi* 37% had severe or gross white nails, compared with 22% of those without naevi. Otherwise no correlation was found with any clinical or laboratory findings.

Further details are shown in the accompanying table.

NUMBER OF NAILS IN EACH HAND EXHIBITING VARIOUS FEATURES OF WHITE NAILS, AS SEEN IN 100 PATIENTS WITH CIRRHOSIS

Character	Number of nails affected in each hand					
	5	4	3	2	1	0
White nails	73	6	1	1	1	18
Distal pink zone	21	14	9	9	12	17
Irregular pink zone	0	3	4	9	13	36
Symmetry of density	24	23	16	14	3	2
Symmetry of distribution	47	16	11	6	2	0

CASE-REPORTS

The following are five typical examples of well-developed white nails in various forms of cirrhosis:

Case 1.—White male aged 44. Chronic diarrhoea for twelve years, aetiology unknown. Huge nodular liver and splenomegaly. Liver biopsy revealed postnecrotic cirrhosis. All the nails exhibited gross opacity with distal pink zones (see figure).

Case 2.—White male aged 72. Postnecrotic cirrhosis with symptoms of hepatic insufficiency for three years. Thumbs showed gross opacity, forefingers severe, middle fingers moderate, and ring fingers slight opacity, while the little fingers were normal. Distal pink zones were present in all the white nails.

Case 3.—Coloured girl aged 16. Hepatosplenomegaly since infective hepatitis at age of 9 years. Postnecrotic cirrhosis following viral hepatitis diagnosed. Chronic ascites present, but no stigmata of cirrhosis. Gross opacity of thumb-nails and severe opacity of other nails. Distal pink zones well marked.

Case 4.—White woman aged 39. Homologous-serum jaundice following multiple blood-transfusions for haemorrhage from placenta praevia at age of 36. Jaundice never cleared completely; gradual downhill course with development of hepatosplenomegaly, persistent ascites, haematemesis, and anaemia. Gross white opacity of all nails, with ivory-like opacity of nails of thumbs and forefingers. Necropsy revealed cholangiolitic cirrhosis.

Case 5.—White man aged 38. Laennec's cirrhosis associated with twenty years' alcoholism. Opacity slight in thumbs, moderate in forefingers, and severe in the rest.

White Nails in Other Conditions

PHYSIOLOGICAL

Many young children aged 1-4 years exhibit various degrees of "classical" white nails, while in perfectly good health and in the absence of any suggestion of hepatic disorder. In all the examples observed in young children the opacity was equal in all the nails, there were a regular distal border and a pink zone, and the intensity was never more than moderate to severe.

Case 6.—Boy aged 2½ years. History and examination were normal apart from one small spider naevus on the hand and well-developed palmar erythema. All the finger-nails showed severe white opacity with narrow distal pink zones of unknown duration. At the age of 3 years the distal pink zones had widened and the opacity was less severe. At the age of 3½ years the opacity had further diminished and was almost graded as slight. In view of this first observation in a child the next case was watched from an earlier age.

Case 7.—A healthy male child, aged 9 months, was found to have no white opacity of the nails apart from the lunula. The nails remained clear until the age of 15 months, when the first suggestion of opaque nail beds appeared, and at the age of 18 months the opacity had become severe.

In normal young women up to the age of 20 some opacity of the nail bed is quite common and occasionally severe.

OTHER DISORDERS

All degrees of whiteness of the nails have been seen in a variety of other disorders, including chronic congestive heart-failure, diabetes (especially in young patients), pulmonary tuberculosis, rheumatoid arthritis, convalescence from viral hepatitis (especially in adolescents), disseminated sclerosis, and some forms of carcinoma. These observations are at present random and few, and a more detailed investigation is being made.

Nature of White Nails

In leuconychia striata and punctata the white areas are in the nail itself, and, as the nail grows, they steadily move towards the finger-tip and are finally eliminated when the nail is cut. Leuconychia totalis is apparently a more diffuse example of the same disorder. These opacities are attributed variously to air-bubbles within the nail, to incomplete keratinisation, or to the persistence of nucleated cells in the nail.

The white opacity described here is entirely different. Neither the white opacity nor the distal pink zone alters as the nail grows. The nail itself is normally transparent, and the opacity evidently results from some change in the nail bed.

The nature of this change in the nail bed is less certain. The lunula is apparently produced by the proximal

portion of the matrix. According to Burrows (1919) the matrix is not so firmly adherent to the underlying vascular connective tissue in the region of the lunula as it is elsewhere, and this separation produces a reflecting surface with apparent opacity. It seems most probable that the opacity of white nails is in the superficial layers of the matrix and is of similar nature to the opacity of the lunula.

Aetiology and Significance of White Nails

The manifestations of cirrhosis include gynaecomastia, spider naevi, cutaneous striae, and palmar erythema. Some or all of these conditions are also seen in children, adolescents, pregnancy, pulmonary tuberculosis, rheumatoid arthritis, congestive heart-failure, and some forms of cancer. If it is accepted that these are manifestations of abnormal steroid metabolism, as many deem likely, then it is conceivable that white nails, which occur in the same range of disorders, may have the same origin.

It has not been possible to relate the presence or absence of white nails or their degree to any of the clinical or other features of cirrhosis of the liver. This lack of correlation is also a feature of the accepted endocrine stigmata of cirrhosis, particularly spider naevi (Bean 1945). It may well be that each separate endocrine stigma reflects the faulty metabolism of a particular adrenal steroid, and that a specific steroid is responsible for the white nails of cirrhosis and other disorders.

Discussion

White opacity of the nail bed giving rise to apparent whiteness of the nails is relatively common and has been observed by me on many occasions in addition to the 82 instances reviewed here. In nearly all these cases the condition of the nails had been entirely overlooked; and in the few where the whiteness had been noted it had been dismissed as due to either anaemia or vasoconstriction. These appear to be the chief reasons for the neglect of white nails as a physical sign.

These nails are common in cirrhosis of the liver and may fairly be added to the list of non-specific physical signs thereof. Their diagnostic value in cirrhosis is limited, since they occur in other conditions, but they are occasionally most helpful in suggesting or corroborating the diagnosis. These remarks are particularly applicable to coloured patients, in whom such signs as palmar erythema and spider naevi are rare or difficult to see.

Apart from young children and adolescents, well-developed white nails have not been seen in healthy people. Their presence is therefore at least a suggestion of ill health, present or impending, and a stimulus for further investigation and observation.

Summary

Opacity of the nail bed with apparent blanching of the nail is common. It was found in 82 out of 100 consecutive patients with cirrhosis hepatitis, and occasionally in certain other conditions.

White nails are easily overlooked; their demonstration and appearance are described.

It is suggested that white nails are endocrine stigmata, comparable with spider naevi, palmar erythema, cutaneous striae, and gynaecomastia.

Well-developed white nails are apparently rare in healthy adults, and their detection may therefore be of some importance.

I wish to thank Dr. R. Bodley Scott for permission to refer to the patient in whom the initial observation of white nails in cirrhosis was made and whose nails appear in the accompanying figure. Nearly all the above observations were, however, made during the tenure of a research fellowship at the Hektoen Institute for Medical Research of the Cook County Hospital, Chicago, granted by the Jerome K. Solomon Memorial Foundation. I am particularly grateful to Dr. Hans Popper and to Dr. Frederick Steigmann, of the Hektoen

Institute, for their advice and encouragement. I am indebted to the photographic department of St. Bartholomew's Hospital for the illustration.

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PSEUDOMONAS PYOCYANEA MENINGITIS SUCCESSFULLY TREATED WITH POLYMYXIN

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SINCE the advent of the polymyxins as therapeutic agents in 1949 little has been published on their use in meningitis caused by *Pseudomonas pyocyanea* (*aerogenes*). Seven cases of meningitis due to this organism treated with one of the polymyxins (of which B and E are the least toxic) have been recorded in the United States (Schoenbach 1949, three cases; Hayes and Yow 1950, Tomlin 1951, Kagan 1952, and Jawetz 1952, one case each). So far as I can discover, no case of *Ps. pyocyanea* meningitis treated with polymyxin has been published in this country. The following case is therefore presented.

Case-record

A boy, aged 5½ years, was admitted to hospital for re-exploration of a cervical-cord ependymoblastoma after a course of deep X-ray therapy. Eight days after operation (Mr. Murray Falconer) he developed a small cerebrospinal-fluid (c.s.f.) fistula at the upper end of the incision, which closed within two days. Two days later (Aug. 24, 1953) he developed meningitis (500–3000 white cells per c.mm.).

Treatment with procaine penicillin 300,000 units b.d. and intramuscular streptomycin 0.5 g. b.d. for four days, followed by oral oxytetracycline 250 mg. eight-hourly for four days, and then with chloramphenicol 500 mg. six-hourly by mouth and 3 g. intrathecally daily for twenty-three days did not produce any sustained clinical improvement.

Culture of c.s.f. on various occasions gave a pure growth of *Ps. pyocyanea*, the sensitivities of which to various antibiotics were as follows:

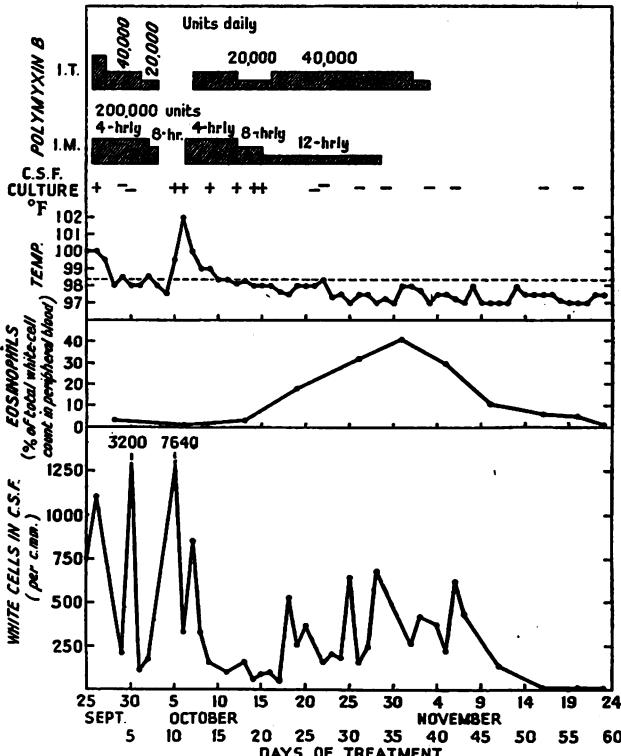
Antibiotic	Organism sensitive	In-vitro concentration
Sulphadiazine	—	10 mg. per ml.
Penicillin	—	100 units per ml.
Streptomycin	—	100 µg. per ml.
Aureomycin	+	100 µg. per ml.
Chloramphenicol	+	50 µg. per ml.
Oxytetracycline	+	50 µg. per ml.
Polymyxin	+	6 units per ml.

Bacteriological Techniques.—The causal organism was isolated from the c.s.f. by inoculating the centrifuged deposit into 50 ml. of glucose broth. During the course of treatment this had the effect of diluting any residual polymyxin, but often growth was not apparent until after forty-eight hours' incubation. Attempts to recover the organism by plating the deposit on solid media failed repeatedly. Initial sensitivity tests were made by the plate method using antibiotic tablets (Evans Medical Supplies Ltd.). Tube sensitivities were determined with doubling dilutions of the various antibiotics in nutrient broth. One drop of a 1 : 300 dilution of an eighteen-hour broth culture was used as the standard inoculum. Results were read after eighteen hours' incubation at 37°C. The sensitivity of the organism to polymyxin was tested again during treatment, and there was no evidence of increased resistance to the antibiotic. Polymyxin levels in the c.s.f. were estimated by the tube method with doubling dilutions of c.s.f. in nutrient broth. The racks were inoculated with a broth culture of *Escherichia coli* (N.C.T.C. 6084), which was sensitive to 0.3 units of polymyxin per ml.

First Course of Polymyxin.—Since the organism was sensitive to therapeutic concentrations of polymyxin alone, treatment with this antibiotic was begun on Sept. 25, 200,000 units being given intramuscularly four-hourly and 40,000 units intrathecally twelve-hourly for three doses and thereafter once daily. Twenty-four hours later the boy's temperature was normal for a few hours, and by the third day it remained normal all day. Simultaneously there was an improvement in the c.s.f., the white-cell count falling to 110 per c.mm. on the sixth day (Oct. 1). Cultures were sterile on the fourth and fifth days of treatment, the blood-polymyxin level twenty-four hours after the preceding intrathecal injection being 19 units per ml. on the sixth day. Treatment was stopped on the eighth day because of these favourable results and because toxic effects had appeared.

Toxic effects were first noticed shortly after the treatment started, when the boy's appetite became very poor and he began to vomit after each meal. He was given an entirely fluid diet (milk and fruit juices with added salt and sugar), but even so vomiting was frequent and, had it continued for long, would certainly have weakened his resistance to the infection and caused serious metabolic imbalance. After two days sacral oedema appeared, and on the third day he had mild oedema of the face, but these features disappeared after forty-eight hours, even though treatment was being continued. A mid-stream specimen of urine at this stage showed no casts and only a trace of protein. The sites of intramuscular injections (buttocks and thighs) showed localised induration and tenderness but no superficial erythema, the injections themselves being painful, even when given slowly. After each intrathecal injection the boy would cry with pain down both legs for about an hour. This was assumed to be due to the irritant effect of polymyxin on the cauda equina. Thorough mixing of the polymyxin solution with c.s.f. before injection made the pain less severe but did not eliminate it. All these side-effects of polymyxin disappeared within forty-eight hours of cessation of treatment. Coincidentally there was a general improvement in his condition and appetite.

Second Course of Polymyxin.—Three days later (Oct. 5) a lumbar puncture, done as a check on his progress, showed a white-cell count of 7640 per c.mm., and a pure growth of *Ps. pyocyanea* was obtained after forty-eight hours' culture. It was assumed that a localised collection of pus, which had not been sterilised by the first course of treatment, had burst



Pseudomonas pyocyanea meningitis treated with polymyxin B

into the c.s.f. The boy's general condition grew rapidly worse, his temperature rising to 103·6°F. Polymyxin-B therapy was therefore restarted (Oct. 6), 200,000 units being given intramuscularly four-hourly and 40,000 units intrathecally daily. Within thirty-six hours his temperature again became normal for a few hours, but did not remain so until Oct. 11. Next day (Oct. 12) the systemic dose was decreased to 200,000 units eight-hourly and further decreased to 200,000 units twelve-hourly (Oct. 15) for the next fourteen days. Apart from four days (Oct. 13-17) during which the daily intrathecal dose was halved, 40,000 units was given daily until the thirty-seventh day (Nov. 3), 20,000 units being given for two further days.

Cultures of c.s.f. showed a pure growth of *Ps. pyocyanea* until Oct. 21, after fifteen days of the second course of treatment. Then the culture was sterile after prolonged incubation (the c.s.f.-polymyxin level twenty-four hours after previous injection was 20 units per ml.), and thereafter it remained so. The c.s.f. white-cell counts ranged between 100 and 500 per c.mm., and the pleocytosis disappeared within two weeks of the end of intrathecal treatment (see figure).

Toxic Effects.—During this second course eosinophilia, xanthochromia of the c.s.f., and a transient mild albuminuria with granular and hyaline casts appeared, the blood-urea level remaining normal. A white-cell count on Oct. 13 (seventh day of second course of treatment) showed a total count of 13,100 per c.mm. (neutrophil polymorphs 84%, eosinophils 3%, lymphocytes 12%, monocytes 1%). The Hb was 9·1 g. per 100 ml., and the red cells showed considerable microcytosis and hypochromia and some anisocytosis. A transfusion of 1 pint of whole blood was given on Oct. 16. Three days later (Oct. 19) a blood-count showed 19,900 white cells per c.mm. (eosinophils 18%, neutrophils 67%), and Hb 12·5 g. per 100 ml. A later blood-count (Oct. 26) showed 18,100 white cells per c.mm. (eosinophils 32%, neutrophils 56%, lymphocytes 11%, monocytes 1%) and Hb 11·9 g. per 100 ml. There was no allergic reaction at any stage, nor was there any past history of allergy. The eosinophilia became even more pronounced and on Oct. 30 was 41% of a total of white-cell count of 14,800 per c.mm. (neutrophils 46%, lymphocytes 13%), with Hb 11·7 g. per 100 ml. A radiograph of the chest at this stage was normal. Eosinophils appeared in the c.s.f. at the same time as in the blood and in about the same percentage of the polymorph-count. Xanthochromia of the c.s.f. became marked soon after the beginning of this course, but while the intrathecal dose was decreased (Oct. 13-17) it was much less so, increasing again with the higher dosage. It disappeared within two days of the end of intrathecal treatment.

Further Progress.—Clinically the boy's improvement was steady and rapid, and a week after the end of treatment he was kicking a football about the ward. Six months after the end of treatment he continues to progress and has shown no evidence of relapse.

Discussion

Pseudomonas meningitis is rare. Stanley (1947) could find records of only forty-one cases of primary infection and twenty-nine (including one of his own) in which the meningitis was secondary to a focus elsewhere. Since then at least eighteen others have been described. The condition will probably become more common as a result of the more widespread use of antibiotics which are effective against most organisms but not against pseudomonas. The mortality in this condition is high. Stanley (1947) found a mortality of 55% in cases due to primary infection and "at least" 86% in secondary cases. If and when it occurs, therefore, it is clearly most important to be able to combat this infection with some safe and powerful agent. Polymyxin B and possibly neomycin (Ditkowsky et al. 1952, Knight et al. 1952) appear to meet this need.

The course of treatment in the present case was much longer than others recorded (except the case of Hayes and Yow 1950, where three courses of treatment were given because of relapse), and, perhaps as a result of this, toxic effects not previously described appeared. The second course of treatment was continued for thirteen days after the cultures became sterile, to avoid another relapse.

It was during the second phase that the new toxic features appeared—considerable eosinophilia (up to 41%) and xanthochromia of the c.s.f. The eosinophilia in the blood, which was also reflected in the polymorph response in the c.s.f., presumably must be due to the polymyxin therapy, there being no evidence of other allergic phenomena or radiographic evidence of any lung changes. The eosinophil-count returned to 6% within thirteen days of the end of the polymyxin therapy. The xanthochromia, like the pain down the legs, was presumably the result of a chemical irritant effect of the polymyxin, for it seemed unrelated to the number of red cells in the c.s.f. It did not appear until early in the second course and was much less severe while the intrathecal dosage was reduced, returning when the dosage was increased to its former level. After the intrathecal polymyxin was discontinued, the xanthochromia disappeared completely within two days. Trauma due to repeated lumbar puncture was not the cause, for the patient had had frequent lumbar punctures during the month before the polymyxin therapy and for several weeks afterwards without xanthochromia appearing.

Signs of renal damage were never severe; even when the urine changes were maximal, the blood-urea level was normal. This is in accordance with the findings of Swift and Bushby (1953). Polymyxins B and E do not usually cause renal damage, but if signs of renal damage appear they soon disappear when treatment is withdrawn. The polymyxin B used in the present case caused no pyrexia, as has been recorded by other workers, and no perianal or perioral anaesthesia as in Tomlin's (1951) case. Pain in the back and down the legs following intrathecal polymyxin injections occurred in the cases of Hayes and Yow (1950) and Tomlin (1951) and in this patient, but ceased after about two weeks' treatment in spite of continued full intrathecal dosage. Similarly the malaise and vomiting, which also were recorded by Hayes and Yow (1950) and Swift and Bushby (1953), disappeared in spite of continued intrathecal and intramuscular treatment. The mild pleocytosis in the c.s.f. which remained at the end of the treatment was probably the direct result of it, for within two weeks of its conclusion the cell-count had fallen to normal levels. This effect was also noted by Swift and Bushby (1951) using intrathecal polymyxin E.

Such was the virulence of the infecting organism, and its resistance to other antibiotics, that this case probably would have proved fatal but for polymyxin therapy. This drug is the one of choice for *pseudomonas meningitis* in spite of its toxic effects, which were not great in the present case, even with long-continued high dosage. Prompt polymyxin therapy in adequate dosage (intramuscular and intrathecal) and continued for at least ten days after the c.s.f. is sterile seems to give a patient with this grave disease his best chance of permanent recovery.

Summary

A case of *Pseudomonas pyocyanea* meningitis following a cerebrospinal-fluid fistula is described. The causal organism was resistant to sulphonamides, penicillin, aureomycin, oxytetracycline, and chloramphenicol, but sensitive to polymyxin B. Recovery followed a long course of intrathecal and intramuscular polymyxin B.

Previously unrecorded toxic effects of polymyxin therapy—severe eosinophilia and xanthochromia of the c.s.f.—are described. Other toxic effects observed were nausea and malaise, pain at the injection site, pain down the legs and in the back following intrathecal injections, and sacral oedema. These effects disappeared in spite of continued polymyxin therapy. Transient mild albuminuria with cylindruria was also present.

I am most grateful to Mr. Murray A. Falconer for permission to publish this case; Dr. K. Anderson, of the bacterio-

logy department, Guy's Hospital, for estimations of the sensitivities and blood-polymyxin levels and the note on the techniques used; and Dr. D. R. C. Willcox, clinical pathologist, Maudsley Hospital, and his staff for daily examination of the c.s.r. for more than two months.

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TRICHOBEOZAR

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BEZOARS are masses of foreign material sometimes found in the stomach and intestines of man and animals. Phytobezoars are masses of unabsorbed fruit and vegetable residue, and trichobezoars are masses of hair. The latter usually accumulate in the stomach for years when persons or animals eat their own hair.

Published reports of hair-balls in man are comparatively few. The first report was that of Baudamant (1779) and the first report of successful surgical removal of a trichobezoar was made by Steltzner (1896). DeBakey and Ochsner (1938) reviewed 172 cases of hair-balls, of which 15 were associated with peptic ulceration and 5 were complicated by perforation. 13 further cases were published up to 1948, including 1 by Parsons (1948) in which the mass was palpable in the abdomen. Nussey and Leask (1949) reported a hair-ball in a woman, aged 40, that completely filled the stomach and formed a cast. Osmond and Price (1951) reported what was thought to be the first successful operation for repair of a perforated gastric ulcer due to a hair-ball in a girl aged 8 years.

Trichobezoars are usually large and solitary but occasionally multiple. The largest on record seems to be that removed by Davies (1921); this weighed 6½ lb. when fresh. DeBakey and Ochsner (1938), however, reviewing the 172 cases then reported, considered that their own example, which weighed 1·6 lb., was of about average size.

It is thought that the stomach cannot expel hair and allied material when ingested, and that ultimately a bolus of ever-increasing size is formed in the stomach. More than 80% of trichobezoars occur in people aged less than 30, and more than 90% in females. The predominance in females is thought to be due to their longer hair, which is more easily pulled out and chewed. In a fairly large proportion of cases there is evidence of mental instability.

While the hair-ball remains small, no symptoms need be associated with it. Later the patient may complain of anorexia, general malaise, loss of weight, or even of a feeling of epigastric fullness or a palpable mass in the abdomen. If the hair-ball is near the pylorus, a condition resembling pyloric stenosis may result, with paroxysmal vomiting and epigastric pain. Ulceration, perforation, and peritonitis may ultimately supervene. The treatment is surgical removal as soon as bezoar is diagnosed. Postoperatively adequate precautions, both physical and directed at the mental state, must be taken to prevent further ingestion of hair.

The following personal case seems well worth reporting because the trichobezoar was found in the terminal

ileum and had given rise to intestinal obstruction. I have not been able to find any similar published case.

Case-report

A girl, aged 7 years, was admitted to the North Staffordshire Royal Infirmary in 1949 with twenty-four hours' history of colicky abdominal pain and vomiting. There was no previous history of any abdominal symptoms whatever.

On examination the general condition was good, but the lower abdomen was distended and showed an early ladder pattern suggesting small-bowel obstruction. A firm sausage-shaped mass was clearly felt in the right iliac fossa. Ileocecal intussusception was provisionally diagnosed, and the abdomen was opened by a right paramedian incision under general anaesthesia. The mass proved to be a foreign body in the terminal ileum 6 inches from the ileocecal valve. It was removed through a small incision in the long axis of the bowel, which was sutured transversely to prevent a stricture from forming. The foreign body was a hair ball. The stomach was palpated, but no further masses were felt. The child made an uninterrupted recovery and was discharged on the twelfth postoperative day. She has remained well since.

A history was later obtained from the parents that the child had been noticed to chew her hair from early childhood.

The specimen was 4 inches long and 1¼ inches in diameter and resembled a thick sausage. It consisted of innumerable black hairs packed together almost inseparably and weighed 12 oz.

Summary

A trichobezoar left the stomach of a girl, aged 7 years, and became impacted in the ileum, causing obstruction which closely resembled intussusception.

My thanks are due to Mr. L. M. Zinck, F.R.C.S.E., for permission to publish this case-report.

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Reviews of Books

The Physician in Atomic Defence

THAD P. SEARS, M.D., F.A.C.P., associate clinical professor of medicine, University of Colorado School of Medicine. Chicago : Year Book Publishers. London : Interscience Publishers. 1953. Pp. 308. 45s.

THIS book deals with the fundamentals of nuclear physics, the injuries caused by atomic bombs, and the administrative plans to meet such disasters in the United States of America. For those unable to attend courses or lectures on these subjects, it sets out the sort of indoctrination they would receive.

Professor Sears is most at ease when he is presenting simplified concepts of modern physics in a readable form. He is not so strong in outlining the rôle of the physician tending atomic bomb casualties : the management of all forms of injury is summarised inadequately in a few pages, and his account hardly presents in realistic perspective the problem likely to be encountered. The casualty figures estimated for airburst explosions make sombre reading ; they apply, it seems, to attacks against unwarned communities, or with very powerful weapons. In either event, blast and burning injuries—about which he says little—would outweigh radiation effects among survivors. On the other hand, the medical aspects of an underwater explosion (when radiation effects would outnumber blast and burning injuries) are not discussed.

Traité de cytologie sanguine

MARCEL BESSIS. Paris : Masson. 1954. Pp. 588. Fr. 6800.

A VOLUME with this title leads one to expect a detailed account of the morphology of normal and pathological blood-cells with illustrations of their appearances as seen under the microscope ; for most books of this type are designed for clinical pathologists and stick to classical

methods of preparation and recognition of blood-cells. Dr. Bessis's book differs from these in adding to classical methods results obtained with other techniques now coming into use. These are cytochemical techniques for showing up particular cell constituents, like fat, phosphatase, or glycogen; the phase-contrast microscope and the possibilities it gives for studying living cells; the electron microscope; the use of polarised or ultraviolet light, and so on. The unusual bulk of Dr. Bessis's book is accounted for by the wealth of illustrations, which show appearances with classical techniques, cytochemical techniques, and phase-contrast and electron microscopy, as applied to almost all types of cells. There are no fewer than 405 text figures—mostly photographs—and 22 colour plates of notably high standard.

Details of these techniques are followed by a short section on the general physiology and pathology of blood-cells, which deals with systems of haemopoiesis, quantitative matters like normal "myelograms" and "splenograms," and abnormalities observed in fixed and living cells, like vacuolisation and ageing. The bulk of the book is a detailed study of each "line" of blood-cells, illustrated by all the techniques used. This section incorporates most of the material that was previously published in Dr. Bessis's smaller book, *Cytologie sanguine, normale et pathologique*, which appeared in 1948; and most of the colour plates of abnormal haemopoiesis are reproduced from that volume. The other illustrations are considerably more numerous and the text has been extended. At the end of each chapter is a good bibliography, showing that Dr. Bessis is familiar with world publications on haematology.

Those who have studied Dr. Bessis's contributions to the medical press will find little new in this book, but for others it presents a unique compendium of information on the application of the newer cytological techniques to the study of blood-cells. It is fair to say that, so far, none of these new techniques has proved superior to the established ones for the diagnosis and control of disease, and they are therefore of little more than academic interest to the clinical pathologist. The research-worker, however, may well get help from cytochemical techniques, and in particular from the phase-contrast microscopy of living cells. In this book he will find a guide to what he can expect to see in human blood and marrow cells.

Acute Anuria

Study Based on Renal Function Tests and Aspiration Biopsy of the Kidney. CLAUS BRUN, 3rd medical department, Kommunehospitalet, Copenhagen. Copenhagen : Munksgaard. 1954. Pp. 215. D. kr. 30.00.

In this book, a well-known Danish nephrophile reviews the subject of acute anuria in relation to 32 patients whom he has treated and investigated. The historical aspects of our knowledge of anuria are well reviewed, but much of this work has been outdated by changes in terminology, and (more important) by the recent functional studies of Bull, and the morbid anatomical observations of Oliver.

By comparison with the results attained by Oliver's microdissection technique, the renal biopsy specimens obtained by Brun are uninformative. Most of the patients were treated conservatively, but intestinal dialysis and even exchange transfusions were used in a few patients; no assessment of the value of such measures is possible, because of the uncertain case-prognosis of this condition. Brun departs from the Bull régime by correcting obvious electrolyte abnormalities, and claims that the clinical improvement outweighs any increased risk of pulmonary oedema; but this is at present rather an open question, in view of the finding of Hamburger and Mathé that cellular overhydration may exist, and be corrected by saline administration. There is no discussion of the use of exchange resins for lowering serum-potassium concentration, or of the possibility of giving hypertonic glucose solutions by polythene catheter into the great veins when patients are unable to tolerate a high-calorie régime by mouth.

This account of anuria is rather diffusely written, and better reviews for the general physician are available (such as that by Swann and Merrill¹); but specialists in kidney disease will find many of Brun's observations, and especially the detailed case-reports, of great interest.

1. Swann, R. C., Merrill, J. P. *Medicine*, 1953, 32, 215.

Carbohydrate Metabolism

Symposium on the Clinical and Biochemical Aspects of Carbohydrate Utilization in Health and Disease. Editor : VICTOR A. NAJJAR. Baltimore : Johns Hopkins Press. London : Oxford University Press. 1953. Pp. 134. 32s.

THIS is a record of the papers read at a conference on the clinical and biochemical aspects of carbohydrate utilisation in health and disease. Many distinguished researchers contributed to the symposium, which was designed not for their mutual interests but for those of the clinician.

In general three main aspects of carbohydrate metabolism are considered—the enzymatic constitution of the individual, the hormonal balance, and the electrolyte pattern in the extracellular and intracellular fluid. Subjects covered include glycogen storage disease (4 types), the effects of hormones on enzymes, hypoglycaemia, including the rare variety associated with hypoplasia of the pancreatic α -cells, the diabetogenic effects of potassium depletion, and the optimal electrolyte replacement for diabetic ketosis. There are unfortunately confusing mistakes in the labelling of two of the diagrams, but the contributors deserve much credit for having compressed so much of interest into so few pages.

Practical Mycology

Manual for Identification of Fungi. SIGURD FUNDER, DR. PHILOS. Oslo : Brøggers Boktrykkeri. 1953. Pp. 146. 39s.

THIS recent addition to the growing list of books on mycology for medical readers can be strongly recommended—either as a simple but entirely satisfactory introduction to the subject, or as a guide to those, not contemplating the special study of mycology, who wish to identify the types of microfungi encountered in routine laboratory work. The biology of the microfungi is adequately explained and mycological technique and methods of examination, as well as the basis of classification, are clearly set out.

A large section on the identification of fungi by microscopy contains an atlas of good line drawings illustrating the characteristic morphology of genera and species, with notes on their systematic position. This section is in three parts, the first of which deals with fungi of general interest, the second with the medical fungi in both saprophytic and parasitic life (with a dichotomous key to the human mycoses), and the third with fungi of importance in plant pathology. A schematic classification of the Thallophyta and a useful glossary of mycological terms complete the work.

Essays on the Applied Physiology of the Nose (2nd ed. St. Louis, U.S.A. : Annals Publishing Company. 1953. Pp. 452).—In a note on the second edition of his well-known essays, Dr. Arthur W. Proetz says : "What can be said of a second edition but that it is the first—revised, amplified, modernized and embellished to the utmost of the author's resources and abilities ?" The book has been amplified by some 50 pages and revised, modernised, and embellished mainly by many excellent new diagrams, and descriptions of equipment and experiments, prepared by the author himself. The general plan of the book is almost unchanged, except for a considerable expansion of the chapter on nasal air currents. Most of this new work was presented at the Royal Society of Medicine in Dr. Proetz's Semon lecture for 1952. It includes an account of the "impingement areas" of the air currents and their close correspondence with the lymphoid patches of Waldeyer's ring. Dr. Proetz's work is very well known to rhinologists and physiologists in this country, and this is a welcome revision of one of the few classical monographs on the subject.

Modern Practice in Anaesthesia (2nd ed. London : Butterworth. 1954. Pp. 622. 65s.).—In preparing the new edition of his excellent textbook Dr. Frankis Evans has made substantial changes. The chapters on anatomy and physiology and on relaxants have been rewritten, and new material on cardiology and on saline infusions and blood-transfusions has been added. The chapters on apparatus and on machines for controlled respiration perhaps follow the manufacturers' leaflets too closely and might be rewritten on broader lines, or omitted, in the next edition. As a whole, however, this is one of the best general textbooks of anaesthesia in the English language.

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Treatment of Hyperthyroidism

In the history of the treatment of hyperthyroidism four distinct periods can be distinguished. During the first, which lasted from the recognition of the disorder until about the end of the 19th century, no effective treatment was employed. The only agent available at that time which could have influenced hyperthyroidism favourably was iodine; but its use was virtually forbidden by the authorities of the day who all agreed on the danger of giving it to hyperthyroid patients. One of the few physicians bold enough to defy the ban was CHEADLE^{1,2} of St. Mary's Hospital: he reported excellent results with iodine, but the medical world was unimpressed. The second period started about 1900, when surgeons became interested, and a lead was given by KOCHER in Switzerland, the MAYO brothers in the United States, and DUNHILL in Australia and this country. At first a hemithyroidectomy was the usual operation, but experience showed that a more radical procedure was necessary if the symptoms were to be completely controlled. So the modern technique of subtotal thyroidectomy was gradually evolved, though it often had to be done in stages, sometimes preceded by ligation of thyroid arteries at a preliminary operation. The best surgeons achieved mortality-rates of 2-5%—a fine performance, for many of their patients were gravely ill. Nevertheless physicians looked on operation as a fairly desperate expedient to which they were driven only by the lack of any positive therapy of their own and by the high mortality of the untreated disease.

This second period lasted until about 1925, when the benefits of iodine, which had been gradually rediscovered during the previous fifteen years, suddenly became apparent to all. Within a year or two a substance which had been regarded as highly toxic to patients with hyperthyroidism was accepted as their salvation. This transformation benefited the surgeon more than the physician, for iodine proved unsuitable for long-continued treatment: usually the maximum improvement was obtained some two to four weeks after the start, and few patients could be satisfactorily controlled for an indefinite time. But iodine was ideally suited to the preparation of patients for operation, and surgeons found that in most cases they could now perform a one-

stage subtotal thyroidectomy. The popularity of the operation increased enormously and probably accounts for the steep rise in the death-rate from hyperthyroidism during the years between the wars. For, though the operative mortality in the best clinics fell to about 1-2%, the mortality in the country as a whole must have been much higher—how high nobody can tell. Hence for the hyperthyroid population as a whole the introduction of the standard iodine-prepared subtotal thyroidectomy was a mixed blessing. In the best clinics it was a very satisfactory procedure, resulting in rapid loss of symptoms, with relatively little danger or inconvenience. But often both iodine and operation were misused. Some patients were allowed to linger for months or years half-treated with iodine, and the surgeon was called in too late or not at all. In other cases the operation was attempted too hastily in a patient not properly prepared; and sometimes it was done without sufficient reason. The inter-war period also saw attempts to treat hyperthyroidism by X rays; but in general radiotherapy was not very successful, because it seldom influenced thyroid function without damaging the skin. There were probably some good results, but also a number of scarred necks and even an occasional skin cancer. The therapeutic response, when there was one, was slow and inferior to that obtained by subtotal thyroidectomy.

The final period opened after the late war, when the thiouracil drugs and radio-iodine appeared on the scene. For a time it looked as though one or other of these might supersede subtotal thyroidectomy as the standard means of treating hyperthyroidism. This they have not done; but their existence has on the whole been beneficial to surgery. For, though neither can improve on the best results of the best surgeons, they offer alternatives which are a good deal better than inferior surgery. And both have helped the surgeon directly. Anti-thyroid drugs of the thiouracil type, used judiciously and followed by iodine, can make the severest case euthyroid by the time of operation, without increasing the operator's difficulties. They are not needed in the milder cases: thus LANGE,³ reviewing work at the New End Clinic, says that of 781 cases 35% were prepared with thiouracil followed by iodine, and 65% with iodine alone. Radio-iodine relieves the surgeon of the technically difficult task of operating on cases of recurrent hyperthyroidism. Through these advances, and the concurrent improvements in anaesthesia, blood-transfusion, and antibiotics, operative deaths have almost disappeared from the best surgical clinics, and all can quote mortality-rates in terms of fractions of 1%. We must still, however, reckon with a certain amount of postoperative morbidity. Postoperative haemorrhage is still seen sometimes, and surprisingly large collections of serum can appear in the wound, causing ugly scars if not promptly attended to. Occasional damage to the parathyroids is probably unavoidable, though the resulting tetany is seldom permanent; the recurrent nerve is divided from time to time, even by the most careful surgeons; and patients also tend to suffer from postoperative hoarseness even when these nerves are known to be intact. Remote consequences include myxoedema and recurrent hyperthyroidism—when too little or too

1. Cheadle, W. B. *St. George's Hosp. Rep.* 1869, 4, 175.
2. Cheadle, W. B. *Ibid.* 1872, 7, 81.

3. Lange, M. J. *Brit. J. Surg.* 1953, 40, 544.

much thyroid tissue is left behind. Recurrent hyperthyroidism can be avoided at the risk of myxoedema, or vice versa, but no known procedure will obviate both.

Patients with hyperthyroidism can fairly be told that the risk of operation is almost negligible, and that complications are unlikely. If things are as well managed as they are at the New End Clinic,³ their stay in hospital need be no more than a fortnight, though presumably they will require two to four weeks' convalescence afterwards before returning to work. Most patients will agree that this is a reasonable price to pay for release from troublesome symptoms. Yet some will hesitate. As a general proposition, it can be said that patients dislike operations; and even a few weeks off work can sometimes dislocate a career or cause grave financial hardship. It is not always justifiable to urge a patient to have an operation when alternative methods of treatment exist, especially when the symptoms are no more than mild. Moreover, in some cases non-operative treatment is preferable on strictly medical grounds; for when exophthalmos threatens to become progressive it is often aggravated by an ill-timed thyroidectomy. In such cases cautious treatment with anti-thyroid drugs provides a more delicate control of thyroid function, though it must always be remembered that over-treatment with these drugs can be as disastrous to the eyes as surgery.

Although medical treatment does not demand any special technical skill, it does demand judgment and perseverance. Unlike the dose of thyroid required to control myxoedema, the dose of anti-thyroid drug required to control thyrotoxicosis is not constant, and neglect to change it with variation of the disease leaves the patient uncomfortably hyperthyroid on the one hand or hypothyroid on the other. The latter state is perhaps the more unpleasant for the patient, especially as it is accompanied by enlargement of the goitre. Such enlargement was not uncommon in the early period of thiouracil therapy, and led many physicians and surgeons to conclude that this type of treatment could not be satisfactory. But, as usually happens, further experience has led to a more delicate control of hyperthyroidism, and there is no reason why patients should not be kept indefinitely as fit as they would be after a thyroidectomy. Simultaneously the safety of medical treatment has improved—a very important matter, for if drug treatment is to compete with surgery it must be as safe as it can be made. The parent substance, thiouracil (particularly when used in the large doses at first thought necessary) was anything but safe. The toxic effects could all be attributed to hypersensitivity, perhaps due to the formation of a drug-protein complex which could act as an antigen. The more common reactions—rashes and drug fever—were fortunately not too serious; but agranulocytosis was often fatal, and there was the possibility that thiouracil might cause more distant reactions of the type of polyarteritis nodosa. Addition of a methyl or propyl group to the thiouracil molecule seemed to decrease the incidence of toxic reactions, and the introduction into clinical use of substances with a mercapto-imidazole nucleus (methimazole, carbimazole) has provided us with even more potent and less

toxic drugs. Nevertheless, even these refined products occasionally give rise to reactions, and agranulocytosis has lately been reported⁴⁻⁶ in 3 patients taking carbimazole, a drug which seemed safer than the others.⁷

It now looks as though no compound of the thiouracil type is incapable of inducing agranulocytosis; and the possibility of this complication—unpleasant out of proportion to its incidence, for it comes without warning and demands urgent action—deters many physicians from using thiouracil compounds at all. Hence it is well worth examining the claims now being made on behalf of potassium perchlorate, which both in chemical structure and in physiological action is entirely unrelated to thiouracil. Whereas thiouracil interferes with the actual synthesis of thyroid hormone, potassium perchlorate stops the process at an earlier stage by preventing the thyroid gland from concentrating iodide, which (unless the blood-iodide level is quite abnormally high) is an essential preliminary to such synthesis. First investigated by WYNGAARDEN et al.⁸ it was introduced into clinical use by GODLEY and STANBURY⁹ at the Massachusetts General Hospital, whose series of 24 cases afforded good evidence of its usefulness. In our present issue, Dr. MORGANS and Dr. TROTTER report their experience in a further 108 cases, and conclude that potassium perchlorate is an effective anti-thyroid agent, though not perhaps quite as potent as methyl thiouracil, even when given in larger dosage. To a few patients it seemed to be a gastric irritant, but no side-effects of the hypersensitivity type were seen. These preliminary results should encourage further study; and if it can indeed be shown that perchlorate is a drug without terrors the case for medical as opposed to surgical treatment will be greatly strengthened. But, however successful the new drug proves, it cannot do away with what is perhaps the greatest handicap of medical treatment—the length of time it takes. None of the present anti-thyroid drugs can cure hyperthyroidism; they merely control it until such time as the disease dies out of its own accord. This may take only a few months or it may take years; and in treating hyperthyroidism medically the quality most needed—by both parties—is patience.

The exact place of radio-iodine in the treatment of hyperthyroidism cannot yet be known. The great deterrent to its use is the fear that it may cause cancer of the thyroid. If it does so, the latent period between treatment and cancer is likely to be of the order of twenty years; so it will be another ten years or so before we can tell whether this fear is real or imaginary. Meanwhile it is already apparent that radio-iodine has the practical disadvantages that it is slow to act and that the right dose for an individual is hard to determine. For the present it is probably best reserved for two types of patient—namely, the elderly and those with hyperthyroidism which has recurred after thyroidectomy.

4. Bartels, E. C. *J. clin. Endocrin.* 1953, 13, 1305.
5. Richardson, J. S., Sarkany, I., Campbell, C. D. *Brit. med. J.* 1954, 1, 364.
6. Harrison, A. R. *Lancet*, 1954, i, 396.
7. Doniach, D. *Ibid.* 1953, i, 873.
8. Wyngaarden, J. B., Wright, B., Ways, P. *Endocrinology*, 1952, 50, 537.
9. Godley, A. F., Stanbury, J. B. *J. clin. Endocrin.* 1954, 14, 70.

Balance

WE publish on p. 769 a memorandum by Sir RUSSELL BRAIN, as chairman of the Staff Side of Committee B of the Medical Whitley Council, announcing salary increases for hospital doctors. These increases arise out of the Danckwerts award, which, by raising the average income of general practitioners in the National Health Service, greatly reduced the financial advantage eventually obtainable by those who spend additional years in training to be consultants. The Government have been satisfied that this financial advantage must, in some degree, be restored; and they are therefore prepared to find the sum of over £3 million that will be needed to raise the salaries of the younger consultants by £400 a year (or the appropriate fractions for part-time posts), and those of senior hospital medical officers by £200, with smaller increases for registrars and for housemen. The new scales will not satisfy those who hold that consultants and specialists should be content with nothing less than the 100% increase on Spens' 1939 figures which general practitioners succeeded in gaining through arbitration. But Sir RUSSELL BRAIN makes it quite clear that the Government have refused from the first to reconsider consultant salaries on a basis of "betterment," and have been equally firm in refusing arbitration; and in view of the consequences, both inside and outside the National Health Service, that would follow a rise of anything approaching 100% in consultants' salaries we believe that in taking this line the Government are right. The task of administration is rather to remove anomalies than to create new ones; and on this occasion the Treasury has recognised the needs of the situation and has responded to practical arguments in a practical way. As for the distribution of the money, there will be some who think it should be different in one way or another. But, since the main object of the adjustments is to induce suitable candidates to make the sacrifices and take the risks involved in seeking consultant status, there are sound reasons for giving the chief increase to those who attain it. For our part we by no means exclude a revision of the present system of grading; for we believe that the status of consultant should be reached through that of specialist—a new rank which should include those now called senior hospital medical officers. But the new scales of remuneration need not stand in the way of this reform, and we congratulate both sides of Whitley Committee B on their sensible settlement of a difficult issue. In these congratulations it would be fitting to include Lord MORAN, who from the moment of the Danckwerts award has insisted that consultants' salaries must be revised so as to correct the imbalance the award created. At a time when most of us were only rejoicing that the general practitioner had been rescued from the position of poor relation, his arguments fell mostly on deaf ears: but their validity became evident when the actual remuneration of specialists at various levels was dispassionately examined. As between specialist and general practitioner, the scales, which had been tilted too far in one direction before the award, were tilted too far in the other direction after it. We may fairly hope that with the present adjustments equilibrium has been reached.

Annotations

VENOUS THROMBOSIS IN THE LEGS

SINCE the 1930s when anticoagulant drugs were introduced into clinical practice, venous thrombosis of the lower extremities has been closely studied. This complication develops most usually after surgical operations or parturition, and less commonly after local trauma. Of the many factors that may favour thrombosis, those which have received most attention are inactivity of the legs from confinement to bed and restriction of respiratory movements owing to pain (both of which may impede return of blood from the lower extremities), injury to the lining of the veins by prolonged pressure on the operating-table, and direct spread of infection in cases of pelvic inflammation. The circulation may be further impaired by lowering of blood-pressure from shock and haemorrhage. The success of efforts at prophylaxis—by exercises in bed, early ambulation, and control of infection by antibiotics and of shock by transfusion—is difficult to estimate, partly because minor cases often pass unnoticed, and partly because the relative importance of the various suspected aetiological factors cannot be evaluated precisely. Certainly these methods have not eliminated postoperative and postpartum thrombosis even if they have appreciably diminished its incidence. Anticoagulants have proved useful in relieving symptoms and in hastening resolution, but they have not sensibly diminished the incidence of pulmonary embolism, or of the postphlebitic disturbances of the venous circulation that lead to chronic oedema and ulceration.

Particular interest therefore attaches to recent studies of cases of thrombophlebitis which have hitherto been termed "spontaneous" and received scant attention. Arising under apparently normal conditions of life, these cases may be a more profitable field for the study of aetiology than is found in the complexly abnormal post-operative state. Homans¹ reports three cases in which thrombosis developed after long journeys by aeroplane or motor-car. Two of the patients were middle-aged men, one of whom had previously had a thrombosis of his femoral artery and venous thrombosis, and the third patient was a 19-year-old girl who also had had a femoral-vein thrombosis. Homans infers that the prolonged maintenance of the sitting posture in these cases was the cause of the thrombophlebitis. He ascribes two further cases to long hours spent at a desk, and to two hours at a theatre with the legs crossed. Homans suggests that people over fifty years of age should move their toes, feet, and lower legs when sitting for long periods and should get up and move about when opportunity offers.

Other lines of approach to so-called "spontaneous" venous thrombosis have yielded more definite information. Hubay and Holden² report that of eight patients admitted to hospital with peripheral venous thrombosis, seven had occult neoplastic lesions and one had tuberculosis. These workers suggest that blood-coagulation may be affected by the physiological response to necrotic tissue. Though admitting that they have seen many patients with venous thrombosis in whom no associated lesion was detectable, they hold that this disorder should alert the clinician to the possibility of an obscure visceral neoplasm. Wegelius³ studied 178 cases of deep venous thrombosis in the lower limbs in the medical wards of the Maria Hospital in Helsingfors. 44% of the patients had congestive heart-failure, 13% diseases of the blood, and 15% infection (generally of the respiratory tract). Like Hubay and Holden, Wegelius notes an association of venous thrombosis in the lower limb with malignant tumours (3.3%), principally of the pancreas or lungs. In 6% of cases no

1. Homans, J. *New Engl. J. Med.* 1954, 250, 148.

2. Hubay, C. A., Holden, W. D. *Surg. Gynec. Obstet.* 1954, 98, 309.

3. Wegelius, O. *Acta med. scand.* 1954, 148, 27.

cause was found. Wegelius found no convincing evidence for the view that the administration of digitalis and mercurial diuretics increases the coagulability of the blood, nor for the claim that erythrocyte aggregation is a major factor in the aetiology of thrombo-embolism.

Clearly we do not know why a person develops deep-vein thrombosis in the legs, whether after operation or parturition, or when he has some "internal disease," or when in apparently normal health. Thus prophylaxis must remain empirical and imperfect. The combined efforts of surgeons, obstetricians, physicians, and pathologists are needed to lighten our darkness.

BEACH POLLUTION

NOT long ago we commented on the risks to the public health which arise from the common practice of discharging untreated sewage into the sea.¹ If the outfall be extended far enough out to sea and consideration be given to the set of tide and current little harm will result, but only too often pollution of a bathing beach may be discovered not by bacteriological finesse but by sight and smell. While coliform bacilli of the types found in the human bowel are rare or absent in water sampled offshore, they are usually to be found in coastal waters. It is true that enteric infections due to bathing beyond reasonable doubt are few, but it would be unwise to deny that the risk exists. Questions of health apart, we do not doubt that the presence of human faeces on the beach brings a resort into popular ill repute. This subject therefore affects not only medical officers of health and sanitary engineers but all those who depend for their living on the seaside holiday trade.

Our French colleagues have shown much interest in these problems and, among other things, have established that what was known to be true of the water is equally true of the fish in it: faecal bacteria are common in the viscera of fish taken in coastal waters but absent from those caught offshore. Guelin,² working at the Plymouth Marine Biological Laboratory, has now shown that specimens of *Ctenolabrus rupestris* (a little wrasse vulgarly known as the pink bream or Jago's goldsinny) which were allowed to swim for an hour in a tank containing *Escherichia coli* continued to harbour this organism for no more than six days after their removal to clean water. Bacteriophages inoculated in the same way persisted for an even shorter time. These were elegant experiments, but we cannot allow the author's claim that they prove that the intestinal flora of warm-blooded animals cannot adapt itself to life in fishes. There are fish and fish, and what may be true in a pink bream may not apply to the whole order of Pisces. Man and guineapig are both mammals, but the bacterial contents of the intestines are quite different.³ One way or another these observations cannot have much bearing on public health since, except for the genitalia and the livers of some larger pelagic fish, fish offal is not an article of diet. One other incidental observation by Guelin calls attention to a technical method of tracing enteric infection which is little used here but which seems to give good results in France. He found bacteriophages of *Esch. coli* in several parts of Plymouth Sound but the phage of *Salmonella paratyphi-B* once only, and that by the outfall of a sewer. The phages of *Salm. typhi* were not found—which contrasts with his experience on the Mediterranean coast.

An inquiry by Moore⁴ into the practical aspects of beach pollution in an anonymous resort in the West of England has produced a notable paper. Sporadic infections by *Salm. paratyphi-B* spread over several years culminated in 1946 in an epidemic attacking 21 people out of a population of about 5000. Popular blame for this accident fell on the town sewage which was discharged

on the beach at all states of the tide, but careful investigation showed that at least half the sufferers had not even paddled. Two years later *Salm. paratyphi-B* was found constantly in the sewer, and this was traced to the wife of the local vendor of ice-cream whose wares had been eaten by 20 out of 21 people infected. Despite this discovery the beach was suspect as the origin of the illness of the 21st patient—a child whose fond parents regulated his diet more strictly than his bathing. A bacteriological survey of water and of sand from between the tide-marks showed that coliform bacilli (including "faecal coli") could be found over the whole 8000 feet of beach, and, as might be expected, they were in general more abundant near the outfall of the sewer. Observations on the tidal currents by means of marker-floats showed that while the general set of ebb and flood was along the shore this was not true throughout the tidal cycle. The presumptive coli count of the water was influenced by these tidal anomalies and by weather conditions. On the basis of these findings the local authority decided to make some alterations in the outfall. It was moved some distance laterally and extended seaward, and advantage was taken of a tidal set away from the shore during the first hour of the ebb to arrange that discharge should be limited to this period. Bacteriological tests when the new plant was in operation did not show a beach free from faecal pollution, but, whereas in the earlier series 35% of samples had shown more than 1000 organisms per 100 ml., after the improvements the figure had fallen to 9.2%.

As in so many problems of public health, the ideal solution demands an almost bottomless purse; but Moore's results suggest that studious and imaginative reconnaissance may lead to great improvements at a small outlay. This paper is indeed a model of method and should be read with care by the health authorities of seaside resorts big and small. The risks to health of beach pollution may be slight; but so long as an uninoculated population has the opportunity of access to human faeces (or its end-products) which may contain *Salm. typhi* or *Salm. paratyphi-B*, so long will enteric fever be found in the Registrar-General's tables.

LYMPHOEDEMA

MUCH concerning lymphoedema praecox remains obscure, but Kinmonth and Taylor¹ have greatly improved our understanding of the condition. Like earlier investigators these workers found that phlebographic and venous-pressure measurements were consistently normal, and it may therefore be presumed that the cause of the swelling does not lie in abnormal venous haemodynamics. In every case intradermal injection of a highly diffusible dye (patent-blue v) revealed a network of abnormally dilated lymphatics. In some cases where large lymphatics could be exposed surgically after their detection by dye, a cannula was inserted and X-ray contrast medium (diiodone) injected. Radiographs revealed dilated and tortuous lymphatics passing upwards through the femoral region into the abdomen. The lymphatics distal to the injection site were also incompetent and valveless. When 2-3 ml. of patent-blue was injected subcutaneously and intramuscularly in a normal limb and the site of injection massaged, normal beaded vessels about 1 mm. in diameter were seen lying near the deep veins. In lymphoedema the lymphatics were dilated and incompetent, and this normal transmission of dye was absent. Information about the efficiency of lymphatic circulation can also be obtained by injecting into the superficial tissues protein labelled with radioactive iodine and measuring the time taken for its removal from the injection site. Kinmonth and Taylor found that the removal-rate on ambulation in two normal people was about ten times that in two lymphoedematous patients.

1. Kinmonth, J. B., Taylor, G. W. Ann. Surg. 1954, 139, 129.

1. Lancet, 1953, II, 1086.

2. Guelin, A. Ann. Inst. Pasteur, 1954, 86, 303.

3. Creecellus, H. G., Rettger, L. F. J. Bact. 1943, 46, 1.

4. Moore, B. J. Hyg., Camb. 1954, 52, 71.

The cause of this abnormal dilatation of the leg lymphatics is not clear, but it seems possible that it is essentially a congenital malformation. Operations for the relief of lymphœdema have been designed either to bridge by skin pedicles what was assumed to be a barrier to lymphatic circulation,² or to excise the mass of redundant subcutaneous tissue in an effort to make the limb more shapely and efficient. If, as now seems clear, the underlying disorder is enlargement and incompetence rather than obstruction of the lymphatics, a different approach may be adopted—namely, ligation of abnormal channels in the femoral region in the hope that lymph will return by alternative and more competent routes. Kinmonth and Taylor treated one patient in this way without success; the operation they found most suitable was superficial lymphangectomy, whereby the oedematous subcutaneous tissue is excised and the exposed muscles covered with free skin grafts which can be most readily prepared by means of an electric dermatome.³ But this major operation should not be undertaken unless the patient is greatly handicapped.

THE MUSCULAR DYSTROPHIES

CLASSIFICATION of the progressive muscular dystrophies has been complex and unclear. The clinical literature is a wilderness of eponyms, and though it is generally held that the disorders are of heredofamilial origin the genetic background has remained confused. Professor Becker, in a new monograph,⁴ analyses the clinical and genetic bases and tries to correlate them. Though the multiplicity of the clinical forms is recognised, and though it is known that the hereditary factors vary, there has been a tendency to regard the different forms as manifestations of a single clinical entity. Becker thinks that this over-simplifies the problem, and finds evidence of two separable clinical entities with three separate genetic streams.

The clinical material surveyed comprises 104 families—most of them belonging to the South Baden district surrounding Freiburg—collected between the years 1904 and 1941 in the various clinics of Freiburg and district. These families contained 259 patients affected by muscle dystrophy, and the total genealogical investigation runs to 6238 persons. Becker has himself examined 159 of the affected patients and interviewed 1844 members of the families. The two clinical forms which he distinguishes are: (1) a shoulder-girdle, or descending form, in which the first or major disability is in the upper limbs, though it may later spread to the lower limbs; and (2) a pelvic or ascending form where the reverse takes place. The two forms never appear together in a single family, and so it follows that they are clinically and genetically distinct. In the descending form there is discernible a definite dominant hereditary pattern; but in addition there are a large number of isolated cases thought to be caused by an unknown, but possibly traumatic, exogenous factor. The pelvic, or ascending, form exhibits two lines of inheritance: the first of these (accounting for a number of isolated cases) is a simple recessive, while the second is a sex-linked recessive. Becker seems to be a little doubtful about this particular concept, since he is constrained to say that the recessivity of the sex-linked gene is not quite regular. Nevertheless, he is able to approach his review of previously published cases with confidence, and to show that in 50 of the 54 families displaying a dominant heredity which have been reported, the cases were, in fact, of the shoulder-girdle type, while of 41 families with sex-linked recessive characters 39 had the pelvic

type of dystrophy. These figures seem impressive, and support the conclusion that there are three independent lines of inheritance.

In the descending (shoulder-girdle) form—which of course may include the face, as in the Landouzy-Déjerine clinical subgroup—the age of onset is between 7 and 25 with a peak at 15; the sex-linked ascending (pelvic) type begins in the first 3 years of life; while the non-sex-linked (or autosomatic) ascending form is most liable to develop in the third decade. The three types vary in prognosis too. The descending form is slow and mild, with a lengthy course, and the patients are economically self-supporting. The sex-linked ascending type progresses rapidly and reaches the upper limbs within the first 10 years; the patients usually die by the age of 20, and rarely enjoy any school life, being gravely disabled throughout. The recessive autosomatic ascending form has a much more protracted course and is milder. The patients can usually manage to get about and the expectation of life is not greatly reduced. The dominant descending form tends to be a pure muscular affection, whereas the other two may show disturbances both of fatty tissue and of bone. More rarely genital underdevelopment may be seen, and so may mental defect.

The logical analysis of a complex problem sometimes leads to a charge that the analyst is attempting to tidy up reality; but that is not the case here. In this clear and thoughtful exposition of a thesis based on a wide survey of genetic and clinical material Becker provides a valuable scaffolding for the further clinical and genetic assessment of the muscle dystrophies.

PYRAZINAMIDE IN TUBERCULOSIS

PYRAZINAMIDE was synthesised during the investigations that followed the discovery of the antituberculous activity of nicotinamide. It was found to be only moderately active against the disease in mice¹ and guineapigs.² In liquid culture media it inhibited tubercle bacilli only in relatively high concentrations³; and on solid media it appeared to have little or no action.⁴ But the first trials in man suggested that its activity was greater than might be inferred from the laboratory results.⁵ The effect, however, was short-lived; many patients relapsed early in the treatment, and decreased bacterial sensitivity was common. Treatment with pyrazinamide and isoniazid together seemed more promising⁶; and McDermott et al.⁷ have now discovered some interesting experimental evidence of this enhanced effect of the two drugs.

They studied the action of several antituberculous drugs by enumerating the viable tubercle bacilli in the spleens of infected mice. Isoniazid causes the population to fall immediately; but it then remains constant despite continued treatment. Pyrazinamide produces a similar change. But with the two together the fall continues rapidly until bacilli can no longer be detected. In mice pyrazinamide and isoniazid have an antibacterial action that is qualitatively different from that produced by any of the standard drugs used singly or together. McDermott et al. treated 61 patients with this combination for three to six months and then continued with isoniazid alone. The radiographic results were better, in their opinion, than in a similar group treated with isoniazid alone. All patients had a positive sputum before treatment; but after six months tubercle bacilli

1. Malone, L., Schurr, A., Lindh, H., McKenzie, D., Kiser, J. S., Williams, J. H. *Amer. Rev. Tuberc.* 1952, 65, 511.
2. Dessau, F. I., Yeager, R. L., Burger, F., Williams, J. H. *Ibid.* p. 519.
3. Dessau, F. I., Yeager, R. L., Burger, F., Kulish, M. *Ibid.* p. 635.
4. Tarshis, M. S., Weed, W. A. *Ibid.* 1953, 67, 391.
5. Yeager, R. L., Munroe, W. G. C., Dessau, F. I. *Ibid.* 1952, 65, 523.
6. Schwartz, W. S., Moyer, R. E. Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration. Washington, 1953: p. 296.
7. McDermott, W., Ormond, L., Muschenheim, C., Deuschle, K., McCune, R. M., Tompsett, R. *Ibid.* p. 319.

were cultured from only 4 (7%) of 53, and three of the four strains were still sensitive to isoniazid.

McDermott et al. compare their results with those obtained with various combinations of streptomycin, *p*-aminosalicylic acid, and isoniazid in the United States Public Health Service investigations. Pyrazinamide and isoniazid seemed to give better radiographic and bacterial results than any of the others. The frequency with which bacterial resistance emerges depends both on the combination of drugs and the type of disease. Differences between two groups cannot, therefore, be attributed to the treatment unless the character of the disease is very similar in the two treatment groups. It would therefore be unwise to claim on the present evidence that pyrazinamide with isoniazid is the most efficient combination so far discovered. But the good results in man, together with the unique quality of its action in mice, certainly indicate that the combination should be more thoroughly investigated. Unfortunately, pyrazinamide may cause hepatitis. McDermott et al. noted impaired liver function in 6 of 66 patients who received the two drugs for eight weeks or more; 4 were jaundiced, and 3 of these became severely ill, 1 dying eight days after the first toxic signs. The drug had been given in daily doses of 50 mg. per kg. body-weight. Hepatitis has also been reported with daily dose of 2.8 and 3 g.^{6,8} the incidence among the 159 patients in the four reports being 7% with 1 death. This seems to justify the conclusion of McDermott et al. that it is inadvisable to administer pyrazinamide with isoniazid in such high dosage as hitherto.

NEUROLOGICAL SEQUELÆ OF INOCULATION

SINCE 1950¹⁰ attention has repeatedly been drawn to poliomyelitis developing within four weeks of inoculation with diphtheria toxoid and/or whooping-cough vaccine; and in the past few weeks our correspondence columns have borne witness to what Dr. Ann Ferguson (March 27) calls the "increasing awareness of the connection between paralytic poliomyelitis and injections of all kinds."

It is timely, therefore, to have Miller and Stanton's¹¹ review of other occasional neurological complications of prophylactic inoculation and serum administration. Of these, the best recognised are the sequelæ of serum administration, which are usually accompanied by serum-sickness but occasionally develop without constitutional symptoms about the seventh to tenth day after injection. The commonest syndrome is pain around one or both shoulders lasting for a few days and followed, as the pain passes off, by atrophic paralysis; the muscles most usually involved are those supplied by the fifth and sixth cervical roots. Considerably less common are generalised polyneuritis, myelitis, and cerebral and meningeal involvement. The same type of neurological complications may develop two to four days after T.A.B. inoculation; but Miller and Stanton point out that radicular involvement is relatively considerably commoner after administration of serum, and meningo-cerebral and spinal-cord involvement after inoculation with T.A.B. With the exception of anterior poliomyelitis, neurological complications after diphtheria immunisation seem to be very rare; Miller and Stanton record transverse myelitis with a lymphocytosis in the cerebro-spinal fluid developing eleven days after an initial injection of 0.2 ml. of alum-precipitated toxoid; and they cite three reported cases—one of cervical radiculitis after the fourth injection, one of motor polyneuritis, and the third of hemiparesis. The position is rather different with whooping-cough immunisation. Here neurological complications, other than poliomyelitis,

8. Phillips, S., Larkin, J. C., Litzenberger, W. L., Horton, G. E., Haimsohn, J. S. *Amer. Rev. Tuber.* 1954, 69, 443.
 9. Campagna, M., Calix, A. A., Hauser, G. *Ibid.* p. 334.
 10. McCloskey, B. P. *Lancet*, 1950, i, 659. Hill, A. B., Knowelden, J. *Brit. med. J.* 1950, ii, 1. Martin, J. K. *Arch. Dis. Childh.* 1950, 25, 1.
 11. Miller, H. J., Stanton, J. B. *Quart. J. Med.* 1954, 23, 1.

are always cerebral; several deaths have been recorded^{12,13} and there have been permanent neurological sequelæ in the form of epilepsy, mental defect, and hemiplegia. Neurological accidents in the prophylaxis of rabies have usually been ascribed to the injection of animal nervous tissue. They occur ten to fifteen days after the first injection and take various forms; the most serious is encephalomyelitis, while ascending polyneuritis and lesions of single peripheral nerves have also been found.

It seems to be established that the basis of serum-sickness is an anaphylactic reaction affecting in particular the blood-vessels; and probably the neurological sequelæ of serum administration have a similar basis, though it is not clear why in some cases the cervical nerve-roots are involved while in others the disturbance is more central. Prophylaxis against rabies involves repeated injections of brain emulsion, and the encephalomyelitis that occasionally ensues is probably an allergic disorder; in some ways it resembles the "allergic" encephalomyelitis produced in monkeys by injection of heterologous brain tissue emulsified with adjuvants. Miller and Stanton suggest that the complications of T.A.B. and whooping-cough immunisation may also be due to allergy, and that the sequelæ of a particular prophylactic inoculation appear to be similar in distribution to the neurological complications of the infective disease concerned. As regards whooping-cough there seem to be some grounds for this suggestion; but as regards enteric fever and diphtheria the connection is far from distinct.

Clinical syndromes similar to those recorded after serum administration or inoculation may develop spontaneously or after non-specific infections. The radicular involvement is exactly comparable to that described by Spillane¹⁴ in 1943 as localised neuritis of the shoulder-girdle (in a series where injection was not regarded as an important factor), and to the 136 cases reported by Parsonage and Aldren Turner¹⁵ under the name of neuralgic amyotrophy; while comparable polyneuritis and encephalomyelitis may occur without obvious precipitating cause. If, as seems very likely, Miller and Stanton are right in suggesting that an allergic reaction in the central or peripheral nervous system is responsible for the cases following administration of serum or inoculation, it is at least possible that a similar mechanism accounts for the "spontaneous" cases.

THE VENOMOUS WASP

NATURE has endowed the common wasp (*Vespa vulgaris*) with a formidable pharmacological armoury. Jaques and Schachter,¹⁶ in a careful study, have isolated from wasp-venom histamine, 5-hydroxytryptamine, and a third potent contractor of smooth muscle which they believe may be identical with bradykinin. These substances were found in large amount; histamine, for example, constituted 2% of the soluble matter in the venom—a concentration far higher than this widely distributed substance is known to attain elsewhere in Nature. Further, some wasp-venoms provoke release of histamine in the skin of the stung one; and all the venoms were found to contain large quantities of hyaluronidase. Thus science makes sense of our readiness to treat *Vespa vulgaris* with distant respect.

Dr. THOMAS CARNWATH, deputy chief medical officer at the Ministry of Health from 1935 to 1940, died on April 2 at the age of 75.

Mr. ARNOLD WALKER has been re-elected chairman, and Prof. A. A. MONCRIEFF vice-chairman, of the Central Midwives Board.

12. Byers, R. K., Moll, F. C. *Pediatrics*, 1948, 1, 437.

13. Toomey, J. A. *J. Amer. med. Ass.* 1949, 139, 448.

14. Spillane, J. D. *Lancet*, 1943, ii, 532.

15. Parsonage, M., Turner, J. W. A. *Ibid.* 1948, i, 973.

16. Jaques, R., Schachter, M. *Brit. J. Pharmacol.* 1954, 9, 53.

Special Articles

REMUNERATION OF HOSPITAL MEDICAL STAFF

A statement by Sir RUSSELL BRAIN as chairman of the Staff Side of Committee B of the Medical Whitley Council

1. NEW INCREASES AGREED

Committee B of the Medical Whitley Council have reached agreement on increases in the rates of pay of hospital medical staff which have been in operation since 1948. The agreement, which has effect from April 1, includes the following provisions :

- (1) The basic scale for consultants is to be £2100 rising by annual increments of £125 to £3100. This new scale gives an increase over the 1948 scale of £400 at the minimum and of £350 at the maximum.
- (2) The new basic scale applies to consultants with C distinction awards, who therefore obtain the same increase as consultants without distinction awards.
- (3) The increases for consultants with B and A distinction awards are, however, limited to £150 and £50 respectively.
- (4) The basic scale for senior hospital medical officers is to be £1500 rising by annual increments of £50 to £1950, an increase of £200 over the 1948 scale.
- (5) Senior registrars will receive £1100, £1200, £1300, or £1400 according to their year of service, an increase of £100 over the 1948 rates.
- (6) Registrars will receive £850 or £965 according to their year of service, an increase of £75 over the 1948 rates.
- (7) Junior hospital medical officers will receive a scale of £775 rising by annual increment of £50 to £1075, an increase of £75 over their 1948 scale.
- (8) Senior house-officers will receive £745, an increase of £75 over their 1948 salary.
- (9) House-officers are to receive an annual rate of £425 for the first, £475 for the second, and £525 for the third and subsequent posts (an increase of £75 over the 1948 rates), but the annual charge made to them for residence is to be increased by £25.
- (10) A maximum of $\frac{3}{4}$ of a session is to be placed on the weighting that part-time consultants and senior hospital medical officers are allowed when their salaries are calculated. This replaces the present maximum weighting of $1\frac{1}{4}$ sessions.
- (11) There is a protection against any individual losing pay on the coming into operation of the new agreement.

The details of the new arrangements are being worked out by the two sides of Committee B, and the full agreement will be transmitted to the Minister of Health and the Secretary of State for Scotland as soon as it is ready.

These increases are the final outcome of lengthy negotiations, and should be judged in the light of the following background and history of events.

2. HISTORY

Before the introduction of the National Health Service it was agreed that the range of remuneration for both general practitioners and consultants in that service should be determined by two Inter-departmental Committees, both under the chairmanship of Sir Will Spens. The Minister of Health and Secretary of State for Scotland on the one hand, and the profession on the other, agreed to accept the recommendations of these committees which became in effect the basis on which professional income in the National Health Service was fixed.

The recommendations of the Spens Committees were framed in terms of the 1939 value of money, and both committees explicitly stated that they left it to others to make the necessary adjustment to present-day values, such adjustment to have regard not only to changes in the value of money, but to increases in income which had in fact taken place in other professions since 1939.

The Consultant Spens Committee went further and stated that the adjustment should have regard to changes in income in other branches of the medical profession.

The Consultant Spens Report was not published until May, 1948, and when the National Health Service was introduced in July of that year hospital staff entered the new service on interim terms, relying on the assurance that the Minister had accepted the findings of the Spens Committee and would incorporate them in the new terms of service.

Subsequently the Government submitted the draft terms of service for hospital staff which, although following the recommendations of the Consultant Spens Committee, applied to them the same betterment factor as was given to general practitioners (20%). This betterment factor of 20% was not accepted by the profession as being an adequate or realistic adjustment of the 1939 figures to post-war conditions, and as early as January, 1949, a deputation from the Joint Consultants Committee and the General Medical Services Committee made joint representations to the Ministry on the subject. The Ministry's attitude at that time was wholly influenced by the white-paper on National Expenditure, and it declined to make any upward adjustment to the betterment factor.

In July, 1949, following discussions on the terms and conditions of service for hospital medical staff, the Joint Committee received certain assurances from the Ministry, among which were the following :

1. That no changes would be made in the terms and conditions of service without discussions in the appropriate part of the Whitley machinery.
2. That remuneration was regarded as a subject suitable for arbitration.
3. That save in exceptional circumstances, and after the conciliation machinery of Whitley had been exhausted, issues of remuneration remaining in dispute would go either to arbitration or for inquiry and report by a committee.

Thereupon the Joint Committee advised hospital staff to accept permanent contracts on the basis of the terms and conditions of service then offered.

Meanwhile there was growing unrest amongst general practitioners about the inadequacy of the capitation fee, and after prolonged negotiations the Ministry in October, 1951, agreed to refer the question of the size of the Central Pool to arbitration, on the understanding that whatever the result of the arbitration might be no additional monies would be paid unless agreement was reached upon a redistribution of the Central Pool. Mr. Justice Danckwerts was appointed adjudicator, and his award was published in March, 1952.

3. A CLAIM SUBMITTED

In June, 1952—shortly before Parliament approved the necessary supplementary estimate to implement the Danckwerts award—the Staff Side notified the Management Side of Committee B of its intention to submit a claim for increased betterment for hospital medical staff in the light of the Danckwerts award. At the outset of negotiations, and before detailed discussions had begun, the attention of the Staff Side was directed to the following statement by the Chancellor of the Exchequer in the House of Commons on 2nd July, 1952 :

"I want to make it clear that the terms of reference of Mr. Justice Danckwerts' award were confined solely to the question of the remuneration of general practitioners in the National Health Service and his award has no wider application. In accepting the results of the adjudication, which was of an exceptional nature, the Government have by no means adopted the view that similar adjustments in other fields should follow. In their view there is no justification for any assumption that the appropriate standard of remuneration for the professional classes is a rate of 100% above that in

force in 1939. They consider that remuneration should be determined in the light of all relevant circumstances."

The Staff Side was left in no uncertainty as to the Government's policy in the matter and the attitude of the Management Side. It was quite clear that in no circumstances could a claim be considered for hospital staff *based on the Danckwerts award*, nor could there be any agreement to submit any such claim to arbitration.

4. LEGAL ADVICE SOUGHT

At this stage the Staff Side decided to take legal advice and consulted Mr. F. Grant, Q.C., who had presented the general practitioners' claim at the Danckwerts adjudication. Amongst other things Mr. Grant was asked whether there were arguments to support a legal claim that the Minister's promise to implement the recommendations of the Spens Committee was implicit in the contracts which consultants had accepted with hospital boards. After studying all the available files, records of past meetings with the Ministry, and other relevant documents, Mr. Grant reached the conclusion that the Staff Side had no claim which was enforceable at law. He did not think that it could be argued that an undertaking by the Ministry to implement the terms of the Consultant Spens Report was a part of the contract on which consultants entered the service. But even if it could be so argued the Minister could claim that the terms of the contract also included an agreement between the Minister and the consultants' representatives that a dispute about outstanding matters concerning the terms and conditions of service should be referred either to arbitration or to a committee of inquiry.

In view of the Government's known attitude towards arbitration, Mr. Grant pointed out that if negotiations broke down in Whitley, the Minister could fulfil his undertaking by referring all aspects of consultant remuneration to a committee of inquiry. The results of such an inquiry could not be foreseen, but one danger was that the findings could in effect replace the Spens Report as the basis of consultant remuneration for the future.

5. BASIS OF CLAIM

During the course of negotiations it became clear that while there was no question of departing from the Chancellor's statement on the application of the Danckwerts award, there seemed to be a realisation that the balance between general practitioner and consultant remuneration had been disturbed, that this factor alone might have an adverse effect on the future recruitment of hospital staff, and that a claim based on such considerations might well form a basis for discussion and possibly agreement. Thus the Staff Side was faced with two alternatives: either, despite the Chancellor's statement, to press its claim for a strict application of the Danckwerts betterment, or to examine the increases which general practitioners had in fact received as a result of the Danckwerts award and to see how far these had disturbed the balance of remuneration.

After very careful consideration the Staff Side reached the conclusion that it had very little choice in the matter. The Government, it was clear, had no intention of departing from the Chancellor's statement, and the profession, in spite of continuous pressure, has still been denied the right of unilateral arbitration. Again, because of the different methods of remuneration in general practice and consultant practice, a straightforward application of the Danckwerts "betterment" of 100% to the "Spens salaries" would have meant that a consultant aged 32 would start at £3000 p.a. and rise automatically to £5000. Again a consultant holding an A merit award would receive £10,000. Apart from the fact that a claim of this magnitude would have been

totally unacceptable to the Management Side, the effect would be again to upset the balance of remuneration between the two branches of the profession.

There were also the inescapable facts that the Government acceptance of the Danckwerts award had been conditional upon an agreed redistribution of general-practitioner income, and that the effect of the award, coupled with the redistribution scheme, had not been to increase the remuneration of individual general practitioners by 100%. For all these reasons the Staff Side considered that the only practicable course was to examine the effects of the Danckwerts award in the general-practitioner field and to relate them to the position of hospital staffs.

It accordingly looked at the percentage increases of remuneration received by general practitioners with varying sized lists, in order to compare them—so far as it was possible to do so—with hospital staff at different levels on the salary scales. Of necessity the comparison could not be precise because of the fundamental differences in the two methods of remuneration.

In the general-practitioner field the effect of Danckwerts had been that the most financially successful general practitioners, with the largest lists, gained virtually no increase of income; again, at the other end of the scale practitioners with very small lists received only a small percentage increase. Practitioners with medium-size lists, on the other hand, received the greatest benefit from the award.

It proved far from easy to translate the comparison into salary increases for hospital staff. The Staff Side felt, however, that, as in the case of general practitioners, if recruitment to the hospital service was not to be affected, the major benefit must be applied to the basic consultant grade in which the majority of hospital staff would make their permanent career rather than to the highest grades where, in any case, taxation would largely nullify the effect of any increase, or to the lower grades in which most practitioners would not expect to have their permanent career.

6. WHOLE-TIME CONSULTANTS

The Staff Side had for some time been pressing the Management Side to review the position of whole-time consultants in the light of the recommendation of the Spens Committee that, in addition to their salary, consultants should receive allowances to cover the expenses reasonably incurred by them in connection with their duties (e.g., car, telephone, membership of learned societies, and purchase of necessary textbooks). Few of these expenses had been met under the terms and conditions of service, and none of them adequately, and it was the intention of the Staff Side that in the claim for increased remuneration the opportunity should be taken of meeting the just grievances of the whole-time consultant.

The solution proposed to the Staff Side for meeting the whole-time consultant's difficulties was that, as part-time consultants and S.H.M.O.s were enjoying disproportionate advantages in the calculation of their salaries, the weighting of sessions should be entirely abandoned, all future part-time consultants and S.H.M.O.s and existing part-time men on promotion to a higher scale being paid unweighted elevenths of the full-time scale.

Apart from the fact that a proposal of this nature would not result in any addition to the whole-time scale, but merely a relative advantage at the expense of his part-time colleagues, the Staff Side felt that it would involve an abandonment of one of the vital principles of the Spens Report to which it could in no circumstances agree. After a very long discussion, the Staff Side agreed that a case had been made for modifying the Spens weighting which at 5 and 6 sessions rises to

$\frac{1}{4}$ elevenths, and that a ceiling of $\frac{3}{4}$ eleventh for weighting should in future be applied. Existing hospital officers would however be fully protected against any loss of salary. Pressure will continue to be exerted on the Management Side to improve the allowances for whole-time consultants.

7. THE SPENS REPORT

The Staff Side is satisfied that the settlement it has achieved does in fact restore the balance between consultant and general-practitioner remuneration which was upset by the Danckwerts award. The differential increases now to be enjoyed by members of hospital staff are a result of a new system of distribution and are no more a departure from the Consultant Spens Report than were the differential increases enjoyed by general practitioners as a result of their new distribution scheme a departure from the General-Practitioner Spens Report. In the face of strong pressure to have it abolished, the principle of weighting for part-time consultants has been retained. The small modification agreed is but a part of the general redistribution of incomes.

The Staff Side is therefore satisfied that the agreement it has made with the Management Side in no way weakens the Spens Report as the basis of consultant remuneration. In their view Spens remains the yardstick of consultant remuneration, and either Side of Committee B is free to seek future adjustments in any grade, if experience shows that the present settlement is working unfairly.

8. CONSULTATION WITH THE PROFESSION

The Staff Side confidently hopes that hospital staffs will regard these increases as satisfactory. Consultants and other members of hospital staffs are, however, entitled to know why it was not found possible to consult them upon the outcome of the negotiations before agreement was reached. This is a difficulty which must always be faced when major issues are at stake. It is implicit in the Whitley machinery that representatives of both Sides have authority to negotiate and eventually to reach agreement. Failure to reach a settlement in Whitley without reference to the profession, would undoubtedly have led to the appointment of a committee of inquiry into the question of hospital staff remuneration in all its aspects. This would have delayed a settlement for a very long time and would not necessarily have led to a final agreement better than the one now reached. Moreover the Staff Side were told that, as an inquiry would probably follow any breakdown in negotiations, it was impossible for the proposed terms of a settlement to be made public, because, if they were rejected, the position of one or other party to the inquiry would be severely prejudiced.

Full consultation with the profession, even had it been possible, would therefore have meant interminable delays and possibly a hardening of the Government's views. Again the Staff Side was informed that one of the bodies represented upon it, the Central Consultants and Specialists Committee of the British Medical Association, had in July, 1953, passed the following resolution :

That the Central Consultants and Specialists Committee expresses its appreciation of the efforts of the Staff Side of Committee B, and of the Central Committee's representatives on the Staff Side, in the matter of the remuneration of hospital medical staffs, and gives such representatives full authority to agree, should they think fit, to such terms as the Staff Side can obtain; provided always that the principles embodied in the report of the Consultant Spens Committee are maintained, and that the committee's representatives will act without further reference to this committee only in case of necessity.

The Staff Side, being satisfied that its negotiations had safeguarded Spens and knowing that it could not refer the terms of the settlement to its constituent bodies,

none the less feels confident that the profession will agree that it took the right course in reaching agreement on the new increases. It realises that hospital staffs will be disappointed to find the increases in remuneration are not retrospective, but the Staff Side was convinced that insistence on retrospective application would have led to a complete breakdown in negotiations.

The Staff Side's task over the past eighteen months has been far from easy. It has had to press its claim during a period of national retrenchment and in the face of the Government's declared policy on the implications of the Danckwerts award. Only experience can show how far the increases obtained will improve recruitment in the hospital field, but in all the circumstances the Staff Side is satisfied that hospital staffs will welcome them as a reasonable adjustment to the position as it exists today.

SCOTLAND IN 1953

THE report for 1953 of the Department of Health for Scotland¹ remarks that during the year the new system of remuneration of general practitioners led to a notable increase in the number of doctors practising in partnership, and also contributed to a more even distribution of patients among doctors. At the end of the year there were 2527 principals participating in the service, of whom 1427 (56%) were in partnership, and there were 273 assistants. Corresponding figures for the previous year were 2438, 1285 (53%), and 306.

The gross cost of running Scotland's first health centre, at Sighthill, Edinburgh,² which was built at a cost of £157,000, is £13,000 a year—without provision for redemption of capital cost, for the remuneration of doctors, dentist, and pharmacist, or for the cost of drugs dispensed in the pharmacy. The Exchequer bears £4500 of this, the corporation £6700, and the doctors £1800. A much smaller health centre is being built at Stranraer; but, apart probably from a further experiment on this scale, in a new town, no further health centres are contemplated pending experience of the arrangement for encouraging partnerships and group practice.³

During the year hospitals in some parts of the country found difficulty in obtaining junior staff, particularly house-officers.

"This was partly due to a temporary fall in the number of graduates coming from the Universities of Edinburgh and St. Andrews arising out of the transition of a five-year course of studies in these universities to a six-year course. Even when this phase passes, however, the number of graduates coming from the Scottish Universities each year will be below the high level of the post-war years, and it will not be possible to rely on house officers for the junior staffing of hospitals to quite the same extent as in these years."

New graduates had no difficulty in finding approved posts in which to spend the pre-registration year called for by the Medical Act of 1950. Most new graduates sought such posts in the teaching hospitals, and peripheral hospitals often had difficulty in filling resident posts. Accordingly boards of management sometimes had to employ senior house-officers instead of house-officers.

During the year the death-rate from respiratory tuberculosis reached a new low level of 23 per 100,000 population—18% below the lowest previously recorded figure of 28 per 100,000 in 1952. Notifications, which had fallen from 167 per 100,000 in 1949 to 144 per 100,000 in 1952, rose slightly to 147 per 100,000.

1. Reports of the Department of Health for Scotland and the Scottish Health Services Council, 1953. H.M. Stationery Office. Pp. 144. 4s. 6d.

2. See *Lancet*, 1953, i, 1038.

3. See *Ibid*, Jan. 30, 1954, p. 250.

Public Health

CONTROL OF DENTAL CARIES

Beginning at the Beginning

ANNE BURGESS
M.B. St. And., L.D.S.

JOHN BURTON
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DENTAL caries is a painful, harmful, and wasteful disease which is almost entirely preventable. Yet we are not preventing it—presumably because the task seems too difficult. Are there then any comparatively simple and practicable measures which could be relied on at least to modify the present deplorable picture of general dental decay? A review of three reports from Scandinavia suggests that there are.

Lessons from Scandinavia

In Denmark, Norway, Sweden, and Finland a big effort has been made to provide good dental care for children. Recounting his observations as the first Gibbs travelling scholar, James¹ says that in Scandinavia as a whole the ratio of dentist to population is higher than in this country (1:2304 as against 1:3333), and the school dental services are of a high standard.

Routine inspection and treatment are carried out in clinics built for this purpose and forming part of the school buildings. A school of 1000 children will often have two surgeries, comfortable waiting-rooms with toys, books, &c., for the children, and probably other small rooms for sterilisation, radiography, and a rest-room for the staff. In Norway dental hygienists are employed, who chart the mouth, and supervise the children as they brush their teeth before going into the dentist. They attend to scaling and polishing, apply fluorine, and give educational talks.

The acceptance-rate for treatment averages 95%. In Denmark assent is assumed unless parents actively object. In Norway, if a child refuses, free treatment is withheld until he has been made dentally fit at the parents' expense.

The dentist : child ratio is high—Bergen has a figure of 1:560 (which is considered too low by those in charge) and Oslo of 1:800 children, with 57 clinics, of which 3 are mobile. (In Middlesex—one of the best-staffed counties in England—the approved establishment is 1:3000 children, and that is not at present maintained.)

The Scandinavian dental schools have many more applicants than they can accept, and after receiving his free education the dentist must spend two years in the public dental service, or (in Denmark) in a public service or as an assistant in a private practice. Private practice is allowed to many dentists working in the public dental services.

Dental propaganda concentrates on (1) promoting oral hygiene; (2) encouraging good dietetic habits, and discouraging excessive sweet-eating; and (3) maintaining public interest in dental affairs.

The Oslo breakfast—a meal of milk, wholemeal bread, margarine, fresh fruit or raw carrot, meat, fish or cheese—is given to each child on arrival at school. This is considered a valuable part of the routine education for dental health, teaching as it does the proper foods to promote dental health and necessitating adequate chewing to promote self-cleansing of the teeth and development of the jaw muscles and bones. Posters, leaflets, and pamphlets and periodicals reinforce the importance of oral hygiene, good diet, and the harmful effects of too many sweets. There is much closer co-operation between the dental profession and the press than exists in this country, and items of dental interest are published regularly.

In so far as the aim of the Scandinavian dental-health education is to enable people to keep caries within reasonable bounds and reduce its harmful effects, this education must be regarded as highly effective. Children (and their parents) accept the services of the dentist as a normal part of school life; and such acceptance is,

in the case of the children, encouraged by prizes for good behaviour in the dental chair. Dentists regard the public dental services as rewarding work with recognised prestige. The community as a whole is interested in dental matters, and parents, teachers, and private dental practitioners co-operate well with the public dental services.

But unfortunately the primary object—to prevent or diminish the incidence of caries—has by no means been realised; for the caries-rate in Scandinavian schoolchildren is actually somewhat higher than it is here. Moreover, in a recent investigation in Sweden it was found that the children spent on the average 1s. 5d. per head per day on sweets. James remarked that the children "appeared to be eating or sucking almost throughout their waking hours."

This educational failure is perhaps not surprising when one remembers that before they start school, with its regular dental care, most of the children are 7 years old and their eating habits are already formed. Children are quick to please their parents by learning to like the sweets which are continually presented to them as desirable—as gifts, rewards, bribes, and treats; and once such a habit is established, it is as hard to cure or moderate as any other addiction. Moreover, the very excellence of the school dental service in Scandinavia must make people regard caries as inevitable, especially as emphasis is placed, by rewards and penalties, on a passive acceptance of cure rather than an active personal endeavour to remain caries-free.

Except in Norway, dental supervision and treatment are not given free to the pre-school child, and the fact that a charge, however small, is made, must tend to create an impression in the parents' minds that pre-school dental care is more of a luxury than a necessity.

MOTHER AND CHILD

Toverud,² has shown that preventive measures begun during the mother's pregnancy cause a greater reduction in caries than those begun even in the first year of life. His advice to mothers emphasised the importance of a good calcifying diet and the minimal use of sugar, as sweets or sweet cakes. Education of the mother before the birth guards against the early introduction of the child to the taste of sugar on dummies dipped in sugared water, honey, or rose-hip syrup, or in the "suckable" sweets so often given in the first year of life. In Toverud's "health station" the children and their mothers were also instructed, by a dental hygienist, in cleaning and brushing the teeth.

"SUGAR CLEARANCE"

Claes Lundqvist³ has tried to discover whether the timing and method of consumption of carbohydrate foods affect the incidence of dental caries. Having established that, until sugar is taken by mouth, the saliva is sugar-free, even if there is hyperglycaemia, he measured the time taken for the saliva to become sugar-free after eating sugar in different quantities and forms, and at different times of day. Of customary foods, candy, honey, and sweetened breads had the highest "sugar-clearance time," and normal toothbrushing habits did not prevent exposure of the teeth to a harmful sugar solution for a large part of the day. To induce everyone to brush the teeth immediately after taking any sweets or sweetened foods is out of the question; but Lundqvist found that, after saturation of the oral cavity with sugar, one rinsing with 20 ml. of water rapidly lowered the sugar content in the saliva. He therefore recommends that the mouth should be vigorously rinsed with water (which is then swallowed) immediately after all meals and also immediately after eating anything sweet.

2. Toverud. *G. Brit. dent. J.* 1949, 86, 191; *Aust. J. Dent.* 1952, 56, 25.
3. Lundqvist, C. *Odont. Revy.* 1952, 3, suppl. 1.

1. James, P. M. C. *Dent. Practit.* 1952, 3, no. 4.

What Might be Done

The exact process by which dental caries is produced is not yet known, but it is a combination of decalcification of the mineral matter and decomposition of the organic matrix of the tooth. Decalcification takes place in an acid medium, such as is created when soluble carbohydrates are available to acidogenic bacteria. The decalcifying solution is kept in contact with the tooth surfaces by any residue of food particles in the mouth.⁴

In this and other countries the incidence of caries was substantially lower during the war and in the years immediately after it, when sweets, sweet cakes, and white bread were scarce or unobtainable.⁵ But this reduction is now being reversed, and the caries-rate is again rising.

In Britain today, then, the situation is that dental caries is on the increase; the dental service to schoolchildren and the priority groups remains grossly inadequate; and the highly refined carbohydrate foods—sweets, cakes, and buns—are increasingly available. This serious state of affairs, and the difficulty of meeting it by traditional means, has directed attention even more urgently to methods used abroad.

Ancillaries.—In New Zealand, where caries is prevalent, the school dental services are operated by dental nurses who, after two years' training, are qualified to do all the routine work—inspections, scalings, simple fillings, and extractions for the pre-school and school children—and also carry out dental-health education. This system has been found to work well.⁶

Other countries have adopted the dental hygienist, whose training lasts one year and who is generally restricted to educational work, and scaling, cleaning, and regular inspection of the teeth. The usefulness of hygienists depends on there being a more or less adequate team of dental surgeons who can delegate the simpler procedures to them. In the absence of enough fully qualified personnel—as in Britain today—the hygienist is unlikely to have much scope.

Fluoridation of Water-supplies.—Fluorine is thought to act by increasing the resistance of the tooth structure rather than by reducing the activity of caries-producing organisms. The U.K. mission which visited the United States and Canada has recommended that controlled investigations of the effect of fluoridation be made in this country⁷; but past experience of preventive measures applied on a national scale (e.g., diphtheria immunisation) suggests that a long time will elapse before the research findings on the efficacy of the fluoridation of water can be implemented.

What then can be done now? Scandinavian experience shows the limitations of even a highly efficient school dental service, and of dental-health education of the public as generally carried out today: existing caries is controlled but its incidence is not reduced. What stands out is the need for dental-health education to be a recognised part of the general health education and supervision of the expectant mother. Stress should be laid on the mother's nutrition—on the advantages of consuming enough protective (and particularly calcifying) foods, and the disadvantages of consuming too much refined carbohydrate. If the child becomes habituated to the taste of sweet substances from the first year of life, later exhortation to reduce the consumption of sweet foods is practically useless. But the taste for sweets is an acquired taste. If a child is not given the usual early training to regard sweet things as "treats," he grows up without any special preference for such things.

Furthermore, mothers should be taught to give the child a drink of water at the end of each meal. Later this can be developed into a more vigorous rinse—but the habit should be begun as early as possible. We believe that a determined effort should be made to spread

this knowledge widely. Money now devoted to the instruction of children and others whose eating and oral hygiene habits, and whose values about dental health, are already formed should be diverted to "educating the educators"—doctors, nurses, health visitors, midwives, the personnel of day nurseries and nursery schools, and teachers in contact with parent-teacher organisations and adolescents in school.

We think it also desirable that the services of a dental auxiliary should be available to mothers and children attending antenatal clinics, infant-welfare centres, day nurseries, and nursery schools. To all children attending the centres, nurseries, or schools, and to those referred by the family doctor, the dental auxiliary would give regular routine inspection, instruction in oral hygiene, and simple treatment where required. Doubtful or difficult cases could be referred to the local-authority dental surgeon or to private practitioners co-operating with the dental service. Even without the evidence about New Zealand dental nurses, our experience in other fields, such as midwifery and nursing, should have convinced us that, in their own restricted fields, ancillaries can achieve greater skill than a general practitioner. Their use in dentistry would release the dental surgeon to practise dental surgery in the fullest sense.

In his report for 1951 the Chief Dental Officer for Middlesex wrote:

"Unfortunately, the nursing and expectant mothers have got out of the habit of visiting the dental clinics, because so many of these have been closed down for long periods. A great deal of re-education will be necessary in order to persuade them of the value of complete dental fitness during the period of gestation and the subsequent nursing period.

"To achieve this re-education it will be necessary to have the co-operation of the medical and nursing staffs who so ably assisted in building up the maternity and child welfare dental services before the National Health Service Act came into force."

This "co-operation in education" is vitally important, and not only for assuring the dental health of the mothers but for preventing a further decline in the dental health of children. The doctors and nurses are ready in the welfare centres to do their part. If the dental members of the team are not forthcoming, then substitutes should be found. In 1921 the *New Zealand Dental Journal* said:

"Public necessity must take precedence over the interests of the individual, or the demands of any dental school, wherever conducted. . . . When the Director of Public Dental Services demands in the near future some 200 assistants to cope with work urgently required, and the Dean of the dental school can promise but a possible 20 or 30, a discrepancy is shown to the disadvantage of the public which cannot be bridged by present methods."

That is still the situation in this country today, and it must be faced realistically.

Tuberculosis in Glasgow

Opening a chest clinic at Belvidere Hospital, Glasgow, on March 26, Commander T. D. Galbraith, M.P., under-secretary of State for Scotland, remarked that since the start of the National Health Service in 1948 more than 1500 additional beds (including 200 in Switzerland) had been provided for Scottish tuberculosis patients. The number of staffed beds—about 5750—was more than three-quarters of the number of new cases last year. "In other words, if the present waiting-lists could be overtaken we would then be able to provide an average stay of over nine months for each newly notified patient even if the present rate of notifications continued." But in Glasgow alone 900 patients were on the waiting-list at the end of last year. New beds could not be brought into commission without more nurses.

"In these circumstances I have been surprised and bitterly disappointed that certain of our Glasgow hospitals have not seen their way to co-operate in a scheme of seconding nurses under training from general hospitals to sanatoria, which has been successfully tried out in the South-Eastern and North-

4. Parfitt, G. J. *Hlth Educ. J.* 1953, 11, 32.

5. Sognnaes, R. F. *Amer. J. Dis. Child.* 1948, 75, 792; *Brit. dent. J.* 1949, 87, 291.

6. Fulton, J. T. *Experiment in Dental Care.* World Health Organisation monograph no. 4. Geneva, 1951.

7. Fluoridation of Domestic Water Supplies in North America as a Means of Controlling Dental Caries. Report of the United Kingdom Mission. H.M. Stationery Office. 1953.

Eastern Regions in Scotland and in many English cities. These schemes have enabled many more beds to be staffed, and it is not surprising in view of the precautions that are now taken that the health of the nurses taking part has been excellent. It is also significant that the nurses have thoroughly enjoyed the work, have found it a valuable part of their training, and have been proud of the part they have played in the fight against tuberculosis."

By improving the facilities for outpatients, the turnover in hospitals could be speeded and the best possible attention be given to patients at home. Commander Galbraith accordingly welcomed the plan to build five new chest clinics in Glasgow, of which this was the first.

Deaths in 1953

According to provisional figures issued by the Registrar-General,¹ the death-rate in 1953 for cancer of the lung and bronchus was 343 per million population of England and Wales. In women the rate remained steady (99 per million, compared with 98 in 1952), but among men it rose to 607 per million from 568 in 1952. The death-rates for all forms of cancer were 2165 and 1836 per million in men and in women respectively, compared with 2151 and 1850 in 1952.

The death-rate for respiratory tuberculosis was 179 per million—a decrease of 16% from the previous year. The rate for other forms of tuberculosis was 22 per million (28 in 1952).

¹ Registrar-General's Return for the Week ended March 27, 1954. H.M. Stationery Office. Pp. 20. 1s.

The rate for maternal mortality (excluding abortion) was 0.65 per 1000 live and still births, compared with 0.59 in 1952—the lowest ever recorded.

Infectious Diseases in England and Wales

Disease	Week ended March			
	6	13	20	27*
Diphtheria	34	22	18	14
Dysentery	1007	1001	1124	1315
Encephalitis :				
Infective	5	1	4	2
Postinfectious	1	2	1	4
Food-poisoning	194	344	159	130
Measles, excluding rubella	2449	2214	2325	2067
Meningococcal infection	27	47	36	35
Ophthalmia neonatorum	24	35	41	34
Paratyphoid fever	15	96	45	20
Pneumonia, primary or influenzal	709	757	705	661
Polyomyelitis :				
Paralytic	14	15	13	15
Non paralytic	4	7	6	9
Puerperal pyrexia	242	239	262	233
Scarlet fever	1379	1480	1282	1492
Smallpox
Tuberculosis :				
Respiratory	740	887	790	785
Meninges and C.N.S.	12	20	13	13
Other	116	98	107	82
Typhoid fever	1	2	2	2
Whooping cough	2042	2096	2548	2558

* Not including late returns.

The Widdicombe File

X. THE PAINLESS APPENDIX *

DEAR LAWSON,

We have never met, but I see that you are a King's man, which means that you have been well brought up and have learnt the basic principles of surgery at the feet of my friends John and Cecil and Harold. You have also learnt what is even more important—to accept the teaching of authority as a working hypothesis only, till you have proved it by your own experience.

You ask me whether I have met an appendix abscess that has developed with no abdominal pain whatsoever until it ruptured. I have, and so will you some day; but you will not be misled if you have listened carefully and examined conscientiously.

Pain is due to tension on nerve-endings, and it is therefore nearly always present at some time in an inflammatory lesion—usually in its early stages. The classical signs of inflammation are, as you know, *Rubor, tumor, calor, et dolor*. The pain arises in tension and is usually most marked when the tension is increasing. It is slight if the tension increases only slowly; it diminishes when the tension ceases to increase; and it disappears when the tension is relieved, or the nerves die—that is, when the abscess bursts or the inflammation goes on to gangrene.

The appendix is insensitive to all those mechanical, thermal, and chemical stimuli that cause pain when applied to the skin or the parietal peritoneum. It responds to an increase in tension either in its lumen or in its walls by a viscero-sensory response—colicky pain referred to the umbilicus and vomiting. This is merely a midgut reflex common to all parts of the alimentary tract supplied by the superior mesenteric artery and its branches when they are subjected to tension: there is nothing to distinguish early appendicular colic from the colic occasioned by unsuitable food or by an aperient. As soon as the walls become inflamed, the visceral stimulation, and with it the colic and vomiting, cease, and true pain follows only if the inflamed appendix lies in contact with some structure able to appreciate pain. In classical appendicitis the appendix lies in its classical position, somewhere in the right iliac fossa, where the parietal

peritoneum responds by pain to the contact of any surface that differs from its normal environment of peritoneal surfaces equally smooth.

May I cite some examples of painless appendicitis I have met?

1. *Pain was absent because the inflammatory process developed only slowly.*—A girl of 22 consulted her doctor one Monday evening because she was feeling unwell. She was due to be married on the Tuesday week. She had been feeling "mouldy" ever since the previous Wednesday, a little mouldier each day, but she had had no pain, vomiting, or disturbance of her normal bowel habit. Her period, which had just ended, was a normal one. The doctor found that her pulse and temperature were normal and her abdominal muscles were not on guard, but she was definitely tender on deep pressure over a well-demarcated area medial to McBurney's point and well above the pelvic brim. On rectal examination no tenderness was found till the uterus was moved by pressing on the cervix.

Though the girl had had no pain, she certainly had a tender appendix. In view of the approaching wedding, I should have been tempted to wait and hope, had the history been a short one; but ten days' malaise meant a slowly progressing infection that could not be expected to subside. The appendix was swollen and a dusky red, and contained thick pus, but the peritoneal reaction had not got beyond a clear effusion. The wedding took place on time.

2. *Pain was absent because the inflammatory process had been aborted by antibiotics.*—A medical student woke up with a sore throat and a temperature the day before his Finals. He gave himself a shot of penicillin, and repeated the dose that evening, and next morning before he went to write his papers. He felt slightly worse that evening, but had no pain and only slight pyrexia. He gave himself an injection of penicillin night and morning for the next eight days till he had been up for his vivas which he succeeded in passing. That evening he felt too ill to celebrate and went to bed early. There, for the first time, he felt a lump in his right iliac fossa. He dressed and sought out the Registrar on duty and asked him to examine him. At operation two hours later he was found to have a gangrenous appendix lying in a small abscess cavity and walled off by omentum.

* This is a copy of Sir Daniel Whiddon's reply to Dr. G. G. Lawson's letter in our issue of March 20.—ED. L.

3. Pain was absent because the appendix was lying in the pelvis.—The missed pelvic appendix is seen several times a year in every large general hospital. The patient has felt ill for some hours, and later has complained of central abdominal colic and vomiting. His temperature has been found elevated, perhaps to 101°F, and his pulse has been accelerated, perhaps to 96; but on palpation of the abdomen no tenderness and no guarding have been discovered. A provisional diagnosis of gastro-enteritis has been made, and the patient has been taken off work and sent to bed, where he has been visited twice daily. His temperature has remained elevated, his pulse-rate has risen slowly, and he has started to look ill. He has refused food. Repeated enemas have produced little beyond flatus. He has then started to get diarrhoea, and the diagnosis of gastro-enteritis seems to be confirmed. Then one day the appearance of a lump above Poupart's ligament, or a gush of pus from the rectum, has established the true diagnosis.

The inflamed pelvic appendix is painless because it lies among viscera that have no pain fibres. It is tender when it is palpated, but it can only be palpated from the rectum.

4. Pain is absent because the patient is not appreciative of pain.—Just as the same wireless programme differs according to the quality of the set on which it is received, so the same painful stimulus produces quite a different sensation in different cerebral cortices. What is agony to one man is a discomfort barely worth mentioning to another. The old are apt to be either insensitive or uncomplaining; at any rate appendicitis in them is very often met in the guise of an abscess appearing without previous symptoms. The man mentioned in my previous letter was an example of such a clinical picture. Any surgeon of my seniority will recall others. Even when there is pain, the old hate to make a nuisance of themselves. They have had many bellyaches in their time. This is another. If it doesn't go tomorrow, a good "clear-out" will put it right. The dose of "health salts" sets up a peristalsis in coils of gut that have been trying to wall off an abscess, and floods the peritoneal cavity with pus.

* * *

Medicine is an entrancing study because it cannot be reduced to set rules. We can learn the typical picture of any disease, which is compounded of the features of the disease process and the way it affects the form and functions of the organ or system it attacks, and of the modifications imposed on that process by the age, sex, and general health of the victim. We must learn the typical picture, but we shall be constantly modifying and enlarging it as we meet further instances of the disease in which some of the familiar features are missing or new ones are added, and by experience we shall learn wisdom.

When I was a student, the Registrar who tried to teach me medicine recounted the story of a conscientious student, who recorded his daily experiences in a notebook. One of his patients suffering from typhoid was caught by the Sister eating the last of two dozen oysters smuggled in by his wife. To everyone's astonishment he improved rapidly. The student made an entry "Oysters are good for typhoid." Shortly afterwards he went on a holiday to Paris with a friend. The friend contracted typhoid, and, remembering the former case, the student bought him two dozen oysters. The friend ate them and died. The student turned back to his former entry and added a footnote—"Oysters are good for typhoid, but not in Paris." Had he lived long enough, seen enough cases of typhoid, observed them as carefully and recorded the results of his observations, this student would have died the wisest typhoidologist in Europe.

If you ever travel to the West Country I hope you will look me up.

Yours sincerely,
DANIEL WHIDDON.

In England Now

4 Running Commentary by Peripatetic Correspondents

AN annual report should be stirring, amusing, telling, revealing, and written with fire—but briefly. Turning its readers from the revulsion which they naturally experience at the sight of it, it should rouse them to passionate enthusiasm for the Cause, whatever that happens to be. Of course some readers are easier game than others: I am easy game myself; partisanship comes so naturally to me that I sometimes think I have Irish blood. But even a born partisan can be choked off so completely by a stodgy report that you can hardly tell him from a Scot.

As a constant reader—perhaps the only constant reader?—of this type of literature, I am in a position to offer a few tips on flavour. First, I can fully recommend the reports of the Muffled Foundation: they have the right air of being breathless (if not silent) on a peak in Darien, with a sea of new things to be done lying straight before them. The Effingham League for Senile Reform also do well, though they are inclined to be almost too moving. The Board of Tightlip err in the opposite direction, mumbling out a quantity of figures; and even when these bear a favourable interpretation the report contrives to sound a decayed and melancholy note. The Royal Association for Psychic Toleration (R.A.P.T.) is spirited enough, but has a told-to-the-children flavour not acceptable to all. Presumably a pen lies behind the printed page of every annual report, and a person behind the pen. Perhaps it has not struck this ambiguous character that he has a reader? Should I offer to publish for his benefit an Annual Report on Annual Reports, this being the first? But no: in the character of Constant Reader, I find my remarks rouse no answering spark in myself—only a Caledonian-type repugnance.

* * *

Once upon a time there were very few maternity hospitals and all the mothers had their babies at home. Some of the bad cases died, and everybody was very sorry. So they built lots and lots of new maternity hospitals to take the bad cases, and not so many died, and everybody was happy. It was such fun for the mothers to go to hospital to have their babies that it soon became hard to find a bed for the bad cases, but all the mothers explained very loudly why their own homes should not be upset by the new babies.

And once upon a time, a bit later than the last time, there were very few geriatric units, and all the grandmothers died at home in the loving care of their children, and everybody was happy. So someone built lots and lots of geriatric units and homes for the aged sick, and the grandmas died well away from their children, and no-one could care less. It was such fun to get rid of the grandparents that it soon became hard to find a bed for the bad cases, but all the children explained very loudly why their own homes should not be upset by the grandmothers.

It is so much nicer to sit right in front of the television, and have plenty of room on the kitchen table to fill in your football pools, and be able to go to the cinema whenever you want. After all, you stamp your cards every week so it's only right that someone else should have the bother of looking after baby and grandma. St. Augustine? Never heard of him.

* * *

The arrival of spring has ended the armistice imposed by "winter and rough weather"; the campaign has opened, and the attackers have taken the field in force with all the latest weapons. With his right hand on the hilt of his drawn sword, and his left clasping a telescope to his martial breast, Lieut-General Sir James Outram, the "Bayard of India," surveys the battle from his panoplied pedestal in the Victoria Embankment gardens. Which side is he backing? The gardeners or the leather-jackets? And what a strange thing it is that these larvae of daddy-long-legs should thrive under the very beaks of thousands of roosting starlings, whose favourite food they are. Do the birds, like some human beings, despise what is close at hand and lust after the exotic and far away?

My wife lately sent an article to one of the shiny magazines. She wrote as a housewife and mother of three children, and the article seemed to me reasonably terse, human, interesting, and practical; but as it described acquaintances, we thought that if accepted it would have to be signed with a pseudonym.

We attacked this problem lightheartedly enough. Perhaps a name from Jane Austen—Emma Woodhouse? No. Emma wouldn't write this. Elizabeth Bennet might, but the name was somehow inappropriate. So we decided to invent an elegant, friendly, well-balanced name that would suggest common sense and charm. My first suggestion of Carol Underwood was rejected out of hand, a judgment which, now, a week later, I think was fair enough. I then suggested Elspeth or Janet Something, but my wife declined to pose as a Scot. We wanted a pleasant-sounding name with a human touch—yet not too down-to-earth, like Martha Butt; nor too exotic, like Berenice, Hildegarde, Carmen, or Aly's; nor too literary, like Imogen or Miranda; still less too Hollywood, like Gloria or Marlene. Then what about a sound, non-committal, correct name like Mary or Ann? The problem then would be to find a suitable surname to go with it. My wife turned down several of my suggestions on the ground that she "knew them at school." Jennifer and Penelope seemed a little young, and I was obdurate about Camilla, which my dictionary says means "an attendant at a sacrifice."

This week's *Lancet* lying on the table suggested anagrams, and we worked out Thea Clent, Tena Chelt, and the sinister-sounding Lethe Cant before we sadly gave up. We were still discussing the matter when the article returned to us with the Editor's regrets.

* * *

The undertaker who preferred to have his operation in the hospital where the mortuary was not so damp (this column last week) reminds me of a post-mortem-room attendant at my hospital many years ago, who needed surgery for a severe disease. Asked by the R.M.O. to choose his surgeon, he named Mr. A. When asked why, he replied "because I have seen more of his work than of the others".

* * *

"Pay no heed to these marks," she said when I was examining her offspring at the clinic. "It's what the doctor calls that popular dirty area."

* * *

The modern operating-table is a beautiful engineering job, enamelled and plated, with lots of handles and a fine miniature railway to which to fasten the dinglum-danglums. But it has two serious defects.

The hinges—or breaks as they are often humorously titled—divide the table symmetrically, without apparent regard for the distribution of the main bends in the human frame. Thus, the central break—for kidneys and gall-bladders—comes where a patient, lying comfortably, keeps his pelvis. Move the body to the break and the feet project from the end of the table while the other end of the table compresses the anaesthetist's chest. Equally, the two minor breaks occur below the knee and about the middle of the scapula. To cope with this we are designing an infinitely bendable table in polyvinyl plastic.

The other defect is more subtle. Tables can be moved skyward or cellarward, usually by footpump, so that the work can be accommodated to the eye level of the surgeon. But our Mr. Short needs a low table, which means that his assistant Dr. Long risks his discs and his cortisone and develops a postural kyphosis, threatening soon to become fixed. Mr. Short will not operate on a box, which might allow a high table and relieve Dr. Long; he is afraid he will fall off. We have tried tipping the table sideways, but surgeons obstinately remain vertical. However, we feel we have the answer at last. In co-operation with the engineer we have devised a neat, fully adjustable, and portable hole-in-the-floor, with which we are confident we shall be able to make Dr. Long comfortable.

* * *

Treating patients is like playing the violin. You can write books on the general principles, but it takes talent to give a performance, and outstanding talent to give an outstanding performance.

Letters to the Editor

LABELS FOR INTRAVENOUS FLUIDS

SIR.—The importance of precision in intravenous therapy is now widely recognised, not only in the volume of fluid administered but also in its crystalloid composition. This precision is hindered by the bewildering variety of labels which manufacturing chemists use to designate their products. Not only are the colours of the labels and the style of printing unstandardised, but different words are used by different firms to describe identical solutions. In particular, solutions of normal saline in 5% dextrose may be labelled in such a way that only careful scrutiny shows that there is salt in the bottle. It is therefore not surprising that from time to time mistakes are made because a label has been misread.

For many years the possibility of this sort of mistake in anaesthetic practice has been recognised and met by a uniform system of marking cylinders of anaesthetic gases. Admittedly the dangers of administering the wrong bottle of fluid intravenously are not so great or acute as those of giving the wrong anaesthetic; nevertheless, dangers do exist and every effort should be made to prevent them. It would be a distinct advance if the manufacturing chemists could agree to label their solutions for intravenous infusion in a standard fashion, and the use of different coloured labels for the different fluids would be a great help to clinicians in the wards.

R. S. HANDLEY

E. W. HART

L. P. LEQUESNE.

IDENTIFICATION OF DRUGS

SIR.—Every doctor has been faced with the difficult task of identifying tablets or capsules for patients. Drugs of widely different pharmacological action are made up in similar form. Conversely, pharmaceutical firms market the same drug in tablets of quite different shape, size, and colour. The problem takes on a more serious and urgent nature when the casualty officer is faced with a comatose patient and some pills are found in the patient's possession. Their rapid identification might enable him to give the correct antidote without delay. Moreover, many patients may swallow dangerous tablets because they confuse them with less dangerous compounds of similar appearance.

My attention was again drawn to the problem when some tablets, probably cortisone, were found in the possession of a patient who had died of coronary occlusion; they could not be definitely identified on sight, even by the staff of the regional centre from whom she had been receiving this drug.

I suggest that all tablets containing drugs on the Dangerous Drugs list should bear a standard imprinted mark. Secondly, tablets in this class should also be stamped with a number or letter code so that by reference to a list supplied to all hospitals, doctors, and pharmacists, it would be possible to identify the dangerous drug in the tablet. The trade-name could be imprinted on the reverse side. I also feel that all capsules containing dangerous drugs should conform to a uniform colour key.

I am writing to the Association of Pharmaceutical Industries to seek their advice and suggestions, and I hope that the co-operation and support of the pharmaceutical firms will be gained in this matter. It would be one of great importance as a safeguard both to the general public and to certain patients in particular.

Farnborough Hospital,
Kent.

M. B. KING.

HOSPITAL, DOCTOR, AND PATIENT

SIR.—While I appreciate how difficult it would be for consultants to make themselves regularly available to visiting relatives, I still think that the letter signed "Parent" in your issue of April 3 raises an important question, to whose consideration I should like to contribute two observations.

Firstly, I have found it necessary to expand my visiting-list by continuing to call on my patients while they are in hospital and, on the same day, on their families. This is the only way in which they can get any information and therefore the only way to prevent the spread of alarm and despondency.

Secondly, at a postgraduate course for G.P.s which I attended recently we were informed, as a body, that patients regarded their family doctor with undue trust and unmerited esteem.

Could these observations be connected, do you think?

YORK.

F. CHARLOTTE NAISH.

SIR.—For quite a long time we have read the complaint that patients in hospital are not told what is the matter, or what is to be done. These complaints have appeared in the popular press; in the reports of judgments delivered in the High Court; and now in your own columns. This seems to raise a question of serious import. In my own case, I try in an emergency to make the patient understand what is going on; and in rare cases (for example, if total removal of the larynx is proposed) I write to the patient's doctor, and to the patient, and then ask him to come for a special interview to ensure he knows all that is implied in the procedure.

But in nineteen cases out of twenty I say (in the outpatient department) "I will write to your doctor: go and talk it over with him." And when a patient is discharged from the wards, the same advice is given. We try to ensure that the family doctor is kept informed of the diagnosis, the proposed line of treatment, our findings, and our recommendations for aftercare. But I do rely on the *family doctor* to tell his patient as much as he thinks suitable. And I feel sure that this is the tradition of many years. I ask you, Sir, to guide us as to whether this old—and, in my opinion, essential—tradition must be sacrificed at the bidding of laymen, who have often little insight into the patients' best interests.

BRISTOL.

E. WATSON-WILLIAMS.

RESPONSIBILITY IN HOSPITAL

SIR.—The letter from Dr. Hamilton (March 27) claiming that the doctor should bear all the consequences of his professional decisions is pertinent and timely. Unfortunately his conclusion depends on the assumption that his professional decisions can always be made in isolation, and this is no longer always true.

A doctor working in a hospital makes many decisions which are modified by the prevailing circumstances in that hospital. If the hospital is understaffed or otherwise inadequate he may have to make what he knows are bad decisions, dictated by expediency. He may, for example, have to give blood to a patient under conditions which involve rejecting the advice of a recent circular on blood-transfusion in at least three separate and important places. If an accident results, such as the circular attempted to prevent, should he be blamed for flouting the advice? It appears rather unjust, to say the least, that he should be held entirely to blame for a professional "mistake" which was forced on him by the inadequacy of the organisation in which he works. His mistake is professional but the causes are administrative, and surely this should be fully recognised before any question of liability is considered. If authority decides that a

hospital is to undertake responsibilities for which it is inadequate, then that authority should accept the consequences of that inadequacy, professional or administrative.

Woolton, Liverpool.

H. E. VICKERS.

THE HOSPITAL MAKES FRIENDS

SIR.—Dr. Hardcastle complained in his letter of March 20 that the reports that he receives from hospital seldom contain any useful information. I am sure that all of us who have worked in general practice will agree that hospital reports are sometimes of no value, and I am equally sure that those of us who work as hospital registrars will say that the general practitioner is usually to blame. It is really a remarkable circumstance that a well-educated man is prepared to send to another a letter which is often devoid of syntax, may contain no words given in the Oxford Dictionary, and is almost always too short to convey any idea of the reason why it was written. Two examples, taken from letters brought to last week's clinic, ran as follows: "Patient's name and address. Recom. for investn. chest condition. Signature"; "Patient's name. ? dust. Yrs. Signature." Even the rather longer letter may be grossly misleading, and I recently received one in which the practitioner failed to mention that the patient had been attending the chest clinic for two months and was to be admitted to a sanatorium in six days' time for treatment of a pleural effusion. Some practitioners' letters are so misleading that I know of one senior physician who tells the students that he never reads the doctor's letter until after the patient has gone!

This is, of course, an absurd situation and may be the cause of some of the "useless" letters written to practitioners. Two such letters ran as follows: "I agree with your diagnosis and think the patient should be given radiotherapy"; "X-ray shows evidence of back pressure on the pulmonary circulation but no other abnormality." No doubt every practitioner has his own collection of prizewinning "useless" reports.

These are amusing stories, but this is a serious problem and I feel convinced that the practitioner does not get a "useful" reply because he does not make it clear what information he requires. Consultants are possibly not, but registrars certainly are, just as stupid as the rest of mankind and cannot be expected to divine the practitioner's wishes. The type of letter that I have quoted, which accounts for perhaps a quarter of those received at hospital, is quite obviously worthless when transferred to other professions. Who would write to the travel agent "? Blackpool" or to the solicitor "Recom. for trust fund"? If the practitioner wishes to know the blood-potassium level or the changes in the electro-encephalogram he must say so, and if he does not wish to know them he must not say merely "Please see and advise."

The practitioner is always in a position to give very valuable information about the patient's home and habits, but it is extremely uncommon for him to do so and a flood of social workers has to be employed to duplicate his work (and to do it rather less well). Having recently left general practice, I realise how much is lost when one does not know the patient's social background, and I have the greatest respect for the G.P.'s special knowledge of it. So far my efforts to benefit from this knowledge have met with no success whatever, and I have never received any reply to the various questions that I have asked numerous different G.P.s.

It may be claimed that the burden of work on the G.P. is too heavy for him to find time to write fully and clearly, but I cannot believe that the burden is in any way lightened by the writing and receiving of useless letters. I have tried talking to the doctor on the telephone, but found that he was unable to give any information

"off-hand," and I have issued three separate invitations to another doctor to call at any time that is convenient to discuss a particularly difficult problem. Once again I have had no reply.

In spite of all this, I believe that the general practitioner is the most important member of the health service, and I most earnestly wish to see more co-operation between practitioner and hospital; but I can assure Dr. Hardcastle that the organisation of such co-operation is weary uphill work.

REGISTRAR IN TEACHING HOSPITAL.

CONTROLLED HYPOTENSION WITH ARFONAD

SIR.—The recent reports of the use of 'Arfonad' have been very interesting. We believe that any hypotensive technique should be used only when it is considered essential for the success of a particular operation. Our present experience with arfonad is, therefore, necessarily small; we have used it in 21 aural fenestrations and 5 craniotomies. We would, however, like to record that our findings are almost identical with those already published in larger series.

The anaesthetic technique recently described¹ for neuro-surgical operations has been used in every case, and it is essential, if oozing is to be avoided even when arterial pressure is low, to ensure a perfect airway, spontaneous respiration, and correct posture. The tachycardia that may follow the injection of gallamine triethiodide should preclude this drug in any hypotensive operation. The standard drip chamber has been used with a pendulum² and fine-adjustment regulator.³ This has allowed satisfactory control of dosage of an 0·1% solution. The ages of the patients in this series have ranged from fifteen to sixty-five years, and the average dosage has been at the rate of 2·3 mg. per minute.

We have been particularly impressed by the control during the induction of hypotension with this drug. The "pressure floor," mentioned by Dr. Scurr and Dr. Wyman (Feb. 13), and the individual variation in dosage required have been confirmed. Difficulty has been experienced in lowering the pressure in 4 cases, but even with a systolic pressure of between 80 and 100 mm. Hg, bleeding has not been troublesome. It seems that the lowering of the pulse-pressure to between 10 and 15 mm. Hg is more important in stopping bleeding than an absolute reduction of blood-pressure. In 4 long cases it was found that, after about 100 minutes, it was suddenly necessary to double the drip-rate to maintain the previously established blood-pressure. This change did not appear to be related to any change in the anaesthetic or any operative procedure. Like others, we have found procaine amide of value in reducing tachycardia. We would also stress the importance of replacing any blood that may be lost; if this is not done, difficulty will be experienced in restoring the blood-pressure to normal.

Cessation of administration has been followed by an immediate rise in blood-pressure, but it has often taken over 30 minutes to return to normal. In the neurosurgical cases, the systolic pressure has been allowed to rise to 90 or 100 mm. Hg before replacement of the bone flap, so that the surgeon could stop any bleeding. The postoperative condition of the patients has been excellent; there have been no cases of prolonged hypotension and no complications attributable to the anaesthetic.

The results published so far suggest that arfonad is a valuable drug, provided it is used with care and discrimination.

ROBERT I. W. BALLANTINE

IAN JACKSON

TOM B. BOULTON.

London, E.C.1.

1. Ballantine, R. I. W., Jackson, I. *Anæsthesia*, 1954, 9, 4.
2. Morton, H. J. V. *Ibid.* 1953, 8, 112.
3. Morton, H. J. V. *Brit. med. J.* 1953, 1, 990.

PREVENTION OF AIRBORNE INFECTION

SIR.—In your issue of March 6, Mr. Baker claims that a continuous-flow aerosol of hexylresorcinol might be used instead of ventilation to control the numbers of airborne bacteria in operating-theatres and dressing-stations, although he admits that no reports of its use for this purpose are available to justify his claims. We have recently completed analyses of an investigation of the use in clerical offices of hexylresorcinol vaporised from the thermal generators described by Mr. Baker. In this situation, no reduction was detectable in the bacterial counts in the air with the vaporisers working normally; and even when the vapour concentration was increased sixfold, and produced some throat irritation among the occupants of the room, the rate of kill of bacteria sprayed from the mouth was equivalent to no more than 6 air changes per hour.

The results of these investigations will be published in full elsewhere.

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O. M. LIDWELL
R. E. O. WILLIAMS.

BLOOD-UREA LEVELS OF WEST AFRICANS IN LONDON

SIR.—The observation of Phillips and Kenney¹ that the plasma-urea level in a small sample of West Africans was as low as 13·9 mg. per 100 ml. prompted us to compare a group of West African students in London with a series of English males of similar age-distribution. Twelve of the Africans were from the Gold Coast and the rest from Southern Nigeria; the Europeans were University staff, students, and technicians.

The urea was estimated on oxalated whole blood, freshly drawn by venepuncture, by Conway's method,² using urease Dunning tablets as the enzyme preparation. All estimations were performed in duplicate; samples from both Africans and Europeans were run in each batch of determinations together with a standard urea solution. We were subsequently able to examine a small series of serum specimens from blood obtained by venepuncture from African technicians at the University College, Ibadan, Nigeria, and sent by air to London in vacuum ampoules packed with ice. We are indebted to Mr. J. P. Garlick for this material and for certain information about the subjects. The data are summarised in the accompanying table.

Sample	No.	Sex	Age (years)		Mean blood-urea (mg. per 100 ml.)
			Mean	Range	
English ..	18	M	28·2	20-42	27·97 ± 1·32
London Africans ..	21	M	26·0*	21-29	24·78 ± 0·84
Ibadan Africans ..	13	{ 12M 1F	{ 16·56 ± 1·57

* Based on 18 subjects.

The mean value for the London Africans compared with the English gives a value of $t = 2\cdot19$ for d.f. 37, which is just significant at 5·0%, so that there is some evidence that, even on a European diet, the African blood-urea level is slightly low. The African subjects had been in England for a period ranging from 11 days to 7 years (mean $2\frac{1}{4}$ years). Plotting the urea level against length of residence in England suggested no obvious relation between the two, but the sample is small and includes very few recently arrived subjects. The mean blood-urea level of the London Africans compared with that of the Ibadan Africans gives a highly significant difference ($t = 5\cdot38$ d.f. 32, $P < 0\cdot0001$). When blank determinations were performed on these sera no evidence of prior decomposition of urea to ammonia was found.

Our results tend to confirm Phillips and Kenney's observation that the blood-urea level is low in Africans of intermediate economic status living on a native diet.

1. Phillips, P. G., Kenney, R. A. *Lancet*, 1952, II, 1230.
2. Conway, E. J. *Microdiffusion Analysis and Volumetric Error*. London, 1947.

in their own country. On questioning 11 of the Ibadan subjects, they all stated that they ate meat daily, and most of them also took beans several days a week and some of them eggs and milk occasionally; these were the only important sources of protein in their diet. We may conclude tentatively that their diet was probably not severely deficient in protein, but is likely to have been lower in this respect than the diet of our English subjects and African subjects in London. Whether the higher blood-urea level in the London Africans indicates that the urea level can rise to near European levels on European diet, or whether African students represent a sample whose urea was already at this level in their own country, the present data cannot decide. It is certainly by no means safe to conclude, without further investigation, that African students in London have enjoyed noticeably better dietetic and general medical conditions in their own country than have the group of Africans resident in Nigeria whose blood-urea has been examined. It would be of interest to examine the blood-urea levels, and perhaps other biochemical variables, in the same individuals both in West Africa and in England after varying periods of residence. It may be noted that, as Barnicot and Wolffson³ showed, the daily 17-ketosteroid output is definitely low in West African students in London, and perhaps not very different from the output in African labourers in Nigeria. The present results serve to emphasise, however, that a low blood-urea level does not necessarily occur in all groups of West Africans, and can, under certain circumstances, be close to the normal values accepted for European subjects.

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N. A. BARNICOT.
F. T. SAI.

THE COST OF PHARMACEUTICAL RESEARCH

SIR.—Your annotation of March 27 on the memorandum submitted to the Guillebaud Committee by the Scottish Committee of the British Medical Association concludes with a reference to the remarks, made in the final paragraph of the memorandum, concerning the N.H.S. drug bill and pharmaceutical exports and research. It is quite true that part of the cost of proprietary preparations "relates to research undertaken by the firms which produce them"; but surely the research component of overhead costs is a proper charge on the purchaser whether this be the State or a private concern? Indeed, it seems not only just but also highly desirable that the State, as the principal purchaser of prescription drugs in this country, should contribute towards the research expenditure from which the community derives so much benefit.

The suggestion in the Scottish memorandum that the N.H.S. may be subsidising pharmaceutical export trade is unrealistic, since the "N.H.S. trade" and the export trade are complementary—each benefiting from the existence of the other. The prices charged for prescription proprietaries in this country and to customers overseas are about the same, after allowing for the difference in distribution costs, and consequently the question of "subsidy" does not arise. If, however, any financial impediment were to be placed upon the research carried on by the pharmaceutical industry it would become impossible to maintain its export trade at the present high level (about £30 million a year) since it is largely upon the development of new and improved drugs that success in export markets depends. There is also the danger that a slackening of research effort in this country would tend to make the medical profession more and more dependent upon manufacturers overseas for essential drugs.

3. Barnicot, N. A., Wolffson, D. *Lancet*, 1952, i, 893.

In such circumstances the probability is that the N.H.S. drug bill would soar well beyond its present figure, and, incidentally, the country's balance of payments would also suffer.

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Secretary, Association of
British Pharmaceutical Industry.

SEXING SKIN

SIR.—There are indications that the skin-biopsy test of chromosomal sex¹ is being used in cases of hermaphroditism in various centres.² These studies will contribute to the theoretical background of errors of sex development in man; and the method is also of practical value to the clinician. But the limitations of the test must be appreciated and a word of caution may be appropriate.

The principal value of the skin-biopsy test of chromosomal sex in practice is in the differential diagnosis of the two main groups of hermaphrodites, when the clinical examination, short of laparotomy, is equivocal.³ These groups are the female pseudohermaphrodites caused by hyperplasia of the fetal adrenal cortex, and male pseudohermaphrodites. The congenital adrenogenital patients have typical female-type epidermal nuclei; cortisone, when administered early, aids in permitting subsequent development along female lines. All male pseudohermaphrodites whom we have had the opportunity of studying to date have typical male-type epidermal nuclei. The latter observation could not have been predicted with certainty and has been rather disappointing, since a proportion of male pseudohermaphrodites have pronounced female characteristics, anatomically and psychosexually. For the male pseudohermaphrodite group, the decision as to whether the patient should be treated as a male or a female must be made on the basis of all available data, and should not be influenced unduly by the male-type nuclei and the inference that the patient bears the male XY sex-chromosome complex.

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MURRAY L. BARR.

DIRECT INGUINAL HERNIA

SIR.—Mr. Brown's letter in your issue of Jan. 23 prompts me to reply. As coincidence would have it, I operated on a girl with a direct inguinal hernia on the morning of Feb. 18, and this issue of *The Lancet* arrived by mail plane that same afternoon.

Although I know that this is a rare condition, I do not understand its complete significance and I hope there will be authoritative replies to Mr. Brown's letter.

Using such references as are to hand in an isolated place like this, where mails are uncertain all the year round and where one does not see another doctor for months on end, I have put together the details of this case.

A normal healthy white girl, aged 17, arrived here by komatik on Feb. 12. She was complaining of a fairly large and painful swelling of the right groin. She had had a smaller painless swelling here for as long as she could remember, but two weeks previously she noticed this swelling had become twice its usual size, and was painful with undue exertion. The lump had never been completely reducible. There was no particular time when the increase in size was noticed.

She had a right inguinal hernia, the lump measuring about 4 cm. by 2 cm. It was not reducible partly because, it was assumed, the hernia was indirect. It was concluded that contents of the hernia were omentum, and that it was potentially dangerous. The left side appeared normal. Arrangements were made for admission to this hospital.

1. Moore, K. L., Graham, M. A., Barr, M. L. *Surg. Gynec. Obstet.* 1953, 96, 641.
2. Hunter, W. F., Lennox, B., Pearson, M. G. *Lancet*, Feb. 13, 1954, p. 372.
3. Barr, M. L. *Anat. Rec.* 1954, 118, 280.

At operation, the hernial sac was found to be very thin, covered with fat and adherent to surrounding structures, the fundus being adherent to the round ligament. Contents were omentum. It conformed in type to the funicular variety of direct inguinal hernia.¹ The sac wall narrowed to a well-defined and thickened neck, and proximal to this was a "secondary" sac, also adherent to a thin transversalis fascia. There was a gap of 3 or 4 cm. between the conjoint tendon and the inguinal ligament. This may have been unusually wide owing to the muscular relaxation with spinal anaesthesia, but was apparently a congenital widening.²

After ligation and excision of the sac, and amputation of the round ligament, repair was effected by the Bassini method. This seems doomed to failure when used to repair a direct hernia in the male, but may be successful in this case.

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Cartwright, Labrador. JOHN S. WHITTAKER.

THE THIRD FONTANELLE

SIR.—While making routine examinations of babies at a postnatal clinic I have tried to assess the frequency of the third fontanelle in non-mongol babies. Now Dr. Hoyle and Dr. White Franklin have published some statistics on this subject in your issue of Feb. 27, and I should like to add my own observations, for they provide more figures on a subject which has hitherto received little attention.

In 1500 non-mongol babies, all aged six weeks or less, a third fontanelle was found in 45 (3%). This figure is lower than Hoyle and Franklin's 4·3% for types 1 and 2 together, but higher than their figure for type 1 alone (1·8%). In my series I have included only those babies in whom the sign could be easily demonstrated to students and midwives, so that most of them would correspond to type 1 (fontanelle occupying an area of 1 sq. cm. or more), but undeniably some fontanelles of type 2 may have been included. However, most of the babies were four to six weeks old when examined, by which time some third fontanelles might have closed.

During the same period I have examined 12 mongols of comparable age (7 at the postnatal clinic and 5 elsewhere): 11 of these had third fontanelles and in only 1 was the sign absent. Incidentally, I agree with Dr. Carter and Dr. MacCarthy (March 6); I have been taught to speak of the third fontanelle in mongols as "Lightwood's sign."

Although there is little doubt that the sign is considerably commoner in mongols, it is, as we have seen, by no means confined to them. I believe it is misleading to regard it as a sign of mongolism. To me it implies poor ossification of the skull—a finding not unlikely in the mongol, but also to be expected in some babies of low birth-weight, especially if premature.

In the accompanying table I have related my own figures to birth-weights.

Birth-weight	No. of babies with third fontanelles	
	Non-mongols	Mongols
Less than 5 lb.	2	5
5-6 lb.	6 = 31	1 = 8
6-7 lb.	23	2
7-8 lb.	11	2
8-9 lb.	2 = 14	1 = 3
Over 9 lb.	1	0
Total	45	11

Anderson et al.³ have shown that birth-weights follow very closely the pattern of a normal distribution curve having a mean of about 7 lb.—i.e., in any large series

- Aird, I. Companion in Surgical Studies. Edinburgh, 1950; p. 534.
- Handfield-Jones, R. M., Porritt, A. E. Essentials of Modern Surgery. London, 1949; p. 590.
- Anderson, N. A., Brown, E. W., Lyon, R. A. Amer. J. Dis. Child., 1943, 65, 523.

there will be as many babies with weights below this figure as above it. The table shows, however, that over two-thirds of the babies with third fontanelles, whether mongol or non-mongol, fall into the lower half of this distribution curve. It is also interesting that the one mongol who did not have a third fontanelle weighed over 9 lb. at birth. In this series, third fontanelles were often associated with delayed closure of the posterior fontanelle and sometimes a widely separated sagittal suture. I might add that 2 babies seen recently with spina bifida and hydrocephalus (not included in the series) had poorly ossified skulls, and in each case the largest skull defect corresponded in position to a third fontanelle.

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R. J. K. BROWN.

THE BIBLE AND MODERN MEDICINE

SIR.—Your review (March 27) of Professor Rendle Short's book refers to the diagnostic problem of Job's ravaging skin disease. The tempo of the drama seems scarcely to match the rapid kill-or-cure course of smallpox. A fascinating alternative clue is offered by recently published cases of psychosomatic or anxiety-induced dermatitis. If we accept that a scrupulous mind, brooding over injustice and the sense of being wronged by authority, may erupt in a generalised eczema, Job's clinical problem is curiously integrated: the Enemy attacks him in the second round, not by an unrelated physical disease, but through Job's very perplexity over undeserved outward disaster to his fortunes and family in the first round. Job's limited understanding can but blame this upon the Almighty, through a faulty correlation in his philosophy between devoutness of religion and material prosperity. Once Job's skin breaks down, the vicious circle is intensified through toxæmia and weariness.

There are, in the Old Testament case-record, corroborative details pointing to an anxiety state: insomnia and terrifying dreams (vii, 4, 14), dread (ix, 28; xiii, 21), shuddering (xxi, 6), and mental confusion in controversy, yet with insight (vi, 3, 26). Besides which, Job loses the moral support of his wife, who counsels merciful suicide.

Doncaster.

CEDRIC C. HARVEY.

CHLOROQUINE IN LUPUS ERYTHEMATOSUS

SIR.—The results of treatment with chloroquine in eight cases of lupus erythematosus may be worth recording. Page¹ reported a good response to mepacrine in this condition. Chloroquine may be more active than mepacrine and does not produce yellow staining of the skin, so its trial seemed justified.

In one patient discoid lesions cleared completely after 13 weeks' treatment with 0·3 g. of chloroquine weekly. This dosage was continued for a further 8 weeks and the patient remained well when reviewed 3 months after treatment had ceased.

In another patient the lesions regressed after 10 weeks' treatment (0·6 g. weekly), but recurred 2 months later and did not respond to doses of 1·05 g. weekly for 10 weeks, after which treatment was discontinued because of anorexia.

In a third patient, treated for 7 months, discoid lesions regressed 13 weeks after dosage had been increased to 0·9 g. weekly. Treatment was discontinued because of anorexia. The eruption recurred 4 weeks later and the patient complained of deafness, tinnitus, and vertigo. She could not hear the conversational voice at a distance of more than 2 ft. from either ear; and tuning-fork tests indicated bilateral nerve deafness. An audiograph revealed uniform loss of air and bone conduction, averaging 25 decibels up to 2048 double vibrations per second, and in the higher frequencies the mean loss was 40 decibels. The result of caloric testing by the Hallpike method was within normal limits. 8 months later an audiograph showed no change and the nerve deafness seems likely to be permanent.

1. Page, F. P. Lancet, 1951, ii, 755.

The remaining five patients showed no improvement. One developed a light-sensitisation eruption during the 8th month, and anorexia and generalised urticaria in the 12th month, of treatment with doses varying from 0.3 g. weekly for 13 weeks to a maximum of 1.8 g. weekly for 7 weeks. A second patient developed additional discoid lesions during the 13th month of treatment with doses varying from 0.3 g. weekly for 8 weeks to a maximum of 0.9 g. weekly for 23 weeks. At this time he complained of dimness of vision, but no optic atrophy was present and the visual fields were normal. Three patients who received 3.0 g. in 4 weeks, 3.6 g. in 12 weeks, and 3.6 g. in 8 weeks respectively, showed no improvement.

When administered over long periods in greater dosage than is normally used for suppression of malaria, chloroquine may produce side-effects.²⁻⁴ Toxic effects occurred in our series, and results were so poor that we considered further trial of chloroquine in lupus erythematosus unwarranted.

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W. A. DEWAR
H. M. MANN.

SEX AND SOCIETY

SIR.—I was surprised to read in your issue of April 3 (p. 737) that the article by Dr. Learoyd in the April issue of the *Practitioner* lacked objectivity. To my mind, it was an admirable article from the point of view of the general practitioner, who may from time to time be consulted by parents on the subject of homosexuality. I agree with Dr. Learoyd that the view expressed by Sir Frank Fletcher (a famous headmaster of a famous public school) in his book *After Many Days* is indeed a model for the treatment of homosexuality, at any rate during the years of adolescence.

E. S. EVANS.

ACUTE LYMPHOCYTOSIS AND EOSINOPHILIA

SIR.—Smith⁵ introduced the term "acute infectious lymphocytosis" to represent a self-limited entity of unknown cause affecting mainly children up to 10 years of age. There are few abnormal symptoms, and therefore the condition often escapes attention. The only constant abnormal finding is the large number of small normal lymphocytes—sometimes as many as 90,000 per c.mm. The number of lymphocytes drops gradually to normal in 2-7 weeks. The condition is mainly sporadic, but occasional epidemics have been described.⁶⁻⁸ Smith believes, therefore, that this is an infectious and contagious disease.⁹

Several authors have mentioned that there is also absolute eosinophilia.^{7-10 11} In four sporadic cases observed by us during the last year we found that the increase in the number of the eosinophils was at least as pronounced as the increase in lymphocytes, and in one (case 5) the eosinophilia was proportionately greater than the lymphocytosis. The findings were:

Case	Total white cells per c.mm.	Lymphocytes per c.mm.	Eosinophils per c.mm.
1 ..	81,000	..	4860
2 ..	60,000	49,200	3600
3 ..	75,000	66,000	3750
4 ..	58,000	50,000	2900
5 ..	48,000	31,200	8640

P. ROBINSON

Director of Public Health.

- Tel Aviv, Israel.
2. Nelson, A. A., Fitzhugh, O. G. *Arch. Path. (Lab. Med.)* 1948, 45, 454.
 3. Alving, A. S., Eichelberger, L., Craigie, B., Jones, R., Whorton, C. M., Pullman, T. N. *J. clin. Invest.* 1948, 27, 60.
 4. Hoekenga, M. T. *J. Lab. clin. Med.* 1952, 39, 287.
 5. Smith, C. H. *J. Amer. med. Ass.* 1944, 125, 342.
 6. Reyersbach, G., Lenert, T. F. *Amer. J. Dis. Child.* 1941, 61, 237.
 7. Finucane, D. L., Phillips, R. S. *Ibid.* 1944, 68, 301.
 8. Barnes, G. R. jun., Yannet, H., Liebermann, R. *Amer. J. med. Sci.* 1949, 218, 646.
 9. Smith, C. H. In *Advances in Pediatrics*. New York, 1947; vol. 2, p. 64.
 10. Landolf, R. F. *Helv. paediat. acta*, 1947, 2, 377.
 11. Dunn, H. G. *Brit. med. J.* 1952, 1, 78.

SELF-HELP AND NUTRITION

SIR.—The article by Dr. Cicely Williams (Feb. 13) reveals many gaps in our knowledge of nutrition in "underdeveloped" countries. The science of nutrition must be founded on economic, nutritional, dietetic, and social surveys; and more knowledge of foodstuffs is needed than is found in analytical tables. Many surveys have been made in the countries of South-east Asia: and these show that malnutrition is mainly found among the poverty-stricken, which may be largely due to pressure of population.

The food taboos and superstitions and the ignorance existing in some countries attract attention by their strangeness, so that their effect in causing malnutrition is often exaggerated. Many years ago, when I began nutrition surveys in Ceylon, I was told that in certain districts all the people were good Buddhists who would not eat anything which had been killed, and so were strict vegetarians. Preliminary surveys of the general diet included surprise visits to schools, when all children aged 8-10 were asked what they had eaten during the previous twenty-four hours. Over 90% of the labouring-class Buddhist children had eaten fish. There are some strict vegetarians or lactovegetarians in India or Ceylon, but the great majority are priests or members of the upper classes.

Much has been heard of the sacred cow of India and its alleged uselessness. Until the advent of motors the greater part of all transport and ploughing in India was by oxen or buffalo. On the fodder available in most parts of southern India, the cows produced only enough milk to rear their calves. Less is heard of the useless sacred cow in northern India where cattle flourish and milk is drunk. The more taboos and superstitions are studied the less simple they appear; some have underlying material values, if only for the upper and priest classes.

Dr. Williams writes:

"Many of them must rely on their own rural ability and intelligence in using what is readily available, such as soya or groundnut powder, mango-seed flour, and sweet-potato leaves. At present these people lack the knowledge and the confidence which alone will produce results."

I would add that nutritionists also lack the knowledge.

Pulses have never been used as staple articles of diet in the same way as cereals. Analytical tables do not tell us why dried pulses, taken daily in more than small amounts, lead to indigestion and flatulence. At one time pellagra was common among the poor whites in the southern States of America. Because analyses showed groundnuts to be rich in proteins and vitamins which should prevent pellagra, the people were urged to eat them, and their reply, "we ain't no peanut eaters," was recorded as perversity; but it is not recorded whether those who recommended peanuts had tried them for themselves. Soya beans are better, for, although they contain a bitter principle and are indigestible because of a trypsin-inhibiting factor, and flour made from the roasted bean will not keep, many Chinese use excellent preparations daily in the form of "milk" curds, fermented products, or sprouted beans; but none of these is easily prepared.

In Ceylon I studied 20 or more leaves eaten by the villagers; these were consumed in small amounts, at infrequent intervals, and very few were ever found on the tables of the well-to-do. When I tried the various leaves myself, I found all of them unpleasant, except in small amount. The most edible were basil (*Basella rubra*), tampala (*Amaranthus gangeticus*), swamp spinach (*Ipomoea aquatica*), and centella (*Centella asiatica*); but compared with them, cabbage is a luxury.

Foods from plants, especially leaves, are bulky and contain much indigestible matter; the proteins are of low biological value and only a mixture of several can supply all the nutrients. There are no vegetable foodstuffs which contain all or nearly all the needed nutrients in digestible form, as is the case with milk, eggs, and the whole carcass of an animal. Furthermore, vegetable foods contain a great variety of

non-nutrient substances, and some of these, such as glycosides, saponins, and oxalates, may not be entirely harmless when taken over a long period.

On the other hand, there are no nutrients needed by man which cannot be found in vegetable foodstuffs. Realising this, laboratory workers have studied the possibility of preparing from them a powder equal in nutritive value to dried milk. Discussing this matter of substitutes for milk I have pointed out¹ that such a powder must be far cheaper than milk if it is to be widely used for the children of countries where the family income is only a few shillings per head per month. The bulk of the material can be prepared from cereals, pulses, roots, and oil-seeds. Probably it would be necessary to add synthetic vitamins and perhaps one or more amino-acids. Obviously the powder must be prepared in factories, for it is beyond kitchen practice.

In an attempt to interest manufacturers of foods and vitamins, I wrote two papers in trade journals,² visited many firms, and corresponded with a large American firm which is preparing amino-acids—particularly lysine—in bulk. I thought that firms preparing cheap foods for livestock feeding might be interested. But they all shied at the financial implications when I pointed out that the bulk of the powders must be prepared in the countries where they would be used and would have to be cheap enough for the labouring classes and the indigent to buy.

The shortage of food in many parts of the world is likely to increase with population growth. More than 25 million tons of oil-seeds and nuts are used yearly in the world for the extraction of oil. Oil-cakes, which are rich in proteins and vitamins, are used for cattle food or fertiliser. It should not be beyond the ingenuity of chemists to assemble, in a digestible and appetising form, the nutrients from these cheap sources.

Ballylickey, Bantry,
Co. Cork, Eire.

LUCIUS NICHOLLS.

HIGH ISOHAEMAGGLUTININ TITRE IN BLOOD-GROUPS A AND B

SIR.—In investigating the selection of possible test serum donors, Brewer³ and Rainsford and Morgan⁴ estimated the iso-agglutinin titre in blood of groups A and B. Rainsford and Morgan found the frequency of suitable donors in the British population to be about 1 : 60 in group A and 1 : 14 in group B. To determine the corresponding frequency in the Swedish population, 1494 group-A sera and 543 group-B sera from the ordinary blood-donors in Stockholm were titrated for the anti-B and anti-A iso-agglutinin titre respectively.

The agglutinin was first tested in a dilution of 1 : 100; only those sera which agglutinated macroscopically in this dilution were titrated in a serial dilution of 1 : 1 to 1 : 256. Serum A was titrated against B and A₁B blood-cells, and serum B against A₁, A₂, and A₂B cells. All titrations and tests were made on tile.

Of 61 A sera which agglutinated B cells in a dilution of 1 : 100, 39 agglutinated A₁B cells in a dilution of 1 : 128 in ten minutes. Of these 39 sera, only 15 agglutinated A₁B cells in a dilution of 1 : 256, which I consider to be the minimum end-titre of an anti-B serum when the loss of activity during storage is taken into account. Only 4 sera showed a stronger agglutination than a + reaction in a dilution of 1 : 256 and were regarded as good test-serum donors.

Of the 543 B sera, 39 agglutinated A₁ cells in a 1 : 100 dilution in fifteen minutes. These 39 sera were titrated against A₁, A₂, and A₂B cells; the results are shown in the accompanying table.

The minimum titre for anti-A serum was taken as 1 : 128 with A₁ cells, 1 : 64 with A₂ cells, and 1 : 32 with A₂B cells. It is seen from the table that 18 B sera fulfilled the minimum requirements. If the loss of activity during storage is taken

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- Nicholls, L. Food Manuf. 1950, 25, 95; World Crops, April, 1950.
- Brewer, H. F. St Bart's Hosp. Rep. 1937, 70, 247.
- Rainsford, S. G., Morgan, W. T. J. Lancet, 1946, i, 154.

NUMBER OF B SERA AGGLUTINATING A CELLS IN TEN MINUTES

Dilution	No. of B sera agglutinating		
	A ₁	A ₂	A ₂ B
1 : 1	39	39	39
1 : 4	39	39	37
1 : 8	39	39	34
1 : 16	39	38	27
1 : 32	39	38	18
1 : 64	39	35	13
1 : 128	37	20	2
1 : 256	27	6	0

into account, 13 B sera (which agglutinated A₂B cells in a dilution of 1 : 64) were suitable as anti-A test sera.

An analysis was made of the sex, age, and Rh-group distribution in the high-titre donors. No correlation was found between the sex and the high titre. There was a preponderance of donors between 20 and 30 years of age. A surprisingly high frequency (30%) of Rh-negative blood (cde/cde) was found in the group-B high-titre sera; no such high frequency was noted in the corresponding group-A sera.

The frequency of suitable test-serum donors in the Swedish population (Stockholm) was found to be 1 : 100 in those with group-A blood and 1 : 40 in those with group B.

Chemistry Department II,
Karolinska Institutet,
Stockholm.

OLOF RAMGREN.

INTRADERMAL ADRENALINE

SIR.—I was glad to notice Dr. Louis Moss's letter in your issue of March 27.

I have been using this new therapy since he described it in a letter to the *British Medical Journal*. My findings corroborate, to a great extent, those of Dr. Moss. I have found that the intradermal injections, with massage of adrenaline cream, give much relief; and allow the patient to use the affected part much more freely.

This seems to me to be a very easy and simple treatment, which can be carried out by the general practitioner in his surgery or the patient's home. Being both cheap and effective, I think it is well worth trying, and it has enabled me to avoid sending some patients to the busy physiotherapy departments.

London, W.C.2.

W. P. JOHNSTON.

BETTER GENERAL PRACTICE

SIR.—May I draw your readers' attention to the comment in the *Observer* of March 28 on Dr. Stephen Taylor's survey, *Good General Practice*, which was discussed in your leader of March 27?

After a short delineation of the main purpose of the survey, the *Observer* says:

"But one point which emerges incidentally from the findings is that some 10 million people living mostly in industrial areas are receiving from their 5,000 doctors a medical service which leaves much to be desired. It would hardly be going too far to say that some of these doctors—perhaps as many as 1,000—are guilty of serious malpractice. They risk the health and lives of their patients by failing to do clinical examinations at the surgery, and rarely on visits. Some do not even possess an examination couch."

It would appear, therefore, that about £10 million are spent each year in providing a "medical service which leaves much to be desired." It is highly probable that most of the 1000 doctors "guilty of serious malpractice" are earning more than many consultants. They are earning three, four, or even five times as much as registrars who, together with housemen, do much of this type of doctor's work for him.

A conservative estimate suggests that £3 million each year is being paid to and accepted by men who are

"risking the health and lives of their patients by failing to do clinical examinations at the surgery, and rarely on visits."

It is common knowledge that registrars are not wanted in general practice in very many areas, and that a higher qualification, particularly the M.R.C.P., is a grave disadvantage. These registrars find their way blocked in the hospital service too, because there is no money for the new posts which are needed in general medicine, general surgery, and midwifery and gynaecology.

Is it surprising that registrars, many of them in their middle and late thirties, married and with children, and with many years of hospital experience behind them, are becoming increasingly bitter?

SENIOR REGISTRAR.

TUBERCULOSIS YARDSTICKS

SIR.—Dr. Tattersall wrote last week a thought-provoking letter on the subject of tuberculosis control.

The reason why the number of cases of tuberculosis on the chest-clinic registers has increased by 20% during the past five years is almost certainly that the number of chest clinics and the facilities they offer have increased.

Dr. Tattersall states quite correctly that tuberculosis will only be controlled by reducing the number of sputum-positive cases—that is, the "known infector pool." He makes the novel suggestion that the certificates of the Ministry of National Insurance should be made available so that the relapse of previously notified cases should be known. I feel that a more sure way would be for the Hospital Laboratory Service to notify automatically the medical officer of health of the results of specimens of sputum containing tubercle bacilli.

I wonder if it would be possible for patients receiving National Assistance who take their own discharge from sanatoria and move to other towns to be followed up through the National Assistance machinery and so avoid being lost sight of, as so often happens.

Whether or not the patient accepts treatment is his concern, but it is very much the concern of others that he should be taught and practises those rules of hygiene that render him a safe member of society.

D. J. AP SIMON.
Bournemouth.

TREATMENT OF VARICOSE ULCERS

SIR.—At risk of seeming captious, I would like to comment on Mr. Maurice Lee's letter of April 3. Many pretty hypotheses have been advanced by surgeons in connection with venous disorders, and it seems to me that a much more critical attitude should be adopted towards some of the too-readily accepted doctrines of the present day.

Referring to the question of arterial spasm in cases of thrombosis, Mr. Lee states that "the equilibrium between inflow and outflow . . . is further affected by the arterial spasm that *always* accompanies a deep thrombosis" (my italics). In my view there is no justification for this statement. On clinical examination one rarely sees evidence of arterial spasm in cases of venous thrombosis, and this clinical observation is supported by plethysmographic studies I made several years ago on patients in the postoperative period. The latter work was not published, but I can assure Mr. Lee that I was not able to demonstrate reduction of arterial flow to the leg in a small number of patients with thrombosis. Had I investigated more patients, I am sure that occasional examples of arterial spasm would have been seen; it is, however, definitely uncommon.

Mr. Lee goes on to advocate the use of vasodilator drugs in the treatment of varicose ulcers, in the belief that they will promote healing. He says that "lumbar sympathectomy will do the same as intra-arterial injec-

tions of tolazoline, and it will be more permanent in its effect." There is, I believe, no authentic evidence that lumbar ganglionectomy is of any real value in the treatment of varicose ulcers, and I would like to ask Mr. Lee whether his contention about the value of tolazoline is not an unjustifiable assumption based on acceptance of an analogous method of treatment.

Mr. Lee is, I think, guilty of a further over-simplification when he says that "pain becomes less as soon as ulceration occurs, probably because there is then an outlet for accumulated metabolites." Can others agree with his initial contention, and what evidence is there that the outlet of metabolites relieves pain?

Finally, Mr. Lee refers to the lack of success of skin-grafting operations, a view with which few would disagree. Nevertheless, he himself was a keen advocate of darning skin-strips through the granulations of varicose ulcers. I wonder what success he has had with this measure and whether he still believes in it.

I must apologise if I seem to cavil, but the treatment of varicose ulcers is a very important matter and I would earnestly plead for a more critical approach to this subject. The surgical literature abounds with enthusiastic articles on dubious methods of treatment for varicose veins, varicose ulcers, and postphlebitic sequelæ. Since the care of so many of these patients is left to relatively junior people, it behoves us to be especially cautious in referring to doubtful aetiological factors and in advocating new methods of treatment.

R. S. MURLEY.

FULL-TIME—PART-TIME

SIR.—The curious letter from two junior part-time consultants (March 27) has stirred me from the undesirable lethargy surrounding a full-time consultant. Undoubtedly there is a need for both types of consultant, and abusing one another does not forward the interests of either. It is obvious that the amount of work done is related to the individual and not to the appointment. The part-timer brings in variety and new experience; the whole-timer, by treating his hospital as a second home, gives it a personal care and interest which could not be expected from a part-timer attending one or two sessions.

As maximum part-time consultants your correspondents do nine sessions. They admit to a mileage of twelve thousand, most of which must be at the Board's expense and from which they should get enough to compensate for the two sessions further they might do on full time. The general experience of consultants with such mileage as this is that they make a good profit on their mileage alone.

A car is equally essential to the full-time surgeon or physician on emergency duty, and the chief bone of contention lies in the failure to recognise this and give him the appropriate allowances, preferably in taxation, for this. It is absurd that, when a doctor's hospital, consulting-room, and home are far apart (so raising his mileage allowance), this offsets the number of sessions lost by changing to part-time. The Board appears to be a double loser, both by losing the services of the doctor in his increased travelling-time, and by actually having to pay him for it. I would like to hear George Schwartz's comments on this arrangement in relationship to solvency in the business world.

The rational way to clearing anomalies and abuse of mileage claims is to allow every medical man a basic allowance for a car, if necessary related to his need to use a car professionally, and to add to this a very much smaller mileage allowance.

The comments of your two correspondents show well the misuse of a doctor's time in travel and in multiple

appointments for a small number of sessions at several hospitals. It also appears a little unfair to protest about the lack of private practice accruing to them from work at a hospital for which they are already fully paid. This was once a fair return for unpaid labour, but old ideas die hard.

I hold no financial grievance against my part-time colleagues, as I realise that the essential difference between our outlooks is whether more money and less time or less money and more leisure represents a higher standard of living. I believe that the widespread impression that full-time consultants get allowances for books and journals, for reprints, for the telephone, for conference expenses at home and abroad, and for the upkeep of their premises should be corrected. Broadly speaking they do equivalent amounts of day labour and bring similar abilities to bear on it. The maintenance of their abilities in first-class order demands the same literary, social, and professional expenses, and this should be recognised. What a doctor does with his overtime is not under discussion.

Northwood, Middlesex.

J. G. BONNIN.

SIR.—It is desirable, as Mr. Langston suggests in his letter of March 27, that there should be no antagonism between whole-time and part-time specialists, but this ideal is unlikely to be achieved while the conditions of whole-time service remain depressed. Consequently, it is up to those part-time consultants who occupy the positions of influence to support whole-timers in their fight for justice. As Mr. Langston was instrumental in securing the election of one whole-time regional specialist to the staff side of Whitley B (for which whole-timers are duly grateful), he must be aware that the other whole-time representative on this committee is a professor of pathology, who, in spite of his distinguished academic record, is not qualified to represent the interests of whole-time specialists in their struggle for existence in the provinces. This fact has been made abundantly clear to all concerned by a letter from Mr. Rufus Thomas, president of the Association of Whole-time Specialists.¹ Incidentally, there are 17 members on Whitley B, so my figure of 15 part-timers is correct.

I am afraid that Mr. Langston's account of the staff side's efforts on behalf of whole-timers does not show events in their true perspective. The announcement of the new mileage rates, which meant increased payments to part-timers and reduced ones for whole-timers, was made in the *British Medical Journal* on Aug. 16, 1952. Subsequently these rates were amended in the General Whitley Council² and whole-timers were placed in the same category as "hospital clerks and porters." It was not until May, 1953, that representatives of the Association of Whole-time Specialists met the management side of Whitley B, for the first and only time. Of course, by then, the victorious management side were not going to surrender the position won, and the few verbal bouquets they distributed to their defeated opponents are nothing for Mr. Langston to rhapsodise about. Surely it is obvious that no whole-timer can have any faith in the staff side of Whitley B unless whole-time regional specialists are adequately represented on it? Mr. Langston himself has criticised the composition of this committee because of the predominant representation of Royal Colleges and Scottish Corporations on it.³ It is, of course, for Mr. Langston and his colleagues holding positions of influence to make this effort to secure unity within the profession, or else to leave the terms and conditions of service to be decided in the political arena, where they have now strayed.

Orpington, Kent.

LEO GILCHRIST.

1. *Brit. med. J.* 1953, i, suppl. p. 12.

2. *Ibid.* 1952, ii, suppl. p. 220.

3. *Ibid.* suppl. p. 174.

A WORD WANTED

SIR.—We have been arguing about a word! Would your readers care to join in?

We are looking for the best antonym to "retrospective." The word we want is intended to emphasise the differences between the two forms of research: the forward-looking planned research, and the backward-looking survey. Some of the suggestions made were: prolective, prolative, prospective, anteroseptive.

Bristol Royal Hospital
for Sick Children.

JOHN APLEY.

NURSING BY THE MOTHER

SIR.—What a pleasure it is to read Mr. Michael Oldfield's letter in your issue of March 20 drawing our attention to the dangers confronting infants and children from the structure and organisation of the hospitals in which they are treated.

"In most hospitals in England," writes Mr. Oldfield, "the child is treated like a miniature adult"; and this was aptly illustrated, for example, when the Sick Children's Hospital in Glasgow was, in a minimum of time, converted into a military hospital, by the substitution of beds for children's cots. The dangers to physical survival, cited by Mr. Oldfield, in wards that contain as many as 35 cots, are paralleled by the dangers to the child's mental and emotional health, studied by Dr. Bowlby and his colleagues. The efforts of Sir James Spence, and those who follow his lead, to make provision for mothers to help in the nursing of their infants, only partially alleviates the conditions. The last few decades have brought so much new understanding of the dynamics of illness in children, that our handling of them in hospital is out of step with our knowledge.

The time cannot be far distant when the construction of new hospitals will be a possibility. Could not the National Health Service call together children's physicians and surgeons and child psychiatrists, together with an architect experienced in hospital construction, to plan a hospital which would be directly designed to meet the specific physical, mental, and emotional needs of infants and children?

Fresh and creative thinking is needed upon the whole problem of the treatment of sick children in hospital. In this should be included reconsideration of the training of the nurses who will care for them and study of the ways in which the help of mothers can be enlisted. Provision should also be made for the use of those recuperative forces in human beings which lie behind the value of "play" in children and the success of occupational therapy in hastening the recovery of inpatient adults.

Such a project would take time, for the problems are knotty, but the very difficulty should be a stimulus to its achievement. We must not let the possibility of building find us without a plan, and, if we start now, we should be ready to meet such opportunity with a coördinated scheme, even if it is at first only on an experimental basis.

Institute of Child Psychology,
London, W.11. MARGARET LOWENFELD.

SIR.—Needless to say, we agree with Mr. Michael Oldfield's views (as far as they go) on mothers nursing their own infants (March 20). But we do not think the mere presence of the mother will attain the desired result of reducing cross-infection. She must be assigned definite duties and responsibilities of individual nursing, with which neither nurses nor sisters must interfere. There must be the closest coöperation between mother and doctor, with no intermediary. Nurses must of course be responsible for hypodermic injections and the taking of temperatures, but these need not be contaminating. Mothers who have been trained nurses, we occasionally found, did not make good "mother-nurses." We could

not understand this until we discovered that sometimes they smuggled in thermometers and were frightening themselves if the temperature rose a little; and a frightened (or cross) mother makes an ill baby, so close is the bond. Now thermometers are banned. Thus, the psychological effect of the mother's presence may be either very good or very bad. It is the doctor's and sister's business to see that the psychology is trained in the beneficial direction, and nipped in the bud if it is not.

We wish to correct a possible misapprehension which may be gained from reading our paper—that by providing the patient with "one nurse only," we meant a trained nurse as well as his mother. It would avoid any misconception if after the words "one nurse only" were added "namely, his mother."

Our principle of *insulation* by guarding the infant at all points from *foreign* bacteria, while leaving him freely in contact with organisms to which he is either congenitally immune or has, by gradual contact in his home, become acclimatised, is much more practicable and logical than trying to surround him in an open ward with an aura of asepsis by the adoption of a technique which is suitable only for the operating-theatre.

Now, as John Bunyan would say: "Concerning the conquest of cross-infection, there be three great lions, old and very fierce in the path, and their names be Apathy, Fatalism, and Ignorance." Apathy on the part of medical staffs; fatalism by trained nurses (because they see that however hard they try it still occurs); and ignorance on the part of the public. If the latter could be abolished, infection would go with it. Why else do maternity wards now hold the proud position of having the lowest percentage of cross-infection when in these wards it used to be so rife? It is primarily, we think, because the public became alarmed and demanded an improvement. There is always a tendency to think: "This is our system (and a beautiful-looking ward). It is sacrosanct. If an infant cannot fit into it—well it's just too bad for the infant." A Procrustean bed!

There is a fourth lion though, but he is a puny fellow; his name is Money-bags. He blows himself up like the frog till he is as large as a cow, but when Ignorance gets to hear of him he can always deflate him with a few vigorous pricks where it hurts most.

But we disagree with Mr. Oldfield that Wellington is in Australia.

Wellington,
New Zealand.

CECILY M. PICKERILL
H. P. PICKERILL.

TREATMENT OF MEGLABLASTIC ANÆMIA

SIR.—I was much interested in the article by Dr. Foy and Dr. Kondi (Dec. 19), and particularly in their statement that "it is well known that whereas all megaloblastic anaemias respond to folic acid, not all respond to vitamin B₁₂".

Though this is a widely held opinion, it should be remembered that exceptions have been reported, and that such observations are of importance in any explanation of the relation between these two vitamins in haemopoiesis. There are well-recorded cases in pernicious anaemia,¹⁻³ while Das Gupta et al.⁴ described a case of nutritional megaloblastic anaemia failing to respond to folic acid but subsequently responding to proteolysed liver. Experimentally, Heinle et al.⁵ have shown that

1. Girdwood, R. H. *Brit. J. Nutr.* 1952, 6, 315.
2. Jarrold, T., Horrigan, D., Thompson, C., Vilter, R. W. *Science*, 1951, 113, 688.
3. Mollin, D. L. *Lancet*, 1948, ii, 928.
4. Das Gupta, C. R., Chatterjee, J. B., Mathen, K. K. *Ind. J. med. Res.* 1949, 37, 455.
5. Heinle, R. W., Welch, A. D., Pritchard, J. A. *J. Lab. clin. Med.* 1948, 33, 1647.

pig anaemia will only respond to folic acid and vitamin B₁₂ when one acts in the presence of the other, although only very small amounts of the other may be required.

I have seen 2 patients with severe megaloblastic anaemia of pregnancy who failed to respond to folic acid. The first had folic acid (20 mg. daily) by mouth for 17 days with no response, but later did well on oral proteolysed liver (15 oz. over 23 days). The other showed no response to folic acid by mouth for 25 days (420 mg.) or to subsequent parenteral folic acid (15 mg. daily) for 7 days; then vitamin B₁₂ intramuscularly (50 µg. daily) for 7 days produced a good response.

This response might be attributed either to a direct response to vitamin B₁₂ or, as with Heinle's pigs, to the fact that the folic acid already present in the patient's tissues could not act until vitamin B₁₂ was present. This response is of further interest in that megaloblastic anaemia of pregnancy is usually said to be refractory to vitamin B₁₂ and fully responsive to folic acid,^{6,7} although Patel and Kocher⁸ record 5 cases which did respond to vitamin B₁₂ without previous folic acid.

Institute for Medical Research,
Kuala Lumpur, Malaya.

P. W. G. TASKER.

MULTIPLE ADENOCARCINOMA OF ILEUM CAUSING INTUSSUSCEPTION

SIR.—Illingworth and Dick⁹ state that "the special importance of simple tumours of the small intestine is that they frequently give rise to intussusception. Indeed, the vast majority of intussusceptions occurring after infancy are due to this cause. Of malignant tumours, an adeno-carcinoma is the most common. It occurs in the ileum more frequently than in the jejunum. . . ."

An Arab boy, aged 8, was admitted to this hospital for observation on Dec. 22, 1953. His parents stated that he had been passing blood from the rectum. They gave a vague history of constipation and attacks of colicky pain. He was a small boy with a distinct pallor. There were no purpuric spots and no mass could be felt in the abdomen. Rectal examination revealed nothing, and there was no blood on the examining finger. An enema produced a good result but no evidence of blood.

Six days after admission he complained of severe colicky pain and vomited several times. A mass was easily palpable in the right iliac fossa, and acute intestinal obstruction due to intussusception was diagnosed. Under general anaesthesia (chloroform followed by "open" ether) a midline incision was made. The mass was found to be an intussuscepted portion of the ileum. The intussusception had been caused by two tumours which were protruding into the lumen of the bowel; it was easily reduced and the condition of the bowel was excellent. The tumour-bearing portion of the ileum was resected and an end-to-end anastomosis performed. No other tumours were discovered.

Glucose-saline solution was given intravenously for forty-eight hours, during which time he received nothing by mouth. He made an uninterrupted recovery and was discharged from hospital on the tenth postoperative day.

12 cm. of ileum was removed; near each resected end was a solid cauliflower-shaped tumour protruding into the lumen of the bowel. The larger tumour measured 4·2 by 5·2 cm., the smaller one was about the size of a strawberry. They were greyish-white, firm, and elastic. Histological examination of the two polyps showed adenocarcinoma infiltrating the coats of the bowel.

I wish to thank Dr. W. D. Bathgate, hospital superintendent, for permission to publish this case, and the pathologist of the Government Hospital, Haifa, for his examination and report.

Edinburgh Medical
Missionary Society Hospital,
Nazareth, Israel.

JOHN L. TESTER.

6. Thompson, R. B., Ungley, C. C. *Quart. J. Med.* 1951, 20, 187.
7. Bodley Scott, R. *Proc. R. Soc. Med.* 1950, 43, 953.
8. Patel, J. C., Kocher, B. R. *Brit. med. J.* 1950, i, 924.
9. Illingworth, C. F. W., Dick, B. M. *Textbook of Surgical Pathology*. 5th ed., London.

Medicine and the Law

Compensation without Negligence

AN interesting comment was made by Mr. Justice Finnemore in a case at Birmingham Assizes¹ after a claim for compensation had been unsuccessfully brought against Birmingham Corporation on behalf of a small girl who had been knocked down and injured by a corporation bus. The judge suggested that children hurt in traffic accidents should be compensated, whether the driver was at fault or not, either by the driver's insurance company or by the State, and he suggested to the defending solicitor that Birmingham Corporation should offer to compensate the girl although she had lost her case.

1. *Manchester Guardian*, April 2, 1954, p. 11.

Parliament

QUESTION TIME

Medically Unfit

Replying to a question, Mr. H. A. Watkinson, parliamentary secretary to the Ministry of Labour, said that of the 303,400 National Service registrants in the 1930 age-class 9500 were estimated to be medically unfit.

Appointment Systems in General Practice

Dr. BARNETT STROSS asked the Minister of Health how many general practitioners saw their patients, using an appointment system; and, in view of the benefit to doctors and patients, whether he would consider circularising all local executive committees, stating the advantages that would follow in time saved and reduction of cross-infection.—Mr. IAIN MACLEOD replied: This information is not available. It is in my view for doctors themselves, in the light of the particular circumstances of their practices, to decide how far they can use a system which seems, when successfully organised, to have many advantages.

Medical Help for African Colonies

Relying to a question, Mr. OLIVER LYTTELTON, Secretary of State for the Colonies, said that colonial territories received considerable assistance from the Government in the form of technical advice and under the Colonial Development and Welfare Acts. Assistance from international sources was only supplementary to that provided by the United Kingdom. The following medical and public-health assistance was given to African territories through W.H.O.:

Nigeria ..	(i) Malaria control (ii) Leprosy control (iii) Yaws campaign	Malariaologist and entomologist Doctors 1 consultant	Supplies and equipment being provided by U.N.I.C.E.F. do. do.
East Africa	Establishment of East African Malaria Institute	1 entomologist, 1 chemist, and 2 field assistants	do.
Kenya ..	3 medical training-schools	Equipment and supplies	—
Uganda ..	(i) Venereal disease survey (ii) Nutrition survey	Mobile investigation team Team of clinical and dietetic experts	—
Tanganyika	(i) Medical teaching (ii) Health survey and health improvement scheme in Buka area	Equipment Nutritionist and physiologist	—
Nyasaland ..	Medical training	Equipment for training-schools	—
Somaliland	Tuberculosis sensitivity survey and B.C.G. campaign	T.B. specialist and 2 T.B. nurses	—

Obituary

JAMES FRANK COLYER

K.B.E., LL.D. Brist., F.R.C.S., F.D.S. R.C.S.

Sir Frank Colyer, who died on March 30 at the age of 87, early won a reputation in his profession which he continued to serve with distinction for some sixty-five years.

As a student at the dental school in Leicester Square his intense activity, his quick absorption of knowledge, his enthusiasm for sports, and his ability to organise the students' societies, impressed his seniors and his contemporaries. He passed the final L.D.S. examination in 1887 before he was 21. He was an ardent follower of the dean of the school, Morton Smale, who believed that a dentist should have a medical qualification, and in 1889 he took the Conjoint qualification from Charing Cross Hospital. It was at this time that he collaborated with Morton Smale in the publication of his first work *Diseases and Injuries of the Teeth*, which afterwards, under his sole authorship became the well-known *Dental Surgery and Pathology*. The later editions he wrote in conjunction with Prof. Evelyn Sprawson.

After holding a house-appointment and a demonstratorship at the London School of Dental Surgery (now the Royal Dental Hospital) he was elected to the honorary staff, and also to the staff of Charing Cross.

In 1900 he was appointed honorary curator of the museum of the Odontological Society, which he had served since 1893, as secretary and editor of their *Transactions*. When the society became a constituent of the Royal Society of Medicine and the museum was lodged in the Royal College of Surgeons, Colyer still remained as curator and reorganised the specimens in their new home. He was president of the odontological section of the R.S.M. in 1919.

The first world war gave fresh outlet for his skill and energy in the treatment of facial and oral injuries at the Croydon War Hospital and Queen's Hospital at Sidcup and his work was recognised by his election as F.R.C.S. in 1916 and his appointment as K.B.E. in 1920.

Colyer's belief in the Hunterian conception of natural history as comprising the whole animate kingdom found expression in his chief work, *John Hunter and Odontology*, and in his series of lectures on Variations and Diseases of the Teeth of Animals which were published in 1936. His last work, which embodied years of thought and study, was *Old Instruments for Extracting Teeth* (1952).

E. S. writes: "J. F., as he was always called, was a dynamic personality, whose energies were at times even disconcerting. He was an indefatigable worker in many branches of dentistry, and in his teaching—and indeed throughout his life—it was the broad principles of dentistry rather than the minutiae which interested him. After he gave up private practice he made his professional home at the museum of the Royal College of Surgeons. Here he held forth to all and sundry on the wonderful collection he there had under his care. As he matured he mellowed, and dental surgeons not only from London and the provinces, but from all over the world, used to visit him in his underground department."

"The career of Sir Frank Colyer," L. L. points out, "refutes the line 'He tires betimes that spurs too fast betimes,' for from his early youth the vital urge in him spurred him on without rest into extreme old age. Even when his beloved collection was packed away in the war, like the grand spirit he was, he went on cataloguing any new specimens, writing a description of those specimens in the few cases transferred to the general museum so that students could benefit by their study—fighting against physical weakness, his vitality bore him upright to the end."

Sir Frank Colyer married in 1895 Lucy Olivier Simpson. She died in 1950, and they are survived by a son and a daughter.

Notes and News

LAW AND MEDICINE

In a presidential address delivered before the section of pathology of the Manchester Medical Society on Feb. 10, Dr. T. Blench said that the Law seeks for certainty but Medicine deals with clinical probabilities. Lawyers chide doctors for differing and also for not being willing to differ. While doctors can be sued as a result of their calling, actions against counsel are statute-barred. Laws were made by lawyers who appreciated their difficulties more fully than those of other people. It is clear that lawyers love words and documents, for the former are elastic and the latter rarely satisfactory even when made by lawyers. On the other hand, Medicine, in contradistinction to advocacy, does not lend itself to verbal analysis and verbal agility. Verbal dexterity in a doctor cannot alter the course of a patient's ailment, while in a lawyer it may change his client's outlook on life. Lawyers and doctors, nevertheless, both take to heart their clients' interest, and at times may identify themselves with it too completely.

A STUDY IN COURAGE

PSYCHOLOGISTS urge us to look to experience, and particularly to early experience, for the key to human behaviour. But just when the key is in the lock, and the door seems to be opening on mental health for everybody, along comes some significant case to remind us that the material is at least as important as what befalls it.

Douglas Bader, whose life-story (so far) is told well and simply by Paul Brickhill,¹ comes of courageous but highly temperamental stock: no native equilibrium, no inborn placidity, has buffered him against disaster: he has had to rely on other gifts. As for experience, his was by no means a good start in life: on the contrary. He was the second child, and three days after he was born he and his mother both had measles; immediately afterwards his mother had a major operation; so they were separated from the start. Moreover when he was a few months old the rest of the family returned to India, leaving him with relatives in the Isle of Man. He was not taken out to rejoin his own mother until he was nearly two years old. Brickhill does not tell us whether the relations in the Isle of Man had included a successful substitute for her; but he makes it clear that Bader's mother, deprived of his company in those early months, was not subsequently able to feel as warmly towards him as she did to his elder brother. For a few months after the reunion the good-tempered small boy presented the subdued appearance of the child who does not fit in, and suffered quietly the assaults of his better-loved brother. Then he began to fight back; and has fought for every worthy cause he has encountered ever since. According to Brickhill, he is always driven by a need to prove himself in his own eyes; and this perhaps is his legacy from those early insecure years—years which might have made another child anxious, depressed, timid, delinquent, or destructive. They made Bader into an outstanding example of tenacity and courage. Courage which, when (as a young pilot in the Royal Air Force, in 1931) he lost both legs in a crash, obliged him to learn to walk on artificial limbs without the aid of a stick; which made him fight to be retained in the Service as a pilot, though R.A.F. regulations made no provision for pilots with no legs; which carried him through the disappointed years when, no longer in the Service, he worked in an office; which sent him back joyously to the air as soon as war broke out; which made him, at thirty, one of the best fighter leaders and tacticians, as well as one of the best pilots, among the inspired few—mostly in their twenties—who fought and won the Battle of Britain; which ensured that he would prove a troublesome prisoner to the enemy, and finally brought him—after three years, and still plotting escape—to the rockbound impregnable castle of Kolditz, whence he and his fellow intransigents were rescued by the Americans.

Bader has been an inspiration to more than his fellow fighting men: his courage has been a pattern for many people crippled in war, and his concern for them has been practical and direct. The book tells of many occasions on which he has gone out of his way to help such disabled people, and to set them thinking constructively. One child for whom he did this had lost both legs after an accident with

burning petrol. "The boy just doesn't realise how serious it is yet," the father said afterwards to Bader. He replied with passion: "That's the one thing he must never realise. You've got to make him feel this is another game he's got to learn, not something that will cripple him. Once you frighten him with it he's beaten."

This splendid virtue of courage does not subsist in isolation: Bader, as Brickhill shows, is a many-sided turbulent person, loyal to friends, stormy, bewildering, and implacable to enemies. To read the book is to be grateful that there are such men alive; and also perhaps that there are not too many of them. A world populated by such dynamic characters would presumably fly apart.

RHEUMATISM AND DISABILITY

THE sixth annual report of the British Rheumatic Association describes the association's efforts to plead the cause of disabled rheumatic persons and speaks with satisfaction of the appointment of the committee which, with Lord Piercy as chairman, is considering the position of house-bound and potentially part-time workers. In his speech at the annual meeting, here reprinted, Sir Walter Monckton, Minister of Labour and National Service, said that 800,000–900,000 disabled people had been on the Ministry's register under the Disabled Persons (Employment) Act, and that the percentage of disabled persons employed in industry was 5 and in Government service 5 $\frac{1}{2}$. More than 35,000 men and women had completed courses at the Ministry's 14 industrial rehabilitation units, and 80% of them went on to training centres or into jobs.

Membership of the association costs 10s. a year. Its address is 11, Beaumont-street, London, W.1.

THE HEALTH OF INDIA

THE report on the activities of the Indian Union Health Ministry for 1953–54 indicates that the Government are prosecuting vigorously their planned campaigns against certain widespread diseases. In the B.C.G. campaign, launched in 1948, over 25 million persons were tuberculin-tested and 8 million vaccinated up to the end of 1953. A national malaria control scheme calculated to protect a population of close on 125 million living in endemic areas, by the setting up of 125 malaria control units, came into being during the year. A department of maternal and child health has been established at the All-India Institute of Hygiene and Public Health in Calcutta; this is a co-operative effort by the Indian government and UNICEF. Construction work on the All-India Institute of Medical Sciences is to start towards the end of this year. It will comprise a medical college, a dental college, a nursing college, a postgraduate centre, a 650-bed hospital, and rural and urban organisations to provide centres for field work. An All-India Mental Health Institute is to be founded in association with the Bangalore Mental Hospital. Finally, a central food laboratory is to be established in Calcutta to help implement the projected legislation to prevent food adulteration. The government of India contributed Rs. 1,290,000 last year to W.H.O. and propose paying Rs. 1,297,000 this year. They are also making a voluntary contribution of Rs. 1,500,000 to the UNICEF local office in Delhi.

STERILISATION OF POLYTHENE TUBING

IN the past six years the plastic material 'Polythene' has played an important part in medicine, especially as pliable tubing for intravenous infusions. Farquhar and Lewis¹ found that this tubing was satisfactorily sterilised by immersion and storage in cetrimide or benzalkonium chloride; but it could be boiled provided that it was shock-cooled. The first of these two methods is generally used. Colker and Norman² now report that polythene tubing which had been kept immersed in a solution containing 1% cetrimide has "often shown growths of Gram negative spore-bearing bacilli of a saprophytic nature." They describe a method of sterilising lengths of tubing by heat in soda-glass tubes containing distilled water. This method, they say, is easily applied.

3-D. IN MEDICAL ILLUSTRATION

THE April number of *Anæsthesia* contains, as illustration to an article on Injury to the Median Nerve by Prof. E. A. Pask and Dr. J. G. Robson, what is believed to be the first anaglyphic stereogram reproduced in a medical journal. A Roye-Vala-Scope is supplied for viewing it so that the reader may obtain the full three-dimensional effect.

1. Reach for the Sky. London: Collins. 1954. Pp. 384. 16s.

1. Farquhar, J. W., Lewis, I. C. *Lancet*, 1948, ii, 244.

2. Colker, J., Norman, R. *Pharm. J.* Feb. 27, 1954, p. 165.

University of Cambridge

The honorary degree of doctor of science is to be conferred on Sir Charles Dodds, F.R.S.

On March 20 the following degrees were conferred :

M.Chir.—* J. F. Bolton Carter, * A. G. Dingley, Alfred Standeven.
M.B., B.Chir.—* A. J. Danby.
M.B.—A. D. Thursz.

* By proxy.

National University of Ireland

The honorary degree of LL.D. is to be conferred on Dr. E. P. Carey and Dr. Philip Lynch.

Royal College of Surgeons in Ireland

At recent examinations the following were successful :

F.R.C.S.I.—D. F. Doherty, J. Kyle, J. G. Maher.
D.C.H.—B. P. K. Ryan, J. B. Shea.
D.O.M.S.—R. E. Tingeay.
D.P.M.—E. Casement, A. C. Fleming, J. P. F. Fogarty, D. C. Hutchison, K. A. McDaid, P. J. Meehan, R. R. Steinert.

Irish Conjoint Board

On April 2 the following candidates, having passed the final examination of the Irish Conjoint Board, were admitted licentiates in medicine and midwifery :

Una E. Batt, A. I. Booth, S. A. A. Carson, Dinshaw Ratanji Chinoy, Margaret T. Coyle, Laura Cullen, Veronica O. Egbuna, Bridget Finnegan, Patricia J. Finnegan, P. D. N. MacAllister, Grainne McCarthy, P. J. Ward.

West Midlands Physicians Association

A meeting of this association will be held at The Royal Salop Infirmary, Shrewsbury, on Saturday, May 8, at 11 A.M.

Diabetic Association

Dr. K. Hallas-Møller (Denmark) will deliver the Banting lecture at University College Hospital School, London, W.C.1, on Friday, July 16, at 2.30 P.M. He will speak on the New Insulins.

International Congress on Thrombosis and Embolism

This congress is to be held from July 20 to 24, at Basle. Those who wish to read papers should write to the general secretary of the congress, Gynaecological Clinic, Basle University, Basle, Switzerland, before May 31.

British Association of Physical Medicine

The annual meeting of this association is to be held at King's College Hospital, London, S.E.5, on April 30 and May 1. The programme includes a discussion on the Scientific Approach to be opened by Dr. A. C. Boyle, Dr. A. T. Richardson, and Dr. Richard Doll.

Grove Hospital, Tooting

This hospital, which was formerly in the South West Metropolitan region, has now been included in the group which forms the teaching hospital of St. George's.

International Festival of Medical Scientific Films

Minerva Medica has organised this festival, which will be held in Turin from May 29 to June 6. Further particulars may be had from the secretariat of *Minerva Medica*, Corso Bramante, 83, Turin, Italy.

Mental After Care Association

The annual general meeting of this association will be held on Thursday, April 8, at Burlington House, Piccadilly, London, W.1, at 3.45 P.M., when the Very Rev. A. C. Don, D.D., and Dr. Henry Yellowlees, will speak.

General Register Office

Mr. Bernard Benjamin, F.I.A., has been appointed chief statistician (civil) in the General Register Office, in succession to Mr. V. P. A. Derrick, who has retired after 34 years in the department.

Congress of World Federation of Occupational Therapists

This congress is to be held in Edinburgh, from Aug. 16 to 21, under the chairmanship of Prof. Norman Dott. The speakers will include : Dr. Henry H. Kessler (New Jersey), Dr. H. Hoyle Campbell (Toronto), Dr. M. A. Perlstein (Chicago), Sir David Henderson, Prof. Walter Mercer, Dr. W. A. Murray, Mr. Robert Stirling, and Mr. G. A. Pollock. Further particulars may be had from the secretary of the congress (Miss Waterston), Astley-Ainslie Hospital, Edinburgh.

International Conference of Geographical Pathology

The International Society of Geographical Pathology is to hold its 5th conference from Sept. 6 to 10 in Washington, D.C. The general subject chosen for discussion is the Geographical Pathology of Cancer. Further information may be had from Prof. Robert A. Moore, M.D., Washington University School of Medicine, 660, S. Kingshighway, St. Louis, 10, Missouri, U.S.A.

Sir Lionel Whitby, Prof. John McMichael, and Dr. P. M. F. Bishop are visiting the Near East under the auspices of the British Council to attend the fourth Middle East Medical Assembly at Beirut from April 9 to 11.

The Proceedings of the conference held last year in Glasgow by the National Smoke Abatement Society are now obtainable (price 7s. 6d.) from the society, 30, Grosvenor Place, London, S.W.1.

CORRIGENDUM—The article on the Mental Health Research fund (see *Lancet*, March 13, 1954, p. 559) appears on p. 10 of the supplement to the January issue of the *Journal of Mental Science*.

Diary of the Week

APRIL 11 TO 17

Monday, 12th

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
 8.30 P.M. Air Commodore T. C. MacDonald, Dr. I. J. Corbett : Medical Aspects of Air and Sea Travel.

Tuesday, 13th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
 8 P.M. Section of Psychiatry. Dr. D. A. Pond : New Physiological Data Bearing on Problems of Consciousness. Dr. Denis Williams : Affective Disorders and the E.E.G.

Wednesday, 14th

ROYAL SOCIETY OF MEDICINE
 4.30 P.M. Section of Physical Medicine. Dr. Doris Baker : Changes in Skin Collagens—A Source of Rheumatic Pains. (Presidential address.)

HARVEIAN SOCIETY OF LONDON, 11, Chandos Street, W.1
 8.15 P.M. Dr. George Warren, Dr. Michael Ward : Health at High Altitudes.

NORTH-WESTERN TUBERCULOSIS SOCIETY
 5.30 P.M. (Aintree Hospital, Liverpool, 9.) Mr. Dillwyn Thomas : Tuberculous Mediastinal Lymph-glands.

Appointments

BURNS, J. P. J., M.C., M.B. Belf., D.P.H. : senior asst. M.O., Wembley and Willesden.

GOLEN, Z., M.B. Polish School of Medicine, Edin. : asst. psychiatrist, Whittingham Hospital, Preston.

LOFTUS, ANTHONY, L.R.C.P.I., D.P.H. : asst. M.O.H. and asst. school M.O., Oldham.

MACLEOD, WILLIAM, M.B. Edin., M.R.C.P.E., D.M.R.-D. : consultant radiologist, Royal Hospital for Sick Children and Deaconess Hospital, Edinburgh.

NABARRO, J. D. N., M.D. Lond., M.R.C.P. : asst. general physician, Middlesex Hospital, London.

ROUSSAK, N. J., M.B. Manc., M.R.C.P. : consultant physician, Withington and Wythenshawe hospitals, Manchester.

North East Metropolitan Regional Hospital Board:

CROCKETT, R. W., M.B. Glasg., F.R.F.P.S., M.R.C.P., D.P.M. : part-time consultant psychiatrist, Oldchurch and St. George's hospitals, Hornchurch.

GRUNBERGER, GEORGE, M.D. Basle, D.L.O. : part-time consultant E.N.T. surgeon, St. Margaret's Hospital, Epping, and Honey Lane Hospital, Waltham Abbey.

MARTIN, D. V., M.R.C.S., D.P.M. full-time consultant psychiatrist and deputy physician superintendent, Claybury.

MASON, MARGARET M., M.B. Camb., F.R.C.S. : part-time consultant E.N.T. surgeon, Ilford and Barking group of hospitals and clinics.

O'SULLIVAN, J. J., M.B., M.R.C.O.G. : part-time consultant gynaecologist, Whippes Cross Hospital.

PRITCHARD, G. C., M.B. Camb., F.R.C.S., D.O.M.S. : part-time consultant ophthalmic surgeon, East Ham Memorial Hospital.

THORNE, N. A., M.D. Lond., M.R.C.P. : part-time consultant dermatologist, Mile End Hospital, St. George-in-the-East Hospital, and St. Andrew's Hospital, Bow.

Births, Marriages, and Deaths**BIRTHS**

BIHARI.—On March 27, at University College Hospital, to Mae (née McMullan), wife of Julian Bihari, F.R.C.S.—a son (David Julian).

JENNETT.—On March 25, at Liverpool Maternity Hospital, to Dr. Sheila Pope, wife of Mr. Bryan Jennett, F.R.C.S.—a son.

THE SECRETIONS OF THE BRAIN*

RELATION OF HYPOTHALAMUS TO PITUITARY GLAND

S. ZUCKERMAN

C.B., M.A. Oxf., M.D. Birn., D.Sc. Lond., F.R.S.
PROFESSOR OF ANATOMY, UNIVERSITY OF BIRMINGHAM

(Concluded from p. 743)

The New Secretions of the Brain

THE PITUITARY HORMONES

The story re-opens in 1895 with the demonstration by Oliver and Schafer that the blood-pressure of an animal rises after the injection of a "concoction" of the pituitary. Howell (1898) soon showed that the effect was due to the posterior as opposed to the anterior lobe of the gland. A few years later Magnus and Schafer (1901) found that the posterior-lobe hormone also has a diuretic/antidiuretic action. And soon afterwards, Dale (1906, 1909) demonstrated that posterior-lobe extracts had an oxytocic action. Concurrently, numerous clinical observations indicated very clearly that the anterior part of the pituitary also had important hormonal functions (see Teel and Cushing 1930). The proof of this was provided in the '20s by the brilliant experimental studies of Herbert M. Evans, Zondek, Aschheim, and others too numerous to mention, which showed quite clearly that the anterior lobe of the pituitary plays a vital part in the control of growth, in the regulation of reproductive processes, and in the maintenance of certain other endocrine organs such as the adrenal cortex.

The histological structure of the posterior lobe did not encourage any of the earlier workers to believe that the active principle which could be extracted from it was elaborated within it. Herring (1908, 1914), whose name is now applied to the hyaline bodies often seen in the pituitary stalk, held that the posterior-lobe hormone was, in fact, produced by the cells of the pars intermedia, and that it passed back into the pars nervosa and up the pituitary stalk. His interpretation was seized upon by many other workers, and particularly by Harvey Cushing (e.g., Cushing and Goetsch 1910, Cushing 1933). Cushing's belief was that the posterior-lobe hormone not only entered the blood-stream, but that after making its way up the pituitary stalk it passed through the ependymal lining of the third ventricle and so entered the cerebro-spinal fluid. Gradually, however, opinion changed. The conventional view today is that there are specific parenchymatous secretory cells in the neurohypophysis, and that these cells are responsible for the secretion of the posterior-lobe hormones (see Gersh 1939).

About the secretory powers of the anterior lobe there never was any doubt. Its structure was clearly glandular, and the only difficulty was to reconcile its apparent cytological simplicity with the complexity of its hormonal functions.

By the time we were fairly clear about the distinction between posterior and anterior lobe function, the infundibular region of the brain again entered the

picture. It did so first as a result of a series of studies started by Karplus and Kreidl in 1909, which showed that stimulation of the hypothalamus led to a number of autonomic effects (e.g., changes in heart-rate, and salivation). These observations were followed in 1913 by Camus and Roussey's demonstration that an adiposogenital syndrome could develop as a result of experimental hypothalamic lesions. As our knowledge continued to grow, it became abundantly clear that in some mysterious way the hypothalamus—the infundibular region of the Ancients—controlled or modulated the endocrine activity of both the anterior and posterior lobes of the pituitary. Once again the question was, How?

This time, however, the problem was both more specific and more complicated. First, it was quite clear that the pituitary consisted mainly of two quite separate endocrine structures—an anterior lobe,¹³ and a posterior lobe.¹⁴ Secondly, by now there was precise knowledge of the nature of nervous action; if the pituitary stalk was not hollow, at any rate it consisted largely of the axons of hypothalamic nerve-cells, which provided an anatomical basis for whatever cerebral control there was of pituitary function (see fig. 3). And thirdly—and most important—answers could no longer depend on speculation based on dogma, however hallowed; the hard facts of observation and experiment were needed.

HYPOTHALAMIC CONTROL OF THE POSTERIOR PITUITARY

The first problem for which a solution seemed to have been found was the control exercised by the hypothalamus over the secretion of antidiuretic hormone. The

13. More correctly designated the pars distalis of the adenohypophysis, of which the other two parts are the pars intermedia and pars tuberalis.
14. Now defined as the processus infundibuli of the neurohypophysis, whose two other parts are the infundibular stem or stalk, and the median eminence of the tuber cinereum—which includes the infundibular bulb or infundibulum.

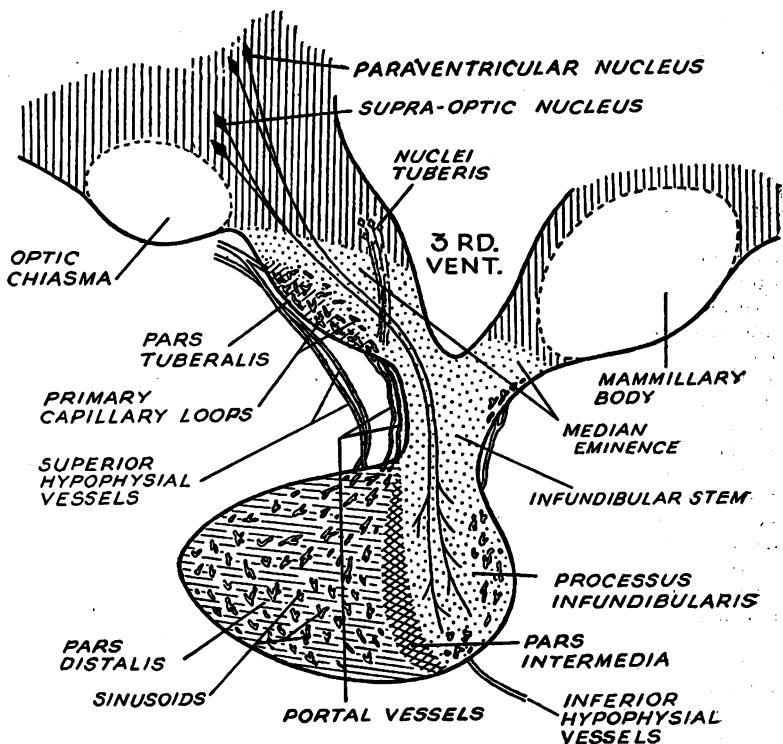


Fig. 3—Diagram to indicate the relations of the pituitary gland to the hypothalamus. The three hypothalamic nuclei mentioned are shown schematically.

* The seventh Addison Memorial Lecture, delivered at Guy's Hospital, London, on Dec. 16, 1953.

explanation seemed simple enough (Fisher et al. 1938). All levels of the neurohypophysis are connected with the terminations of the axons of cells in the nuclei supraopticus and paraventricularis of the hypothalamus (particularly the former). Presumed secretory cells ("parenchymatous glandular cells") are present in the median eminence and infundibular stem, as well as the infundibular process (Gersh 1939). The whole neurohypophysis, including, as it does, part of the floor of the third ventricle, is thus concerned in the secretion of hormone, and all of it is under the control of the hypothalamus. Sever the pituitary stalk, and the part of the neurohypophysis distal to the section atrophies completely—owing to the interruption of the trophic influence of the hypothalamus—and no longer can any hormone, antidiuretic, pressor, or oxytocic, be extracted from it. Destroy the nuclei supraopticus and paraventricularis and remove that control completely, and the whole neurohypophysis involutes; and diabetes insipidus supervenes, owing to the cessation of secretion of antidiuretic hormone. Or completely divide the supraoptico-hypophysial tract, and the cells of the nucleus supraopticus degenerate. The reason why hypophysectomy itself is only occasionally followed by diabetes insipidus is also straightforward; the operation very rarely removes all of the neurohypophysis, and the cells of the part which remains hypertrophy to compensate for the loss of the rest.

These observations and interpretations seemingly provided all that could be asked for in trying to understand the control exercised by the hypothalamus on the diuretic/antidiuretic balance. And since the hypothalamus is a major autonomic motor centre which is linked, as far as one knows, with all the afferent zones of the brain, they also made it possible to understand how various forms of afferent stimulation are tied up with processes in which posterior-lobe hormones are involved. Thus they help to provide an explanation for the effects of emotion on water diuresis (e.g., Verney 1947, Noble et al. 1950, Taylor and Noble 1950), and also to understand the nature of the nervous pathways concerned in the reflex stimulation of milk discharge (Harris 1951). In short, while one might not know exactly how it all worked, there could be no doubt about the general nature of the link between the brain and the posterior pituitary.

HYPOTHALAMUS AND ANTERIOR PITUITARY

If the connection with the posterior lobe of the pituitary seemed, on the face of it, clear enough, that with the anterior was anything but obvious. Here one goes on being confronted by a most bewildering puzzle. First, there is no doubt that the anterior lobe of the pituitary regulates several bodily processes, and that the timing and intensity of its different physiological activities accord with the steps of those processes; or, to put it in the teleological terms used by Bayliss and Starling (1904), that the secretions of the anterior lobe are regulated by the needs of the body. We know that some of this regulation is effected by hormonal or metabolic interaction. For example, when, under the stimulus of the gonadotrophic hormone of the anterior pituitary, an excess of oestrogen is secreted by the ovaries, the pituitary becomes inhibited, and the gonadotrophic stimulus weakens. Or if we follow Wilhelmi (1948), when the peripheral carbohydrate level falls, adrenocorticotrophic hormone (A.C.T.H.) is released from the pituitary, as part of the mechanism concerned in stabilising peripheral carbohydrate levels; then, as an effect secondary to the subsequent secretion of hormone by the adrenal cortex, gluconeogenesis occurs and the level of blood-sugar rises. But some regulation is undoubtedly of a more direct nervous kind, and is presumably mediated by the hypothalamus. For example, it has been shown (Harris 1948a) that in an animal such as a rabbit, which normally

ovulates after the stimulus of mating, direct unipolar or bipolar stimulation of the hypothalamus can result in rupture of the ovarian follicles, provided the experiment is done during the oestrous phase of the cycle. Presumably normal mating also starts a train of nervous stimulation which culminates in the firing of the relevant hypothalamic neurons. Another example is the anestrous ferret, which becomes oestrous in the winter months if it is exposed to additional light. While the main visual centres of the brain are apparently not involved (Le Gros Clark et al. 1939), the primary receptor for the response is the retina (Thomson 1951, 1954), and the stimulus is presumably also relayed to the hypothalamus before it activates the pituitary. And to take a last but perhaps now more familiar, even if more debatable, example, a painful stimulus leads to a reflex release of A.C.T.H. from the anterior pituitary; certain workers (e.g., de Groot and Harris 1950, Fortier 1952) believe that the hypothalamus is once again an intermediate station for the response.

But—and here is the essential difficulty—few workers believe that the glandular cells of the anterior lobe obtain their secreto-motor innervation from the hypothalamus (see Harris 1948b),¹⁵ or that there is any other kind of secreto-motor innervation (e.g., via nerve-fibres along the pituitary blood-vessels).

How, then, are the "reflex" responses of the anterior pituitary controlled?

THE PITUITARY-PORTAL VEINS

The possibility which is now attracting the greatest attention is that the critical anatomical link between the hypothalamus and anterior pituitary is provided by the very axial-stalk vessels which Lieutaud described nearly two hundred years ago. The part they played then was as a channel for the pituita; they derive their present importance from the possibility that they convey a so-called "chemotransmitter" from the hypothalamus to the pituitary.

We owe their rediscovery, and their first fairly complete description, to Popa and Fielding (1930a and b, 1933), who gave an account of what they were the first to call the hypophysio-portal system of veins. According to these workers, the axial-stalk veins collect blood inferiorly from the pars distalis (anterior lobe) and pars intermedia, as well as from the pars tuberalis and pars posterior, and then ascend the stalk as parallel veins "which after a short course, acquire thick neuroglia sheaths." Popa and Fielding believed that superiorly, beneath the infundibular recess of the third ventricle, the vessels lost their neuroglia wrapping, and formed a network of very fine channels which they describe as a secondary distributing net. Popa and Fielding were persuaded of the correctness of Cushing's opinion about the direction of flow of the posterior-lobe hormone, and it was their view that the current in the portal vessels was from below upwards, and that colloid material was transported from the pituitary to the hypothalamus, where in fact they demonstrated it histologically, as had Collin (1928) before them. Since then the contrary view has gained ground, particularly as a result of the researches of Wislocki and King (1936), Green and Harris (1949), and Barnett and Greep (1951a); and most—but not all—observers now believe that the direction of the blood is from above downwards. The secondary distributing net of Popa and Fielding has thus become the primary net, comprising a dense mesh of capillary loops in the pars tuberalis, while the true secondary net is represented by the connection

15. The early death in 1952 of Vazquez-Lopez, the most recent protagonist of the opposite view, has unfortunately removed from the scene one who might have helped solve the problem, which has clearly to be settled before we are going to reach anything like a final answer to the question of the control of anterior pituitary function.

of the main portal vessels with the sinusoids of the pars distalis (see fig. 3).¹⁶

As already indicated, it was the disbelief in the existence of any nervous connection that made it necessary to consider the possibility that the pituitary-portal veins are in some way involved in the presumed control which the hypothalamus exercises over the anterior lobe of the pituitary. The hypothesis that has been advanced (Harris 1948b) is that some unknown "chemotransmitter" is liberated, as a result of nervous stimulation, in the vicinity of the portal vessels, into whose primary capillary loops it passes. The "hormone" then passes down the longitudinal channels on the stalk into the sinusoids of the anterior lobe, and is so able to influence the secretory cells of the pars distalis.

In the light of Harris and Jacobsohn's (1952) experiments on pituitary transplantation, few could doubt that the portal vessels play some special part in the economy of the anterior lobe; for these two workers found that pituitary tissue is more likely to "take" successfully if it is transplanted under the median eminence of the brain, where the grafted tissue can come into relation with the proximal stumps of the portal vessels, than anywhere else. On the other hand, the attractive theory of which the portal vessels constitute the central feature is essentially based on what may be called purely negative considerations. Indeed, the chemotransmitter or chemotransmitters had to be conjured into existence only because without them we could seemingly explain nothing about the mechanisms involved. Moreover, the theory is hardly as precise as the facts which it has to explain. The anterior lobe of the pituitary controls many functions; and we have either to suppose that the gland is differentially activated by different kinds of chemotransmitter, or that, once activated by a single stimulus, the gland of itself adjusts its secretions according to the needs of the body. If it is the former which is implied, we are well beyond the area of fact. If it is the latter, the hypothesis merely transfers the critical problem we are trying to understand—how the reflex functions of the pituitary are controlled—from the hypothalamus to the pituitary itself.

THE PITUITARY-PORTAL HYPOTHESIS

The specific evidence which it has been suggested (Wingstrand 1951a,¹⁷ Harris 1952, Mazzi 1952) supports the idea that the pituitary-portal vessels are the controlling link between these two structures, derives partly from observations on the effects of direct stimulation of the hypothalamus, partly from studies of the behaviour of pituitary grafts, and partly from studies of the effects of section of the pituitary stalk.

The first line of evidence, however, merely indicates that experimental stimulation of the hypothalamus can lead to responses such as ovulation—without in any way showing what the link is between the hypothalamus and the anterior pituitary. Correspondingly little can be drawn from such evidence as is available about the behaviour of pituitary grafts. The genetic relationship of host to donor has not always been as close as is desirable in experiments of this kind, and the results in some cases reflect the fact that very little pituitary tissue has survived. All but a few reports also imply that the

grafts do not maintain full reproductive function. On the other hand, it seems to be agreed that a transplant of anterior pituitary tissue in the anterior chamber of the eye will release A.C.T.H in response to a suitable stimulus—in spite of the fact that it is completely separated anatomically from the hypothalamus.

The information that is available from experiments in which the pituitary stalk has been sectioned is also equivocal, some observers reporting very little, if indeed any, and others considerable, derangement in processes which are under the control of the anterior pituitary (e.g., reproduction). Harris (1952) has suggested that in those instances in which the operation has not interfered with reproductive function, the pituitary-portal vessels have regenerated; and on the basis of work carried out in collaboration with Jacobsohn (1952) he has concluded that the anterior pituitary does not function properly except when the pituitary-portal system is intact. An alternative explanation of the conflicting results of stalk section reported by different investigators is that the operation almost inevitably divides one or more small vessels supplying the gland, with variable amounts of resulting and lasting damage due to infarction (Greep and Barnett 1951).

Studies in my own laboratory (Thomson and Zuckerman 1953) suggest that complete division of the pituitary stalk in the female ferret does not necessarily interfere with the presumed relay of impulses to the pituitary from the hypothalamus—even when no vascular connection of any kind has re-formed between the gland and the infundibular region. The particular response studied was the reaction of the ancestral animal to additional light in the winter months. The operations were carried out in the summer months, and a piece of waxed paper inserted between the proximal and distal parts of the stalk. Most preparations were defective for one or other of several technical reasons—usually movement of the paper between the time of the operation and the subsequent autopsy. In two, however, there was no question but that the animals reacted to light despite either destruction of the median eminence and disappearance of the primary capillary net, or complete separation of the pituitary from the hypothalamus, determined from serial sections of a block consisting of the sella turcica, the pituitary, and the overlying part of the brain. In one animal a three-dimensional reconstruction showed that the paper was still in position, that the processus infundibuli had atrophied completely and that the proximal stump of the stalk was attached to the scar tissue surrounding the plate of paper. The pars distalis, which the paper completely separated from the base of the brain, showed no histological abnormalities, and was normal in size. There was no vascular connection of any kind between it and the region of the median eminence.

This observation disposes both of the view that the integrity of the pituitary-portal veins is essential for the "reflex" activation of the anterior pituitary in responses of the kind that we are considering, and of the generalisation that the anterior lobe of the pituitary will not function properly unless the vessels are intact. It is also incompatible with the idea that the signal which triggers the pituitary of the ancestral ferret to produce gonadotrophin is some chemotransmitter that is elaborated in the hypothalamus, and which passes down the pituitary-portal veins. On the other hand, it does not exclude the possibility that there is a chemotransmitter(s), or, given that one exists, that this is conveyed to the pars distalis via the systemic blood-stream. Nor, needless to say, do our observations mean that what applies to the ferret necessarily represents general vertebrate physiology. In many birds, for example, all or most of the arterial blood which passes to the pars distalis traverses the capillary loops of the primary capillary net of the portal system, and in the species concerned these vessels are presumably

16. Popa and Fielding (1933) knew that other observers before them had seen the hypophysio-portal vessels. They do not, however, appear to have known about de Bordeu's controversy with Lieutaud, since the earliest of their references is to Lothringer (1886), who described an intermingling of epithelial cells with large vessels at the point where the pars distalis and pituitary stalk come together.

17. Wingstrand, while adhering to the pituitary-portal hypothesis, recognises that "the decisive proof of the route of the impulses from the hypothalamus to the pituitary is lacking."

essential to normal pituitary function (Wingstrand 1951a and b, Benoit 1951).

Our observations do, however, underline the critical consideration that what matters in experiments in which the stalk is divided may well be the extent to which the anterior pituitary suffers as a result of infarction, following on the interruption of its ordinary blood-supply, or from some other cause. In the rat Greep and Barnett (1951) and Barnett and Greep (1951b) found that immediately after the operation the reproductive system becomes hypoactive to an extent which varies with the amount of damage suffered by the anterior pituitary, but that it may then recover slowly, although rarely completely. Recovery is, however, independent of restoration of the pituitary-portal vessels. Tang and Patton (1951), on the basis of experiments on male guineapigs, go a step further and state that there is practically no evidence of impairment of anterior pituitary function after stalk section, and that this is so despite no regeneration of the stalk vessels. In ferrets whose pituitary stalks are divided, the anterior lobe is occasionally normal in size, and at other times smaller and changed in microscopic appearance. In the former, but not the latter, instance the operation has presumably damaged some small vessels supplying the gland.

The fact is that no two operations on the pituitary stalk of an animal are likely to produce precisely the same type of lesion—regardless of the intention of the investigator. Circumstances make it difficult to standardise the operation, and variation in minute anatomical disposition between animals cannot be counterbalanced by visual control. Moreover, unfavourable though the position is with mammalian species used in experiments on the stalk, it appears to be worse with birds, where the main afferent blood-supply to the pars distalis is, apparently, via the portal vessels. Experiments may show that anterior-lobe function is not the same after division of the portal vessels, and one may consequently draw the conclusion that some local chemotransmitter is involved (Benoit 1951). A more obvious interpretation would, however, be that an ischaemic anterior lobe cannot function properly.

In evaluating experiments of the kind we are discussing, it is clearly not enough, therefore, to be told that the stalk was completely divided. Where pituitary hypo-function supervenes, we also need to decide whether the effects observed were not due to unintentional damage to the pars distalis, or even to damage to adjacent parts of the hypothalamus.

While our observations on the ferret conflict with the pituitary-portal hypothesis, they fail to take us a single step closer to an understanding of the precise way the response to light in this animal is, in fact, mediated. And unless we are prepared to overlook the critical lack of those facts which should be there if we are to understand the physiological mechanism involved, the same unfortunate conclusion applies, in my judgment, to all experiments which seem to show how the hypothalamus is linked to, and is involved in, the "reflex" activation of the anterior lobe.

SECRECTIONS OF THE HYPOTHALAMUS

It is paradoxical that while the "chemotransmitters" which activate the anterior lobe seem so illusory, an increasing number of researches in recent years are nevertheless leading to the view that hypothalamic neurons do, in fact, secrete hormones. These, however, are concerned with the neurohypophysis—not the adenohypophysis. I have already referred to the fact that Collin, as well as Popa and Fielding, had noted that so-called colloid inclusions could be found in the hypothalamus. E. Scharrer independently made the same observation, and in 1928 published the first of a series of papers concerned with the peculiar secretory appearance

of cells in the nuclei supraopticus and paraventricularis of the vertebrate hypothalamus, and with their close relationship to capillaries. He argued convincingly that the histological appearance of neurosecretion had a functional significance, and represented neither post-mortem changes, nor degeneration phenomena, nor fixation artefacts; and also that the colloid in the hypothalamic nuclei had not migrated into the brain from the pituitary, as had been suggested by Collin. Few, however, seem to have been convinced, and Scharrer, as he himself states (Scharrer and Scharrer 1940) failed to throw further light on the problem by experimental methods. It was, as he points out, difficult to know what pharmacological tests to apply to extracts of the two hypothalamic nuclei. At the same time the contention of Ranson and his colleagues that the hypothalamus could not takeover the function of the neurohypophysis, when the latter was ablated, obviously affected views on the possible significance of the hypothalamic secretion.

The position was transformed overnight in 1949, when Bargmann discovered that Gomori's chrome alum-hæmatoxylin-phloxine stain could be very effectively used to demonstrate cytoplasmic inclusions not only in the neurons of the nuclei supraopticus and paraventricularis, but also throughout the length of their axons. His observations have now been confirmed by many workers, including Scharrer and his colleagues. No neurons other than those of these two nuclei and of the mammillo-infundibular nucleus are chromehæmatoxophil¹⁸ (Smith 1951). At the same time, experiment has suggested very strongly that the neurohypophysis itself is not a primary secreting organ, but that the posterior lobe hormones (the pressor, antidiuretic, and oxytocic principles) are elaborated by the neurons in the nuclei supraopticus and paraventricularis, and also possibly by their axon terminals in the neurohypophysis (e.g., Bargmann and Scharrer 1951, Hanström 1952a and b). For example, it has been shown (Hild 1951, Stutinsky 1951a) that when the pituitary stalk is tied or cut, the part of the neurohypophysis distal to the ligature rapidly becomes depleted of material which stains with Gomori's alum-hæmatoxylin, whereas so-called Gomori-positive material accumulates within the axons immediately proximal to the ligature. Corresponding observations, which seem to indicate that there is a flow of some substance from the cell body down the axon, have been made in invertebrates in which "neurosecretion" has for long been accepted as a normal phenomenon. For example, Ellen Thomsen (1954) has used a single strand of silk from the silkworm to ligature the axons coming from a few secretory neurons in the brain of the fly, and has demonstrated the damming-back of some substance immediately proximal to the knot. Yet another demonstration of this "flow" has been provided by Drager (1950), who removed the pituitary from a certain species of snake and filled the empty sella turcica with fibrin-foam. Two to four weeks later, when the animals were killed, spherical droplets with staining properties identical with those of the granules in the hypothalamic nuclei, were found in the fibrin-foam.

Transplantation experiments also suggest that the processus infundibuli does not secrete the hormone it contains. Thus, Stutinsky (1950, 1951b) transplanted the "gland" to the capsule of the kidney, and found that in its new position it rapidly becomes depleted of Gomori-positive material which, on the other hand, piled up in the proximal part of the neurohypophysis which was not removed. A corresponding observation is based on the

18. The following terms have been used to describe cells which stain electively with chrome alum-hæmatoxylin: Gomori-positive; c.H.P. positive; chromehæmatoxophil. Smith states that the axons of the mammillo-infundibular nucleus mingle with those of the two other nuclei which react to the stain.

fact that neurosecretory granules disappear from the hypothalamus and neurohypophysis when animals are kept thirsty. If the pituitary stalk is cut in such animals, which are then allowed to drink ad lib, granules soon reappear proximal to the cut, but not in the part below (Hild 1953). Moreover, the granules first reappear in the cell bodies themselves, as opposed to the axons (Ortmann 1951).

Valuable evidence has also been obtained in a series of experiments carried out on large groups of Alsatian dogs by Zetler (1953) and Hild and Zetler (1953). These workers have found that the concentration of posterior lobe hormone in the anterior hypothalamus¹⁹ varies, in parallel with that in the processus infundibuli, according to the state of hydration and dehydration of the body. They have also shown that, whereas the concentration of posterior lobe hormone is much higher in the normal processus infundibuli than it is in the hypothalamus, the reverse is true after the pituitary stalk is tied. The concentration of hormone distal to the ligature rapidly falls, while that in the hypothalamus increases. Zetler and Hild have also provided evidence that the substance which has an affinity for Gomori's chrome alum-hæmatoxylin is almost certainly not the active hormone, but some carrier material. This observation is interesting in view of the recent synthesis by du Vigneaud (1953) of polypeptides with the properties of posterior lobe hormones.

The general conclusion to which all these newer studies are pointing is that the posterior lobe itself is little more than a storage organ for hormones produced in hypothalamic nuclei. On the other hand, Bodian (1951), in a very careful reassessment of the histological structure of the neurohypophysis of the opossum, holds that, while this conclusion is in general true, the terminals of the axons in the tractus hypophysius may also be involved in the process of secretion. Bodian believes that "the morphological complexity of the nerve terminals becomes more readily rationalised as a mechanism for serving to increase the ratio of cell surface to cell volume, and perhaps thus favoring an enhancement of the secretory process in the pars nervosa, as compared with the hypothalamic nuclei." He also believes that the pituicytes (Gersh's parenchymatous secretory cells) are adapted so as to bring the nerve-fibre terminals into closer relationship with the blood-vessels which intervene between the lobules of the processus infundibuli.

The idea that the axon terminals may play a part in the secretory process can be related to some recent observations of Vogt (1953). This worker has found that extracts of the anterior hypothalamus have the same ratio of pressor to antidiuretic activity as characterises true posterior-lobe extracts, but that oxytocic activity is relatively very low. She has, therefore, suggested that the "molecule" of posterior-lobe hormone secreted by the anterior hypothalamus is either modified as it travels down into the processus infundibuli, or that the latter actually elaborates oxytocin. Either way, this experimental observation could be taken as according with Bodian's anatomical view that the nerve terminals play some active part in the production of the posterior-lobe hormone.

EVIDENCE FOR POSTERIOR-LOBE SECRETION

With all these new findings and new ideas coming forward, it is obviously essential to reconsider the facts which sustain the conventional view that the neurohypophysis itself is a secretory organ. As the history of the subject shows (compare, for example, van Dyke 1936, with his 1939 review of the subject), recourse can hardly be made to histology for proof that the posterior lobe is a secretory organ. Nor can we take the fact

(e.g., Geiling 1935) that posterior-lobe hormones can be extracted from isolated pars nervosa tissue as indicating that the hormone is elaborated there—it might well have been produced, as the new theory suggests, in the hypothalamus. In view of this possibility, the only kind of evidence that could be taken as proof that the pars nervosa is itself a secretory structure would have to be derived from tissue-culture experiments. And even so it could be argued—if it turned out that cultures of posterior lobe do not produce hormone—that such a result was only to be expected in view of the fact that none is produced even by the posterior lobe *in situ* once it is released from hypothalamic control.

The evidence from tissue-culture experiments is far from convincing—in spite of the frequency with which it is cited. Geiling and Lewis (1935) prepared cultures of pars nervosa and intermedia taken from rats and mice, and allowed them to grow for up to fifty days. The pars nervosa tissue gave rise to an abundant growth of long, flat, radiating cells, and of neuroglia-like cells. The cultures were found to have both a pressor and melanophore-expanding action, but there is a suggestion, too, that the nutrient medium itself had a slight pressor effect.²⁰ A test for antidiuretic action was made with only one culture, and it gave no more than "some indication" of the presence of an active antidiuretic principle (Lewis 1938). What one does not learn from reports of experiments of this kind is: (a) how rigid the controls were; (b) how specific the tests were for posterior-lobe hormone²¹; and (c) whether such activity as was demonstrated in the culture was not due to the persistence of hormone that was there already (a point which applies regardless of the negative results of a few control cultures of connective tissue to which a solution of posterior-lobe hormone had been added).

Anderson and Haymaker's (1935) observations are equally indecisive. These authors found that there was no growth of pars nervosa elements in cultures of posterior-lobe explants taken from 8-day-old rats. The cultures were extracted after 6 days, and the melanophore-expanding principle—a product of the pars intermedia—was shown to have increased. This principle was also found in some cultures which were left for 9 or 12 days. No oxytocic hormone could be demonstrated, but some antidiuretic effect was observed, presumably in 6-day-old cultures, in three tests on dogs.

This seems to be the best evidence that can be cited about the secretory capacity of posterior-lobe explants. What little it indicates is far too inconclusive to provide any challenge to the idea that the so-called posterior-lobe hormones are, in fact, secreted by hypothalamic nuclei.

This new thesis also hardly conflicts with any of the facts—as opposed to interpretations—which Ranson and his colleagues disclosed in their classical series of researches on the cat and monkey. Both old and new theories agree that once the tractus hypophysius is interrupted, the distal part of the neurohypophysis atrophies and soon becomes free of hormone. According to Ranson's interpretation, the change is due to the interruption of a trophic and secretomotor innervation. According to the newer view, it is essentially due to the blocking of channels along which hormone flows. A more difficult issue to reconcile is the amount of retrograde degeneration that occurs in hypothalamic nuclei after division of the axons which form the tractus hypophysius. In agreement with earlier workers (e.g., Kary 1924, Lewy 1924), Ranson and his colleagues (Fisher et al. 1938) hold that all the cell bodies in the nuclei supraopticus and paraventricularis (particularly in the former)

20. It is not stated that the nutrient medium had no effect, but merely that it had no "appreciable effect on the blood-pressure."
21. On this point see van Dyke (1936); also Noble et al. (1950), Pickford (1952).

19. Abel (1924) was the first to show that extracts of the hypothalamus had pressor and oxytocic activity.

involute. Stutinsky (1951a), however, does not agree that this is so—he claims that a very large number of neurons remain functional. The difference, however, is mainly one of emphasis. Fisher, Ingram, and Ranson (1938) themselves point out that a fully developed diabetes insipidus will not occur unless the entire neurohypophysis, including the centre part of the tuber cinereum, is removed, and that "in general the intensity of the diabetes insipidus is proportional to the degree of interruption of the supraoptico-hypophysial tract." This is in fair agreement with the neurosecretory view, according to which sufficient antidiuretic hormone will be released into the blood-stream to maintain the diuretic/antidiuretic process in balance, as long as a critical amount of the two relevant nuclei is intact.

POSSIBLE CONTROL OF ANTERIOR LOBE BY POSTERIOR-LOBE HORMONE

One final question needs to be raised, even though it cannot be pursued in detail. Is there any evidence that posterior-lobe hormone—the hypothalamic "chemo-transmitter" which has been revealed by all these post-war researches—can itself activate and control the many functions of the anterior lobe? The simple answer is: so far, none that stands up to close examination. For example, it is known (e.g., Nagareda and Gaunt 1951, Stutinsky et al. 1952) that strong and non-physiological doses of posterior-lobe hormone can stimulate the release of A.C.T.H. But much more will need to be revealed about this response (for example, its differentiation from a reaction due to the stress of the experiment) before we shall be in a position to evaluate it properly.

The anatomical facts that bear on the point also need close scrutiny. The median eminence in birds and in most mammals that have been studied is differentiated into an inner ependymal zone; a middle coarse-fibre layer; and an outer so-called glandular layer which is devoid of cells and which essentially consists of very fine nerve-fibres, believed to be dendrites or possibly axons of the nuclei tuberis infundibularis, set in an interstitial "colloid" (e.g., see Nowakowski 1951, 1952, and Wingstrand 1951a and b). The central fibre layer consists of the axons of the nuclei supraopticus and paraventricularis, which terminate at all levels in the stalk and infundibular process of the posterior lobe. Only this layer stains selectively with chrome-alum-hæmatoxylin, the outer glandular layer, which is in contact with the pars tuberalis and the primary capillary loops of the pituitary-portal vessels, being apparently devoid of the Gomori-positive granules which mark the flow of the posterior-lobe hormones. In some mammalian species the outer layer is reduced in thickness, and, according to Hanström (1953), is partly represented by tissue of corresponding histological appearance around the capillaries deeper in the eminentia. This occurs in certain Hyracoidea, Artiodactyla and Primates—including the orang-utan.

Gomori-positive granules have been demonstrated in the vessels of the posterior lobe (Hanström 1952a and b), but under normal conditions they apparently do not occur in those of the anterior lobe.²² Again, the very fine fibres which have been diagnosed as nerve-fibres in the outer "glandular" zone have not been proved—at any rate in mammals²³—to come from the nucleus tuberis infundibulu-

22. According to Stutinsky (1951a), when the stalk is cut and the normal flow of the granules affected, they may pile up in the outer "glandular" zone of the median eminence, and may even get into the primary capillary loops, as well as into the third ventricle.

23. Wingstrand has provided convincing histological evidence that they do so in birds. The nucleus tuberis infundibularis, which is said to be "Gomori-negative," is distinct from the nucleus mamilllo-infundibularis, which is said to be "Gomori-positive" (Smith 1951). In man both are described as forming part of the "lateral hypothalamic area" (Clark 1936).

laris, and opposing views are held about their nature (cf. Nowakowski 1952, Hanström 1952b). Indeed, Palay (1953) failed to confirm that they were present at all in the rhesus monkey. He believes that the only nerve-fibres in the median eminence are those of the middle zone which, while they may approach the radicles of the pituitary-portal veins, never establish contact with them. Palay's view is that the vessels and nerves of the median eminence are similarly arranged in man, the cat, rabbit, guineapig, and rat (but not in the mouse), where fibres have been described as terminating on the vessels.²⁴

Histological study thus provides no indication that "Gomori substance" normally can or does enter the pars distalis, and it cannot, therefore, be taken to support the view that posterior-lobe hormone activates the anterior lobe. If there is a hypothalamic chemo-transmitter, which controls this lobe, its source would, by exclusion, have to be the very fine "nerve-fibres" of the outer glandular zone—in those species where they exist. There is no cytochemical evidence that this is so,²⁵ nor has a substance specific to this region alone been recognised pharmacologically. In short, it is not quite clear on what grounds, other than the presence of interstitial colloid, the outer zone of the median eminence has been called "glandular"—unless it merits this name because of its close anatomical association with the pars tuberalis of the adenohypophysis.

Conclusion

We can only conclude, therefore, that if the posterior-lobe hormones control the varied and varying functions of the anterior, this is not yet apparent from the evidence before us. In drawing our parallel between the present and the past, we must rest satisfied for the moment with the fact that modern science has not only established that the infundibular region of the brain does produce a vital essence, but that it has also apparently discovered the pathway by which this essence moves down the pituitary stalk into the posterior lobe of the gland. Swedenborg's "genuine or fresh" infundibular spirit and Luschka's fine tubes have thus taken real shape and meaning. So too, have the axial-stalk vessels discovered by Lieutaud two hundred years ago. But what principle, if any, these convey, and how the "reflex" responses of the anterior lobe are controlled, are two problems which still challenge our curiosity—as they have done for many years past.

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- 24. Both Wingstrand and Benoit refer to nerve-fibres forming loops in the outer glandular zone, and approaching the primary capillary net of the portal vessels. Wingstrand, however, has never observed the fibres terminating on the vessels.
- 25. As already noted, an interstitial—as opposed to intra-axonal—colloid is present in the external glandular layer, but whether this is evidence of "secretion" is debatable.

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TRIGEMINAL NEURALGIA PATHOLOGY AND TREATMENT

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PAINS in the face may result from lesions that are demonstrable by simple examination, by special investigation, or by dissection at necropsy. On the other hand, there are varieties of continuous or periodic facial pain for which no cause can be found either in life or after death.

Trigeminal neuralgia (Fothergill's disease, prosopalgia, facial tic, or tic dououreux) is one of those maladies for which no definite pathological basis has been discovered. In diseases where a physical lesion exists, removal of the lesion usually gives relief; but the problem in conditions such as trigeminal neuralgia is entirely different, and surgical treatment consists in division at some peripheral or central level of the pain pathways concerned.

Characteristics of the Pain

The essential feature of major trigeminal neuralgia is that the pain is spasmodic and not continuous. It occurs in lightning flashes which usually are only momentary but occasionally last for as long as a few minutes. The pain is confined to the distribution of the trigeminal nerve. When the facial muscles on the affected side go into spasm during an attack, this spasm is more in the nature of "flickering" than of true contraction. In severe cases the pain may recur many times a day. Commonly there are periods of freedom, but eventual recurrence is usual—possibly after an interval of years.

The pain is initiated by any slight movement of the face, as in chewing or speaking; and a light touch—say to the side of the nose—may bring on an attack. In an attack the patient remains completely still, often holding a hand near his face, not touching it but as if for protection against any further stimulus. This unwillingness to touch the painful area is of great diagnostic significance, since in other types of facial pain the patient usually rubs his face in an attempt to get relief. The pain commonly originates from a localised area, known as the trigger-point. At the end of an attack the patient is completely free from pain, although there is always great apprehension of a further attack.

Neuropathology

No definite pathological change in the trigeminal pathways or the contiguous tissues has been found to account for the pain of trigeminal neuralgia. Organic lesions, such as acoustic neuromata and aneurysms, can of course cause pain indistinguishable from that of trigeminal neuralgia but in most cases no such lesion is present.

Harris (1926, 1937) suggested that the pain of trigeminal neuralgia is of peripheral origin, because in an untreated case there is never any objective loss of sensation or evidence of trophic disturbance. He argued that if the pain were central in origin, peripheral nerve block

or neurectomy would be unlikely to give relief. In many of his cases the pain had followed difficult dental manipulations; and, because trigeminal neuralgia usually affects the lower two divisions of the trigeminal nerve (that is, the divisions that supply the teeth), he argued that the pain might be due to septic filamentous neuritis secondary to dental sepsis. He drew attention to the prevalence of right-sided neuralgia, and suggested this was possibly due to the fact that, in the right-handed majority, the teeth in the left side of the mouth were more thoroughly brushed than those on the right, with the result that sepsis was more frequent on the right side.

Dandy (1934), from his experience of operations on the cerebellopontine angle, believed that trigeminal neuralgia was due, in many cases, to irritation of the nerve by a tumour, by an aneurysm, or by loops of the branches of the basilar artery, particularly the superior cerebellar artery.

Frazier et al. (1937) concluded that the thalamocortical mechanisms were at fault and that the severe and overwhelming quality of the pain in trigeminal neuralgia was due to misinterpretation and over-estimation at the higher neural centres of a normal peripheral message. To substantiate this hypothesis, Lewy and Grant (1938) described 6 cases of trigeminal neuralgia in which necropsy revealed gross structural changes in the thalamocortical connections. They pointed out that trigeminal neuralgia arises largely at an age when degeneration of the brain is most likely; they further emphasised the absence of structural changes in the peripheral mechanisms, though Lewy and Frazier (1935) thought that the threshold for pain in the peripheral mechanisms was below normal. The high incidence of trigeminal neuralgia in patients with disseminated sclerosis may seem to support this hypothesis. On the other hand, most workers argue that cerebral degenerative changes, as judged by the clinical findings, are rare in trigeminal neuralgia.

In 5 cases of trigeminal neuralgia in which I did air-encephalography, there was no evidence of ventricular distortion or enlargement to suggest a thalamocortical lesion. In most cases there is not a single neurological sign to point to the presence of an extrapyramidal or pyramidal lesion. Moreover, on the hypothesis of imbalance of the thalamocortical mechanisms, it is difficult to explain the remissions that occur so commonly. Possibly, however, a neural message could be misinterpreted centrally without any evident structural change being present.

Wyburn-Mason (1953) implied that, as a result of distortion of the neural pathways of the first and second cervical nerve-roots, the patterns of the pain plexuses of the skin of the face became abnormal. Weddell and his associates, in a series of important papers (Weddell 1941, Weddell and Sinclair 1947, Weddell et al. 1948), have shown that in the skin pain fibres from several sources are interwoven, and only when this complex structure is intact is a pin-prick registered in the normal way. When, because of nerve damage, the normal neural pattern in the skin is replaced by a simpler mesh-work, a pin-prick is registered protopathically. This possibility of alteration in the pain meshworks of the skin interested me many years ago, and in 3 instances the trigger-points of the skin were excised and were examined by the late Prof. A. F. Bernard Shaw; on no occasion were changes found in the pattern of the skin-pain plexuses.

Another possibility is that the pain may arise from excessive spasm or dilatation of a blood-vessel, the impulses merely being transmitted by the trigeminal pathways.

PERSONAL OBSERVATIONS

Of 250 personal cases 176 were treated by operation: the trigeminal pathways were approached extradurally

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TABLE I—DISTRIBUTION BY AGE AND SEX OF 250 CASES OF TRIGEMINAL NEURALGIA

Age (years)	No. of cases	
	Male	Female
20-29	1	1
30-39	6	12
40-49	15	17
50-59	24	29
60-69	36	60
70-79	11	34
80-89	—	3
90-	—	1
—	93	157

via the middle fossa. Although the middle meningeal artery varied in size, neither the artery itself nor its larger branches were ever found to be in such a position that they might beat against the third or second divisions of the nerve or against the ganglion. On one occasion only was a large artery discovered passing through the foramen ovale with the third division of the nerve. Usually large veins run along the margins of the divisions as they enter the ganglion; and, though these are often found congested at operation, it is doubtful whether they ever produce pain. On no occasion was there evidence of an angioma, either about the ganglion itself or along the territories of the second and third divisions. Sometimes the dura mater was thick, sometimes thin; sometimes it stripped easily from the bone, and sometimes it was densely adherent to the periphery of the middle fossa. Sometimes it would strip easily from the second and third divisions and from the ganglion itself; sometimes it was so adherent it had to be reflected by means of sharp dissection. In my opinion, it is not in the dural variations that the source of trigeminal neuralgia will be found. Obvious narrowing of the foramen ovale or foramen rotundum and constriction of the relative divisions was never found.

Thus no constant change was discovered that might account for trigeminal neuralgia in this series.

Histological Findings

Lengths of the third and second divisions, pieces of the ganglion, and lengths of the posterior root were removed and sectioned, care being taken to avoid artefacts. Of 15 specimens none was found to show any lesion. These examinations were also carried out by Professor Shaw.

Pieces of skin forming the trigger-points of the pain at the corner of the nose were excised as an ellipse in 3 patients. The pain plexuses in the skin were examined by the method of Weddell (1941); in none of these 3 instances was there any obvious alteration in the pain-plexus pattern, but Professor Shaw and I considered that there was an increase in fibrous tissue. As large nerve-roots pass, for example, along or through muscle-planes, they are surrounded by the equivalent of a synovial tunnel, which ensures that the nerve can slide freely without traction or distortion whenever the limb is made to move. Perineural adhesions resulting from inflammation will prevent the free slide of a large nerve along a neighbouring tissue and give rise to perineuritis

TABLE II—SITE OF PAIN IN 250 CASES OF TRIGEMINAL NEURALGIA, ACCORDING TO AFFECTED DIVISION OF FIFTH CRANIAL NERVE

Division affected	No. of cases	Division affected	No. of cases
<i>Unilateral :</i>			
1st .. .	5	3rd rt and 2nd and 3rd lt..	1
2nd .. .	54	2nd lt and 3rd rt .. .	1
3rd .. .	38	2nd lt and rt .. .	1
1st and 2nd .. .	34	3rd lt and 2nd and 3rd rt .. .	1
2nd and 3rd .. .	80	2nd lt and 2nd and 3rd rt	1
All .. .	34	—	—
—	245	—	5

and to pain. My suggestion is that a similar condition occurs about the peripheral filaments of the nerves, producing what could be termed perifilamentous adhesive neuritis. This differs from Harris's original hypothesis only in that he regarded the peripheral lesion as a mild interstitial neuritis. In my opinion, most of the evidence favours the conclusion that the lesion is essentially peripheral.

These histological experiments should be repeated, because trigeminal neuralgia can perhaps best be explained on Weddell's hypothesis.

Material

The age and sex distribution of 250 consecutive personal cases of trigeminal neuralgia is shown in table I. In 82 cases the left side was involved and in 163 cases the right side, while in 5 involvement was bilateral. The sites of the pain are shown in table II.

The disorder had been present for up to 3 months in 13 cases, for 4-6 months in 15 cases, for 7-12 months in 32 cases, for 13 months to 5 years in 95 cases, for 6-10 years in 39 cases, for 11-20 years in 25 cases, for 21-30 years in 4 cases, and for 31-40 years in 1 case; in 26 cases the duration was not recorded. The shortest history was 1 week, and the longest over 40 years.

Blood-pressure

In 64 cases there was no record of the blood-pressure. Of the remaining 186 cases, there was hypertension in 96 (51.6%) (see table III). Patients were classified as

TABLE III—DISTRIBUTION BY AGE AND SEX OF 96 CASES OF HYPERTENSION IN PATIENTS WITH TRIGEMINAL NEURALGIA

Age (years)	No. of cases	
	Male	Female
20-29	1	1
30-39	—	—
40-49	5	4
50-59	6	14
60-69	17	25
70-79	4	18
80-89	—	1
90-	—	—
—	33	63

hypertensive if the diastolic blood-pressure was 100 mm. Hg or more (see table III). It is very doubtful whether hypertension *per se* is a significant factor in the production of trigeminal neuralgia; many people above the age of 60 have hypertension without suffering also from trigeminal neuralgia.

Surgical Relief

Since trigeminal neuralgia is not caused by any lesion that is otherwise injurious to the patient, the only object of operation is to relieve pain. Moreover, the pain does not become intractable or incurable if surgical treatment is withheld or delayed. After root section regeneration of the trigeminal pathways is impossible, and after destruction of the ganglion by alcohol it is unlikely; so relief obtained by root section or alcohol ganglion block is likely to be permanent. On the other hand, resection or alcohol block of the trigeminal pathways distal to the ganglion may give only temporary relief.

Division of the trigeminal pathways causes numbness in the territory of the face concerned, and numbness is a positive sensation carrying with it a disagreeable feeling of cold, stiffness, and swelling. Should the pain be unrelieved by destruction of a trigeminal pathway, the patient's burden is increased by this added disagreeable sensation. Therefore unless there is a definite probability that trigeminal section will result in relief, this manoeuvre should not be undertaken.

I believe that it is wrong, in the interests of permanent cure, to render the whole of the face numb when only

TABLE IV—TREATMENT OF 250 CASES OF TRIGEMINAL NEURALGIA

Initial treatment	No. of cases	Subsequent treatment
<i>Injection:</i>		
Gasserian ganglion	47	—
2nd division	1	
3rd division	6	
3rd division and infra-orbital nerve	1	
Infra-orbital nerve	17	Ganglion injection in 6 cases
Supra-orbital nerve	1	
Infra-orbital and supra-orbital nerves	1	
Total	74	
<i>Operation:</i>		
Complete root section	15	Complete section in 3 root cases
Fractional root section	113	—
Intracranial 2nd-division neurectomy	38	Complete section in 1 root case
Avulsion of supra-orbital nerve	1	—
Avulsion of infra-orbital nerve	9	—
Total	176	

one area is painful; in my experience, it is not true that a patient's morale is undermined by fear of a possible return of the pain with consequent need for further operation. On the contrary, I have found that most patients prefer to have as little done as will give immediate relief from pain for a reasonable length of time, and that if further operation does become necessary they show no undue apprehension.

In this series, of the 250 patients, 34 had pain in all divisions and 172 had no pain in division 1 (see table II). Among these 172 the disorder had been present for several years, and therefore spread of pain to division 1 is by no means inevitable even after a long period. As table IV shows, complete root section or ganglion block is not necessarily inevitable following incomplete operations, such as fractional root section, peripheral neurectomy, or peripheral nerve block.

Controlled fractional block of the ganglion is not technically possible by injection; so if the ganglion is injected in all cases, whether or not the first division is affected, the danger of paralytic interstitial keratitis must be greater than with fractional root section, by which the ophthalmic fibres can be spared in suitable cases.

Where the first division is affected, the advantage of ganglion injection over complete root section is that it avoids the danger of facial paralysis. Regarding danger to life, I have been operating on the trigeminal pathways by the extradural middle fossa approach for more than twenty years without a single death. Operation is very much easier for the patient, because it eliminates the usually very distressing experience of having a needle plunged into the face. In this series there is no doubt that the patients treated by operation were much more grateful than those treated by injection.

The advantages of fractional root section in suitable cases are outstanding: the cornea can be left sensitive, the numb area confined to the affected divisions, and the motor nerve spared. In this series there was no instance of permanent facial paralysis after complete or fractional root section. In my opinion, fractional root section is the method of choice in all cases where the first division is not affected. Where the first division is affected, alcohol injection and root section are equally efficient. Root section is a precise procedure, and I have never yet failed to section the root when this has been necessary; even the most expert, however, can fail to introduce a needle into the ganglion.

There is now a tendency in some centres to approach the posterior root via the middle fossa intradurally. The advantage of this method is the avoidance of facial paralysis and of bleeding into the middle ear. The intradural approach, though now safe in most hands,

must, by its very nature, carry a greater risk to life than the extradural approach. The actual section of the root fibres is equally precise by either method.

Intracranial extradural neurectomy of the second division is a most valuable procedure in suitable cases. By this means, the territory of only the maxillary division of the face need be denervated when the pain is confined to this area. Occasionally, when doing a fractional root section I also do neurectomy of the second division when it is essential that no fibres of this division be spared but no fibres of the first division sacrificed. With neurectomy of the second division alone, there is no danger of paralytic interstitial keratitis or of facial paralysis.

Extracranial alcohol blocks of the second and third divisions are safe and produce local denervation only. Their chief disadvantage is that the relief is temporary, lasting at most two or three years.

Avulsion of the supra-orbital or infra-orbital nerve is not a serious undertaking and is worth trying in old people when the trigger-point seems to be in one of these areas. The relief gained, however, is merely temporary.

Although procaine injection into the gasserian ganglion has not been applied in this series, it will often bring to an end a bout of trigeminal neuralgia and provide a period of remission.

Lastly, I would emphasise again that where the ophthalmic division is unaffected, fractional root section by the middle fossa extradural approach is, in my opinion, the treatment of choice.

Summary

A series of 250 cases of trigeminal neuralgia is analysed.

On the basis of histological studies it is suggested that the lesion is essentially peripheral, consisting in "perifilamentous adhesive neuritis."

Relief of the pain by surgical treatment is discussed.

I should like to take this opportunity of thanking Prof. F. J. Nattrass, Dr. W. Ritchie Russell, and Dr. R. Whitehead for their helpful criticisms in the preparation of this paper.

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ANÆSTHETIC EXPLOSIONS PREVENTION BY WITHDRAWAL METHOD

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THE causes of anæsthetic explosions and the current methods for their prevention in Great Britain have been described by Lowe (1950) and Hadfield (1952). In the U.S.A. more elaborate precautions are taken owing to the greater danger of static sparks and the use of ethylene. Electrostatic hazards have been discussed by Bulgin et al. (1949), Magee and Bracken (1952), and Roberts and Hewer (1953).

Whenever explosive gases or vapours are in use, there is always a risk of explosion, be it remote, since the possibility of their being ignited by a static spark cannot be entirely ruled out. There are occasions when the use of an explosive agent (diethyl ether in particular) is highly desirable in the presence of a known source of ignition—e.g., diathermy—and many anæsthetists finding themselves in this position have their own methods of minimising the risk of explosion.

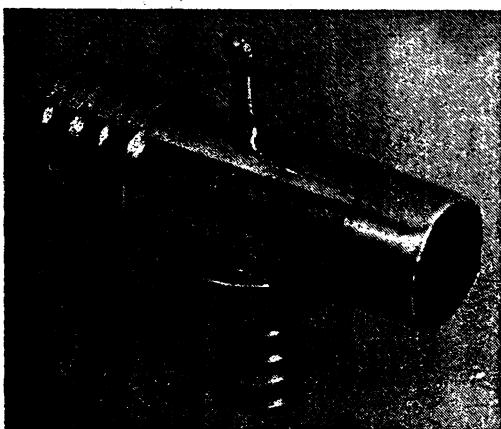


Fig. 1.—T-junction with tap.

A serious type of anaesthetic explosion, often fatal to the patient, is that which happens when a collection of gases in the room is ignited at some distance away from the anaesthetic apparatus; a flame travels across the room and "lights back" through the leak-point in the apparatus; the gases inside the apparatus and the patient's air-passages then explode. The method about to be described prevents this type of explosion.

Withdrawal Method

In the ordinary way explosive gas mixtures are allowed to escape through expiratory valves or other leak-points from the anaesthetic apparatus into the atmosphere of the room in which the anaesthetic is being administered.

By the withdrawal method the gases are not allowed to enter the atmosphere of the room; they are withdrawn out of the room through a pipe from the apparatus. This is achieved quite simply by the use of a T-junction, which is plugged into the anaesthetic circuit, the gases being led away from the junction through a length of rubber tubing ("withdrawal tubing") connected to it. The withdrawal tubing leads away through a door or a window or through the floor (see below) to a safe place.

T-junction (fig. 1).—The horizontal limb has a male connection at one end and a female connection at the other end; it plugs into, and makes continuity with, any part of an anaesthetic circuit with standard connections. The vertical limb is a tube of $\frac{1}{2}$ in. internal diameter and can be shut off from the horizontal limb



Fig. 2.—T-junction in use with semi-closed ("semi-T-piece") anaesthesia. Valve unit could be removed altogether, if desired.

by a tap. $\frac{1}{2}$ in. rubber tubing is connected to the vertical limb and may be of any length, since only the very slightest resistance (equal to a pressure of less than 0.5 cm. of water) is offered to the escape of gases along this tubing.

Clinical Use

"SEMI-CLOSED" CIRCUIT

Fig. 2 shows the method in use with a continuous-flow semi-closed circuit. The T-junction may be interposed between the valve-mount and the endotracheal adapter, or angle-mount to face-piece. When the tap of the T-junction is open, gases will pass along the withdrawal tubing rather than through the expiratory valve, there being more resistance in the latter; the reservoir bag collapses until almost empty.

If positive pressure is required for artificial respiration, the expiratory valve is first screwed down and the tap

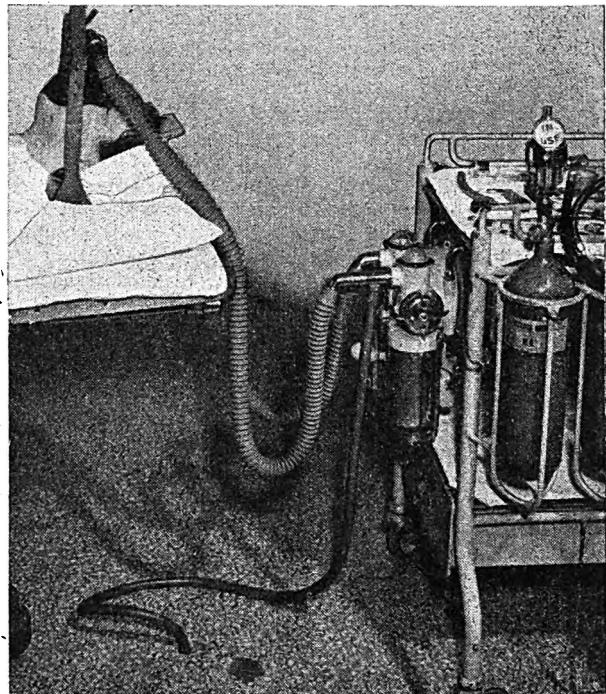


Fig. 3.—Withdrawal method in use with circle absorber, explosive gases being led away through floor.

adjusted, in much the same way as an expiratory valve, to increase the pressure in the circuit.

If the patient is breathing spontaneously, an anaesthetic administered in this way is a cross between a semi-closed circuit and my T-piece technique (Bullough 1952). I call this "semi-T-piece anaesthesia."

The flow-rates of gases, &c., are exactly as for semi-closed anaesthesia or my T-piece technique.

CARBON-DIOXIDE ABSORPTION CIRCUITS

"Closed Circle"

When a "closed" circuit is in use with "badal" oxygen, plus ether or cyclopropane, and the apparatus is gastight, it will usually be found that the reservoir bag becomes distended periodically and some gases must be allowed to escape. This is because, almost invariably, for various reasons, more gases are run into the circuit than the patient can absorb. Conversely, if the bag does not become distended, it is highly probable that there is a considerable leak in the circuit.

Clearly the "closed" circuit cannot be relied on entirely to eliminate ignition of gases outside the apparatus.

First, all expiratory valves, &c., are securely shut off; the T-junction is plugged into the expiratory port

of the absorption unit (fig. 3) and the hosing connected to the T-junction; the tap is turned off. Whenever the reservoir bag becomes distended the tap is opened, the bag is squeezed until half-empty, and the tap is closed again. The excess gases pass away along the withdrawal tubing out of the room.

Circle Absorption with Intentional Leak

This is a common technique, nitrous oxide and oxygen being the basic mixture, with total gas-flows of 1-5 litres a minute. If ether or cyclopropane is added, the administration may be managed in the same way as for a "closed" circuit when low gas-flows are used. If flows of more than 3 litres a minute are used, the tap on the T-junction may be adjusted to allow a continuous leak at any desired pressure.

If the patient is breathing spontaneously and the junction is placed between the patient and the absorber (fig. 3), some "rebreathing" can take place along the expiratory hosing. Owing to the design of the junction, however, this is very slight, provided the gravity valves are working freely. In addition, a high flow of fresh gases prevents any appreciable accumulation of carbon dioxide. "Rebreathing" will not take place if artificial respiration is in progress, or if the junction is placed between the absorber and the bag, as is easily arranged on other types of apparatus, or when a bag is used in place of the concertina on the type illustrated.

To-and-fro Absorption

Figs. 4 and 5 show how this method may be used during to-and-fro absorption. A small tap (fig. 4), formerly used for running gases into this type of bag, is now used to lead gases away. Alternatively, a T-junction (fig. 5), with unions of a suitable size, is interposed between the bag and the canister.

Disposal of Gases

The gases may be led away through any length of withdrawal tubing through a door or a window, to a safe place, preferably out of human reach, where they will not be ignited by cigarettes, &c.

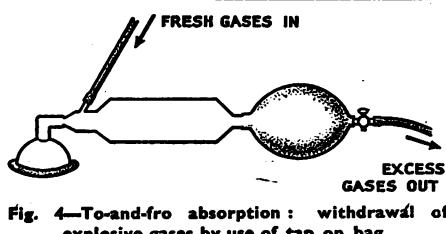


Fig. 4—To-and-fro absorption : withdrawal of explosive gases by use of tap on bag.

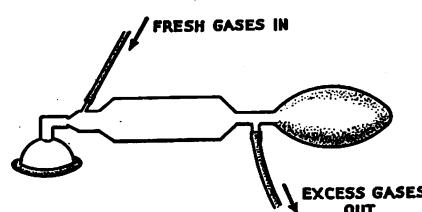


Fig. 5—To-and-fro absorption : withdrawal of explosive gases by use of T-junction.

A more convenient method is to lead the gases through a hole in the floor placed near the head of the operating-table (fig. 3). This has been done at hospitals in the Dartford group by installing a metal pipe which leads through the floor to the outer wall of the building, and up this wall out of human reach (fig. 6). (Back-pressure in the pipe is negligible, less than 1 cm. of water.)

A perforated box or cage surrounds the end of the pipe as an additional safeguard against cigarette ends, and a warning notice is placed on the cage. It is hoped to find a gauze, like Davy gauze, which will prevent ignition and "lighting back" of emerging gases.

Discussion

The safety of this method depends on the anaesthetic apparatus, and the junction between apparatus and patient, being leakproof at the pressure at which the anaesthetic is being administered.

A great deal of the anaesthetic apparatus at present available in this country was designed before the risk of explosion had become what it is today. Electrical apparatus is now in almost constant use ; techniques involving artificial respiration, and therefore high pressure in the apparatus, are also the rule rather than the exception in many operating-theatres.

In the apparatus illustrated in fig. 3 there are a dozen places where leakage can take place, excluding the rubber parts. Such an apparatus is difficult to keep gastight, and one is inevitably led to the conclusion that new apparatus should be designed to remain gastight under present methods of usage.

A gastight junction to the patient can fortunately be achieved with a cuffed endotracheal tube. If rupture of this cuff would be highly dangerous, a second cuff could be applied to the tube. Face-masks with inflatable rims are available which will form a gastight junction to moderate pressure in a high percentage of patients.

During artificial ventilation of the lungs, pressures in the circuit of 20 cm. of water are common and pressures of 40 cm. of water or more are not uncommon ; in some circumstances far higher pressures are used for short periods. Clearly leakage from the circuit is far more likely to take place during artificial respiration than when the patient breathes spontaneously.

When the patient is breathing spontaneously, the pressure inside any circuit need not rise above 4 cm. of water. When the semi-T-piece method is used, the pressure will be less than 1 cm. of water, at which pressure leakage is quite easily prevented in present-day apparatus. I consider that this technique can be safely used with explosive anaesthetics in the same room as a known source of ignition, and have so used it for the last three years.

If this method is adopted as an additional safeguard against anaesthetic explosions, I suggest that, when pipes are laid to carry anaesthetic gases into an operating-theatre, an additional pipe be laid to carry them out again.

Quite apart from preventing ignition of anaesthetic gases, this method relieves all operating-theatre personnel from the necessity of breathing noxious anaesthetic gases and vapours emanating from the anaesthetic machine.

Summary

A simple method of preventing ignition of anaesthetic gas mixtures in operating-theatres, &c., is described : the withdrawal method.

The gases are prevented from entering the atmosphere of the theatre.

A T-junction, with a tap, is plugged into an anaesthetic circuit ; a pipe attached to this conveys gases from the theatre to a safe place outside.

There is a need for anaesthetic apparatus of a new design, easily kept gastight to the pressure used in

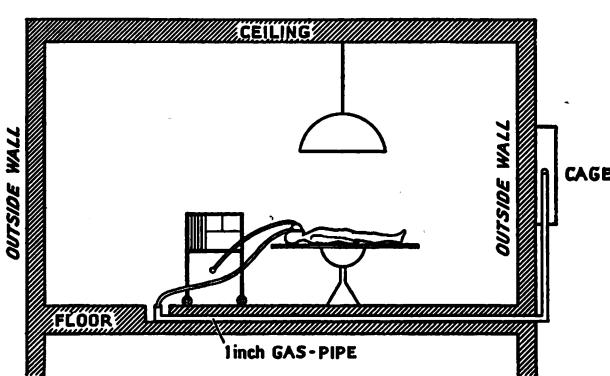


Fig. 6—Disposal of explosive gases through pipe under floor to outside of building.

clinical anaesthesia today. Only when the patient is breathing spontaneously can leakage from apparatus at present available be easily prevented.

Operating-theatre personnel are relieved from breathing anaesthetic gases by the withdrawal method.

I wish to thank Dr. M. Mitman, Dr. R. G. Henderson, C.B.E., and Dr. T. S. Cochrane, superintendents of the hospitals in the Dartford Group, for their interest in this method and for its installation in the operating-theatres in the Group; the hospital engineers for installing the apparatus to my specification; the British Oxygen Company for assistance in developing the method and for making the T-junctions; and Messrs. Woods & Porter, West Hill, Dartford, for the photographs. The T-junction may be obtained from Messrs. Charles King Ltd.

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CLINICAL TESTS FOR KETONURIA

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ALTHOUGH the clinical tests for urinary ketones are essentially qualitative, it is customary for clinicians to give them a quantitative significance based on certain characteristics, such as the intensity of the colour reaction and the rapidity of development of a colour, or by comparing the results of tests of different sensitivities. The usual tests vary so much in technique and interpretation that it is difficult to compare the results of different workers, especially when + symbols are used.

Friedemann et al. (1946) have reviewed the many ways in which the nitroprusside reaction may be used for detecting ketone bodies, and have drawn attention to the variety of methods and sensitivities reported.

Some workers state that the colour given by the nitroprusside reaction is due mainly to the presence of acetone (King 1951, Stanley 1943), whereas others state that it is due to both acetone and aceto-acetic acid (Harrison 1947). All workers agree that β -hydroxybutyric acid gives no reaction with sodium nitroprusside.

Few textbooks adequately present either Rothera's (1908) or Gerhardt's (1865) test.

Describing the Rothera test Todd et al. (1953), Lawrence (1950), and Harrison (1947) do not indicate that the urine must be saturated with ammonium sulphate to give the maximal sensitivity.

Bayliss (1950) adds 2 or 3 drops of a "concentrated" sodium nitroprusside solution, whereas King (1951) adds 8-10 drops of a 0.25% solution in 1% nitric acid.

The time allowed for the colour reaction to develop before its intensity is read varies from 1 to 30 minutes (Fearon 1946, Haler 1951, Lawrence 1950), or is not mentioned at all (Carter and Thompson 1953, Hawk et al. 1947).

Descriptions of Gerhardt's ferric-chloride test are also at variance. The strength and quantity of ferric-chloride solution used is often omitted. No workers agree about the time of boiling the urine to distinguish the colour given by aceto-acetic acid from that given by non-ketone substances, only one of them emphasising that the boiling should be prolonged (Hutchison and Hunter 1951).

* In receipt of a scholarship grant from the Royal Free Hospital Endowment Fund.

It is therefore not surprising that clinicians do not usually relate the results of the tests with actual concentrations of ketone bodies present in the urine. It follows that the clinical tests for urinary ketones are of limited value in following the progress of a patient in ketosis. We report here studies of the Rothera nitroprusside and Gerhardt ferric-chloride tests, and include observations on a recently developed "nitroprusside tablet." † The object is to assess the significance of these tests so as to provide a more precise interpretation than has been possible hitherto. The relative merits of the tests for routine use were also studied.

Methods

Since the urine of patients with ketosis was not always available when required for study, it was necessary to add ketone bodies to normal urine. Preliminary experiments indicated that urines to which known concentrations of acetone and aceto-acetic acid had been added gave reactions of the same colour and intensity as those given by similar concentrations found in the urine of ketotic diabetic patients. To determine the relative proportions of acetone and aceto-acetic acid in the urine of ketotic patients, estimations of the individual ketone bodies were made by the method of Thin and Robertson (1952) on specimens of urine giving positive results to Rothera tests.

Stock solutions were made from aceto-acetic acid prepared by the method of T. E. Friedemann (personal communication) and from 'Analal' acetone and the concentrations determined (Thin and Robertson 1952). These solutions were added to normal urine to give concentrations of aceto-acetic acid ranging from 0 to 2000 mg. per 100 ml. in steps of 50 mg. per 100 ml. Further dilutions were made when necessary. The three tests studied were applied to these specimens of urine according to the methods described below. After preliminary trials each test was finally repeated twenty times on different occasions. In the Gerhardt ferric-chloride test the colour due to aceto-acetic acid is distinguished from that given by excreted products of certain drugs by boiling the urine and repeating the test. To establish the minimal time of boiling required to remove all the aceto-acetic acid present, 20 ml. aliquots of urine containing 25, 100, and 300 mg. of aceto-acetic acid per 100 ml. were boiled vigorously in a 50-ml. beaker for 5, 10, 15, and 20 minutes respectively, and the test was repeated after cooling and adjusting the volume to 20 ml.

TECHNIQUE OF TESTS

Rothera's Test

Of the various techniques reported that recommended by Friedemann et al. (1946) was found to be the most satisfactory. About 5 ml. of fresh urine is saturated with ammonium sulphate, and 10 drops of 2% sodium nitroprusside solution is added. The solution is well mixed, and 10 drops of concentrated ammonia (sp. gr. 0.880) is added. The purple colour due to the presence of acetone or of aceto-acetic acid is allowed to develop for 15 minutes. The reasons for selecting this particular technique are as follows :

(1) The urine must be saturated with ammonium sulphate to give the maximal sensitivity and to reduce the interference of non-ketone substances.

(2) A minimal quantity of sodium nitroprusside is used so as not to confuse a trace reaction with a colour due to excess reagent.

(3) The colour due to aceto-acetic acid reaches a maximal intensity in about 10 minutes, and that due to acetone in 20-30 minutes. After this time the colour begins to fade. Also, several sulphhydryl compounds give red colours which develop in a few seconds but fade within 3 or 4 minutes. By choosing a time of 15 minutes false positives are avoided and a maximal colour is obtained.

† 'Acetest Reagent Tablet' manufactured by Miles Laboratories Ltd. (distributors Don S. Monand Ltd.).

Gerhardt's Test

Ferric-chloride solution 10% is added drop by drop to about 2 ml. of fresh urine. A precipitate due to phosphates usually forms but redissolves on further addition of ferric chloride. A reddish-brown colour may indicate the presence of aceto-acetic acid. If such a colour does develop, the urine must be boiled in an open vessel—e.g., a beaker—for at least 15 minutes to decompose the aceto-acetic acid to acetone, most of which boils off. If the boiled and cooled urine still gives a reaction similar to that of the unboiled urine, it is due to substances other than aceto-acetic acid.

TABLE I—CONCENTRATION OF KETONE BODIES IN URINE OF 21 KETOTIC DIABETIC PATIENTS

Acetone (mg. per 100 ml.)	Aceto-acetic acid (mg. per 100 ml.)	β -Hydroxy- butyric acid (mg. per 100 ml.)	Total ketones (mg. per 100 ml.)	Ratio of aceto-acetic acid to acetone
5.9	62.3	188.2	256.4	10.1
13.3	95.6	198.6	307.5	7.2
13.8	120.0	244.1	377.9	8.7
13.7	136.8	157.2	307.7	10.0
49.0	94.8	435.7	579.5	1.9
13.2	106.4	173.0	292.6	8.1
13.4	64.9	156.6	234.9	4.8
4.1	17.3	179.0	200.4	4.2
2.2	16.0	45.5	83.7	7.3
2.8	24.1	52.8	79.7	8.6
2.4	30.9	75.5	108.8	12.9
1.7	15.8	57.3	74.8	9.3
2.0	19.8	75.7	97.5	9.9
3.3	33.2	88.8	125.3	10.0
4.4	66.2	110.6	181.2	15.0
1.8	19.1	34.8	55.7	10.1
1.3	13.0	37.5	51.8	10.0
1.2	7.2	14.0	22.4	6.0
2.3	40.0	49.5	91.8	17.4
2.1	30.9	62.7	97.5	14.7
0.9	9.5	87.0	97.4	10.5

Mean ratio of aceto-acetic acid to acetone 9.4 ± 3.6 .

Nitroprusside-tablet Method

This tablet contains sodium nitroprusside, glycine, disodium phosphate, and lactose. The technique adopted for this test is that described by the manufacturers. A tablet is placed on a clean white surface, and one drop of urine is allowed to fall gently on to it. At the end of 30 seconds the purple colour which develops when the test is positive is compared with the three shades of colour on the scale provided with the tablets. When the test is negative, the tablet remains unchanged in colour except for a slight creaminess due to the colour of the urine. In common with all nitroprusside reactions for ketone bodies the colour will continue to develop for several minutes. For this reason the colour scale is designed for use at the end of 30 seconds.

TABLE II—SENSITIVITIES OF ROTHERA TEST TO ACETONE AND ACETO-ACETIC ACID ADDED SEPARATELY TO NORMAL URINE

Result	Acetone (mg. per 100 ml.)	Aceto-acetic acid (mg. per 100 ml.)
Trace	25	1
+	100	5
++	200	10
+++	300	15
++++	400	20

Results

The levels of the different ketone bodies occurring in the urine of a series of ketotic diabetic patients whose ketosis ranged in severity from mild to precomatose are presented in table I. The levels of β -hydroxybutyric acid are included, although this ketone cannot be detected by the clinical tests for ketonuria.

A deep purple, through which it was only just possible to see transmitted light, was given by a solution of 400 mg. of acetone per 100 ml. in urine with the Rothera test. This depth of colour was called ++++. A faint purple was given by 25 mg. of acetone per 100 ml. This

TABLE III—SENSITIVITY OF GERHARDT TEST TO ACETO-ACETIC ACID ADDED TO NORMAL URINE

Result	Aceto-acetic acid (mg. per 100 ml.)
Trace	25
+	50
++	100
+++	150
++++	200

was called a "trace." +, ++, and +++; reactions were assigned to proportionate levels between these extremes.

Solutions of aceto-acetic acid were found which gave colour reactions corresponding to the intensities of colour given by the acetone solutions mentioned above. The concentrations at each level for both acetone and aceto-acetic acid are shown in table II.

In determining the sensitivity of Gerhardt's ferric-chloride test the use of a standard solution of aceto-acetic acid was found to be undesirable, because its preparation was lengthy and its stability poor. It was therefore necessary to prepare an arbitrary standard which could be easily made up and did not deteriorate quickly. A solution of ethyl acetone dicarboxylate in urine gave a colour with ferric chloride which closely matched that given by the addition of ferric chloride to urine containing aceto-acetic acid. A 1% solution of ethyl acetone dicarboxylate in normal urine gave, on the addition of ferric chloride, a colour which corresponded to a strongly positive Gerhardt test such as is found in severe ketosis. This colour was called +++, and on analysis was found to be equivalent to about 200 mg. of aceto-acetic acid per 100 ml. The lowest level at which a definite colour could be clearly detected without the aid of a control tube was about 25 mg. of aceto-acetic acid per 100 ml. As before, +, ++, and +++; were assigned to

TABLE IV—EFFECT OF BOILING URINE ON GERHARDT TEST

Duration of boiling (min.)	Aceto-acetic acid		
	25 mg. per 100 ml.	100 mg. per 100 ml.	300 mg. per 100 ml.
0	Trace	++	+++
5	1/2 trace	Trace	++
10	Negative	Negative	Trace
15	Negative	Negative	Negative

reactions lying proportionately between these extremes (table III).

Table IV shows the result of boiling the urine containing various concentrations of aceto-acetic acid for different lengths of time. If only a little aceto-acetic acid is present, 10 minutes' boiling should be sufficient to remove it; but, if larger quantities are present, 15 minutes' boiling is necessary to ensure that no aceto-acetic acid remains.

The determination of the sensitivity of the nitroprusside tablets is much simplified by the use of the colour scale provided with the tablets. The concentrations of acetone and of aceto-acetic acid which corresponded most closely to each shade on the colour scale are shown in table V.

TABLE V—APPROXIMATE SENSITIVITIES OF NITROPRUSSIDE TABLETS TO ACETONE AND ACETO-ACETIC ACID ADDED SEPARATELY TO NORMAL URINE

Result	Acetone (mg. per 100 ml.)	Aceto-acetic acid (mg. per 100 ml.)
Detected	..	25
Trace	..	50
Moderate	..	250
Strongly positive	..	800

Discussion

Table I shows that there is usually about nine times as much aceto-acetic acid as acetone present in the freshly voided urine of ketotic patients, which is in agreement with Folin (1934), who found a ratio of 10 to 1. With the Rothera test aceto-acetic acid yields a colour about twenty times as intense as that of an equal concentration of acetone (table II). Therefore only about a two-hundredth of the colour produced is due to acetone. Even in severe ketosis levels of acetone greater than about 50 mg. per 100 ml. have not been observed. It follows that for practical purposes the Rothera test can be regarded as a test for aceto-acetic acid only.

Table II shows that a deep purple (+++) is given by 20 mg. of aceto-acetic acid per 100 ml. In our experience clinical signs of ketosis do not develop when the urine contains less than about 50 mg. of aceto-acetic acid per 100 ml. Owing to the extreme sensitivity of the Rothera test concentrations of this level and greater all give +++ reactions; hence differing degrees of clinical ketosis cannot be distinguished by the test. However, when the concentration of aceto-acetic acid in urine is very low, it is possible to detect differences in the colour intensity by a standardised technique. Table II shows that 1 mg. of aceto-acetic acid per 100 ml. can be detected, but it is not clear at present whether the detection of such small amounts of ketone bodies in the urine is of any help in assessing a patient's clinical condition. It appears that, unless a very carefully standardised technique is used for the Rothera test, misleading results will be obtained. Such a technique takes at least 15 minutes.

The Gerhardt test is more useful clinically than Rothera's test because it is considerably less sensitive and covers a wider range of ketone levels (table III). Unfortunately it has a serious disadvantage in that several drugs in common use produce excretory substances which give a colour with ferric chloride similar to that given by aceto-acetic acid. It is fairly easy to distinguish the colour due to drugs from that due to aceto-acetic acid by boiling the urine and repeating the test. Table IV shows that 15 minutes' boiling in a beaker is essential to ensure that all the aceto-acetic acid is removed. Momentary boiling in a narrow test-tube, as is usually done, is inadequate. Any routine test involving this amount of time is obviously impractical for ward use. Thus it seems that both the Rothera and the Gerhardt tests are far from ideal for ward and clinic use. Though laboratories using standardised techniques may achieve satisfactory results, it is unreasonable to expect nurses to devote the time necessary for the proper performance of these tests.

Little advance has been made in urinary ketone tests since the introduction of Rothera's test in 1908 until the recent production of a tablet form of the nitroprusside reaction. The tablet method appears to overcome many of the objections to the previous tests. The sensitivity of the tablets to aceto-acetic acid is roughly intermediate between that of the Rothera test and that of the Gerhardt test (tables II, III, and V). By the use of this test detection of the lower levels of ketonuria, which are of doubtful significance, is avoided. Clinical trials on a large series of ketotic patients will be necessary to establish a more exact relationship between the ketone content of the urine and the patients' condition. Clinical symptoms of ketosis are not evident when the ketone test shows less than a "trace" reaction by this method. As with the Rothera test, practically no colour is contributed by the acetone present, even in the urine of severely ketotic patients.

The advantages of the tablet method for general use are unquestionable. The tablet is stable and non-caustic, no obnoxious fumes or ammonia are evolved, and no other reagents or apparatus are required. It provides

the clinician with a standardised procedure which is so simple that variations are unlikely. The nitroprusside reaction in this form is specific. The presence of blood-glucose, protein, creatinine, and the excreted products of commonly used drugs such as salicylates, phenazone, barbiturates, and phenol has no effect on the test. It is almost impossible to see a positive reaction with the older tests in a specimen which is grossly contaminated with blood. When the tablet is used, such a small amount of urine is required that the reaction is neither masked nor influenced by the presence of blood.

A major consideration in the routine testing of urine is the large amount of time taken. In this respect the tablets effect a very considerable saving. The Rothera test, as usually done, takes about 5 minutes, and the Gerhardt test about 2 minutes when negative and 6 minutes when positive (this allows only 2 minutes for boiling, which is inadequate for removing large amounts of aceto-acetic acid). Since the tablet method takes less than a minute, about 4 minutes is saved on each Rothera test. There would be a further saving of about 5 minutes on each Gerhardt test. If both of the older tests were superseded by a tablet test, about 10 minutes would be saved on each examination of urine. Gray and Millar (1953) have claimed that with 100 specimens of urine to be tested for sugar 9 hours is saved by using a tablet method. It appears that about 16 working hours would be saved on 100 urine tests done by the nitroprusside-tablet method. The tablet methods for sugar and ketones may be used simultaneously within a minute.

In view of the great clinical importance of tests for urinary ketone bodies the Rothera and Gerhardt tests seem to be unsatisfactory in comparison with other biochemical tests, such as those for glucose. The tablet adaptation of the nitroprusside reaction, in addition to being simple, quick, and reliable, provides an indication of the degree of ketosis, and seems worthy of more extensive clinical trials. For the detection of minute traces of ketone bodies Rothera's test is the most sensitive.

It is realised that the level of ketonuria is not always a reliable indication of the degree of ketonaemia. A rapid and accurate method of estimating the plasma-ketone level is required. Further studies on this problem are in progress.

Summary

The sensitivities of the Rothera, Gerhardt, and nitroprusside-tablet methods for detecting urinary ketones are compared, and their suitability for clinical use is discussed.

The earlier tests have several disadvantages, such as the absence of a standardised technique, and the large amount of time involved when the tests are correctly made.

The need for a simple and quick clinical method for detecting urinary ketone bodies is largely met by the introduction of the nitroprusside tablet.

The quantitative levels of the individual ketone bodies in the urine of patients in different degrees of ketosis are presented.

We wish to thank Dr. Una Ledingham, F.R.C.P., for her support and for making available the facilities of the diabetic department. The work was aided by a grant from the Royal Free Hospital Endowment Fund.

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POTENTIATION OF CORTISONE BY GLYCYRRHETINIC ACID

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WITH continuing restriction of supplies of cortisone in this country, any substance which might prolong or intensify its therapeutic action is worth investigating. Hitherto all efforts to produce such potentiation have failed; *p*-aminobenzoic acid, insulin, and other substances have not been proved useful in this respect. Some workers have found that gold therapy not only fails to increase cortisone action but actually reduces it—i.e., the two substances are antagonistic. When therefore Borst and his colleagues (1953) found that liquorice, in addition to a mineralocorticoid action, appeared to potentiate the action of cortisone in Addison's disease, we felt that a clinical trial in other conditions would be well worth while. Card et al. (1953) found in a case of Addison's disease that glycyrrhetic acid, which occurs in liquorice in the form of its glycuronide (glycyrrhizinic acid), had effects on weight and electrolyte balance similar to those found after the administration of deoxycortone and cortisone. It seemed to us that this substance might be tried, in conjunction with small doses of cortisone, in cases of rheumatoid arthritis, to see whether this had any anti-inflammatory effect such as would be seen with larger doses of cortisone alone.

Methods

Eleven patients (six male, five female) were selected for study; their ages ranged from 39 to 65 years. Eight patients were treated in hospital, and these had a preliminary period of rest in bed. Most of the patients were also placed on a basic régime of physiotherapy. Each patient was then treated with cortisone. When the clinical condition was judged to be stationary inert lactose capsules were given in addition to cortisone for two days as a control; these capsules were identical with those containing glycyrrhetic acid. A course of glycyrrhetic acid 0.5 g. daily was then given, usually for five to seven days; during and after this course the dosage of cortisone was unaltered. The eleven patients received altogether fifteen such courses of glycyrrhetic acid.

Two methods of stabilising the patient on cortisone were followed:

1. In the first method, used eleven times, the patient was given small doses of cortisone (15–37.5 mg. daily) until the clinical condition became static, with symptoms and signs only suppressed in slight degree; glycyrrhetic acid was then added.

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2. In the second method, used four times, larger doses of cortisone (37.5–100 mg. daily) were given until a remission was obtained; the dosage of cortisone was then progressively reduced until a slight relapse resulted; glycyrrhetic acid was then given without further adjustment of the dose of cortisone.

Assessment

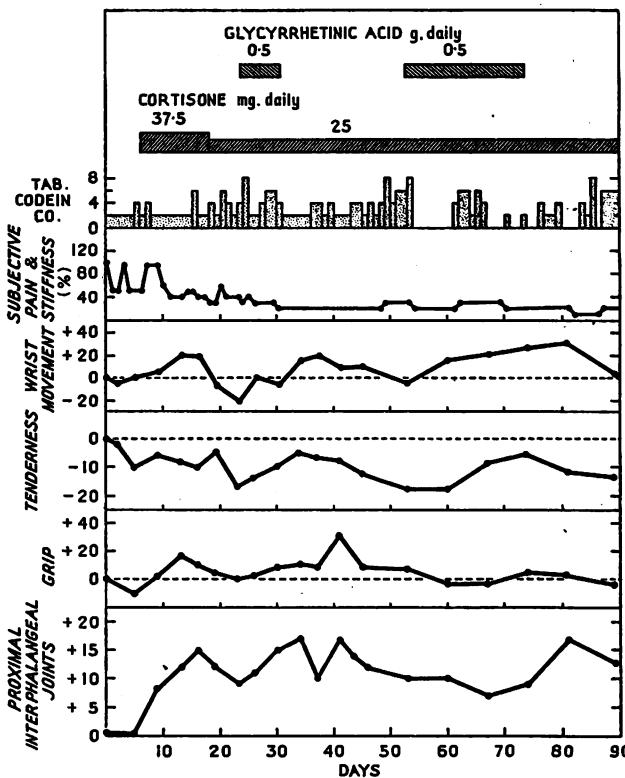
A combination of subjective and objective criteria was used for assessing the progress of the patient. Subjective assessment was based on: (1) the patient's own estimation of the degree of pain and stiffness expressed as a percentage of the pain and stiffness present at the onset of the trial; (2) the number of tablets of aspirin needed each day to relieve pain; (3) the grip of each hand, as measured with a dynamometer; (4) tenderness, as estimated by the application of gradually increasing pressure by the observer.

The range of movements of various joints—usually the wrists—was measured when applicable. In addition the degree of swelling of the proximal interphalangeal joints was measured by the use of Wheatsheaf rings; this has proved a reliable and sensitive method of measurement when used by the same observer (Hart and Clark 1951).

Results

On the whole, the results of the investigation were discouraging. In five patients the results were wholly negative; and in five others the results were probably negative, though certain unusual features were present. In only one patient was there any convincing evidence of potentiation of cortisone by glycyrrhetic acid.

This patient, a woman aged 51, had had rheumatoid arthritis for two years. She was admitted to Westminster



Findings in case of rheumatoid arthritis treated with glycyrrhetic acid.

The amount of pain and stiffness before starting the trial was estimated at 100%. Wrist movements, tenderness, grip, proximal interphalangeal joints swelling: "0" represents the state at the onset of the trial; "+" figures represent improvement and "-" figures deterioration. The measurements were appropriately standardised.

Hospital on June 13, 1953, and after three successive subjective and objective assessments at intervals of three days had given fairly constant readings, she was treated with 37.5 mg. of cortisone daily. Within a few days she had a satisfactory remission, confirmed by all the subjective and objective criteria. After twelve days the daily dosage of cortisone was reduced to 25 mg., and within twenty-four hours there was a partial relapse, confirmed by further measurements taken four days later. A course of glycyrrhetic acid was then given for seven days, with considerable improvement according to all methods of estimation (see figure). When the glycyrrhetic acid was stopped there was a further relapse. She was discharged on 25 mg. of cortisone daily, and attended the outpatient department once weekly. A further course of glycyrrhetic acid was then given, this time for three weeks. This immediately produced great symptomatic improvement, shown by the fact that the patient took no codeine tablets for seven consecutive days. Later there was objective improvement also. When the glycyrrhetic acid was stopped the objective improvement continued for several days, and then a further relapse occurred. The patient has since been satisfactorily maintained on 37.5 mg. of cortisone daily.

In several other patients there was a suggestion that glycyrrhetic acid might have a somewhat prolonged action; improvement occurred while a course of the drug was being given, but no relapse followed when the drug was stopped. It is more likely, however, that most of these inconstant improvements were due to the cumulative effect of rest in bed and small doses of cortisone. The absence of relapse when glycyrrhetic acid was stopped is strong presumptive evidence that this drug was not responsible for the improvement.

Discussion

It is notoriously difficult to assess impartially the progress of patients with rheumatoid arthritis. Spontaneous remissions and relapses are frequent, and seriously handicap the most objective observer. The patients respond so readily to suggestion that improved performance-tests often merely reflect the enthusiasm of the investigator. Despite these pitfalls, we believe that from this small series of cases of rheumatoid arthritis it is justifiable to conclude that glycyrrhetic acid has no distinct or constant potentiating action on cortisone. Possibly it may occasionally have a relatively mild effect—indeed, in the case described here it appeared to exert an effect equivalent to 12.5 mg. of cortisone. The inconstant improvement noted in several other patients supports this view, but such a feeble and inconstant action is unlikely to be of therapeutic value in treating rheumatoid arthritis.

Summary

Eleven patients with rheumatoid arthritis were treated with glycyrrhetic acid 0.5 g. daily, usually in courses lasting from five to seven days. The patients had previously been stabilised with symptoms only partly relieved on small doses of cortisone, which were continued during the administration of glycyrrhetic acid.

In only one patient was there any convincing improvement with relapse when the drug was stopped. In this case the drug had a potentiating action equivalent to 12.5 mg. of cortisone daily.

Any potentiating action by glycyrrhetic acid is too slight and inconstant to be of value in the treatment of rheumatoid arthritis.

We wish to thank Mr. William Mitchell, Ph.D., of Messrs. Stafford Allen & Sons Ltd., for supplies of glycyrrhetic acid, and Prof. N. F. MacLagan, F.R.C.P., for his advice.

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LIQUORICE EXTRACT IN ADDISON'S

DISEASE

SUCCESSFUL LONG-TERM THERAPY

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THE deoxycortone-mimetic action of the juice and extract of liquorice has been demonstrated in normal persons (Borst 1950) and in patients with Addison's disease (Groen et al. 1951, Card et al. 1953, Parrish and Alpert 1953). The triterpene constituent, glycyrrhetic acid (Card et al. 1953, Pelser et al. 1953b), and its diglucuronate, glycyrrhizinic acid (Groen et al. 1951, 1952), have also proved effective in brief investigations in this disease. In the case described here liquorice extract was administered over a longer period.

Case-report

A housewife, aged 54, was admitted on April 19, 1952, with the classical features of Addison's disease. Weakness and loss of appetite and weight had been present for a year; brown pigmentation of the skin for nine months; and slowness of thinking for three months. Vomiting, faintness, and yawning had been frequent in the three weeks before admission. The history was negative regarding previous illnesses, operations, residence abroad, and family history of tuberculosis. The patient had a generalised "sun-tan," especially distinct over pressure areas, nipples, and axillæ; while black pigmented spots were present on the lips, tongue, and buccal cavity. The pulse-rate was 80 per min.; the blood-pressure was 85/55 mm. Hg, and there was no orthostatic hypotension.

Investigations

Table I summarises the biochemical and blood-pressure changes before and 1, 5, and 17 months after treatment with liquid extract of liquorice B.P. (Boots). When the daily dose was increased to 60 g. the blood-pressure, blood-urea, and serum-electrolyte values were restored to normal; and they have remained so, despite great reduction in the dose to prevent undesirable rises in blood-pressure. Serum-potassium and fasting blood-sugar values have fluctuated little, while results of blood-counts, hepatic tests, and urinalysis with microscopy have revealed no abnormality throughout.

The main pharmacological observations are summarised in table II, which shows the blood-pressure and general effect with, singly, liquorice extract (B), large doses of salt (C), and deoxycortone acetate (D), and a combination of liquorice extract and salt (E), compared with two separate-control phases (A) of one week without treatment. In each therapeutic phase (table II) the index of response adopted was the mean value of the four-hourly blood-pressure readings on the last day. This index was shown to be more reliable than body-weight in this patient. Each phase (B-E), with one exception, lasted one week or a multiple thereof. The exception was during combined liquorice and salt therapy (E₂), when, after two days on 60 g. of liquorice and 12 g. of salt daily, this treatment had to be terminated abruptly owing to premonitory pulmonary oedema with increased transverse diameter of the cardiac silhouette radiographically, associated with ankle oedema. Headache, which is a usual accompaniment of overdosage with liquorice (F. E. Revers, personal communication), was not present. This situation had occurred previously after two weeks of combined treatment with 30 g. of liquorice extract and 12 g. of salt daily (E₁). It can be concluded from table II that 60 g. of extract of liquorice by mouth daily and the 5 mg. of deoxycortone by intramuscular injection daily were about equipotent and more than adequate to control the disorder; whereas 12 g. of supplementary salt alone proved insufficient for stabilisation after a three-week trial.

Two other interesting actions of liquorice extract were evident. A cumulative effect was observed immediately after each of the two abrupt cessations of treatment due to incipient pulmonary oedema (F); the blood-pressure failed to drop to normal until a further seven days and 10 days respectively had elapsed. This cumulative effect was also observed later when the blood-pressure remained normal for up to two days after abrupt cessation of therapy. Secondly, increased sensitivity in the response to liquorice therapy was observed. For instance, a smaller dose (30 g.) five months after admission

TABLE I—BLOOD-PRESSURE AND BIOCHEMICAL FINDINGS BEFORE AND 1, 5, AND 17 MONTHS AFTER START OF LIQUORICE EXTRACT THERAPY

Phase	Blood-pressure (mm. Hg)	Serum-electrolytes (mg. per 100 ml.)			Blood-urea (mg. per 100 ml.)	Fasting blood-sugar (mg. per 100 ml.)	Neutral 17-ketosteroids (mg. per diem in urine)	Kepler test "A" value	CO-combining power (vols. %)
		Na	Cl (as NaCl)	K					
Before treatment	85/65	275	445	31	60	98	0.48	4.8	..
1 month later (60 g. ext. glycyrrh. liq. daily)	135/80	345	579	17	29	95	62
After further 4 months (30 g. ext. glycyrrh. liq. daily) ..	130/80	325	555	18	34	100	0.62	4.5	63
After further year (4½ g. ext. glycyrrh. liq. daily) ..	125/80	315	573	19	35	96	0.76	9.2	60

(after completion of the pharmacological observations recorded in table II) maintained a normal blood-pressure, whereas in the first few weeks this dose was clearly inadequate. Reductions, to 3 g. daily at the time of writing (January, 1954), have continued; and latterly the maintenance of the desired blood-pressure has required very fine readjustments. Thus it was recently observed and verified that after a week on a daily dose of 2.5 g. the blood-pressure fell from normal to 110/70 mm. Hg, but the pressure rose to 150/90 after a daily dose of 3.5 g. daily for a further week. Such discrimination between doses differing by only 1 g. daily was not found in the initial phase of treatment with liquorice extract.

Discussion

Pelser et al. (1953a) provided the first evidence of the successful long-term treatment of Addison's disease solely with liquorice extract or its constituents. Their four patients were maintained in electrolyte equilibrium for periods ranging from one to two and a half years. The patient described here has now enjoyed good health for over a year as an outpatient and avers that this medicine is both palatable and free from undesirable effects on digestion or bowel habit.

The initial control in our patient required the large dose of 60 g. of liquorice extract daily. The absence of a favourable response earlier to half that dose tempted us to abandon this treatment. As treatment continued,

TABLE II—COMPARATIVE EVALUATION OF VARIOUS TREATMENTS

Treatment (in addition to ordinary diet)		Duration (weeks)	Mean blood-pressure (mm. Hg) on last day of study period	Effect
A	Nil	1	85/55	—
B	Ext. glycyrrh. liq. 5 g. t.d.s. 10 g. t.d.s. 15 g. t.d.s. 20 g. t.d.s.	1 1 1 1	70/55 80/55 105/80 135/80	Nil Nil Slight Definite
C	Sodium chloride 12 g. daily " "	1 2 3	80/60 85/55 110/75	Nil Nil Slight
D	Deoxycortone acetate (intramusco.) 5 mg. daily 2.5 mg. daily	1 1	140/80 110/70	Definite Slight
A	None	1	80/60	Nil
E ₁	Ext. glycyrrh. liq. Plus sodium chloride 10 g. t.d.s. 12 g. daily	1 2	145/90 175/100	Definite Very definite
F	None (following E ₁) ..	1	125/80	Cumulative
E ₂	Ext. glycyrrh. liq. Plus sodium chloride 20 g. t.d.s. 12 g. t.d.s.	1 ^{1/2} ..	160/90 ..	Very definite ..
F	None (following E ₂) ..	1 ^{1/2}	120/80	Cumulative

however, the initial insensitivity to this therapy was soon reversed, and the patient's present maintenance dose is 3 g. daily. Pelser and associates (1953a) also observed increasing sensitivity to liquorice therapy. They considered that there was no evidence that this resulted from regeneration of adrenocortical remnants—a view confirmed by the present observations. In the present study a cumulative action of extract of liquorice was also observed.

The action of liquorice extract is thought to be purely deoxycortone-mimetic (Borst et al. 1953, Pelser et al. 1953b). In our patient during continuous therapy with liquorice extract there were no significant changes in the results of the Kepler test or fasting blood-sugar levels to suggest any cortisone-like action by the extract. Determinations of urinary 11-oxysteroid excretion by the method of Talbot et al. (1945), slightly modified, showed that, compared with the normal range (0.15–0.40 mg. per 24 hr.) the value was below normal (0.025 mg. per 24 hr.) when no treatment was being given and above normal (0.5 mg. per 24 hr.) during treatment with 15 g. of liquid extract of liquorice daily. This suggests that the excretory products of liquorice extract may interfere greatly with the results obtained by this test. In another case of Addison's disease we sought by a modification of the method of Norymberski et al. (1953) to establish whether a similar interference disturbs the assay of urinary 17-ketogenic steroids. Apparently there is no such disturbance; for a normal value was obtained while the patient was receiving 60 g. of the liquorice preparation and 6½ mg. of cortisone daily. It was further shown (J. M. Stowers, personal communication) that the liquorice preparation was itself a powerful reducing agent of the copper in the Talbot test for urinary corticoid assays (Talbot et al. 1945). Repeated determinations of the urinary neutral 17-ketosteroid excretion gave uniformly low results, as Hudson et al. (1953) have also found.

Liquorice therapy therefore does not appear to influence androgen metabolism. Although the skin pigmentation of our patient did not change significantly after the institution of liquorice therapy, the finger-nails appeared to become appreciably paler, suggesting that liquorice therapy may reduce melanin deposition in growing structures. This view was supported by microscopic study of the cut free ends of the nails, at various stages; but this observation has not been checked biochemically.

Patients with Addison's disease vary considerably in their sensitivity to liquorice or its constituents. Thus, Borst et al. (1953) reported that the deoxycortone-like effect of liquorice was absent in their three patients with Addison's disease, but that 10 mg. of cortisone restored fully the effect of the liquorice on mineral metabolism. I recently made a similar observation (to be published) in a patient who, on two attempts, could not be controlled adequately on liquorice therapy alone, although he responded to deoxycortone alone, and later to the combined administration of 6½ mg. of cortisone and 60 g. of liquid extract of liquorice daily.

As with deoxycortone, for the maintenance of the more severe cases of Addison's disease liquorice must be administered along with cortisone. A synergistic action between these two drugs has been demonstrated by Borst et al. (1953), who described a patient who remained well for at least a year while receiving 16 g. of liquorice extract and 10 mg. of cortisone daily.

Thus it seems that Addison's disease may be treated over long periods with liquorice extract or its constituents, aided when necessary with concurrent cortisone therapy. Pelser (1954) has described a patient in whom the effect of glycyrrhetic acid on electrolyte metabolism, although satisfactory, was potentiated by small doses of cortisone. The merits of liquorice therapy are its apparent effectiveness and safety, and the absence of undesirable side-effects, as well as its palatability, convenience, and cheapness.

Summary

A case of Addison's disease, well maintained for over a year on liquorice extract alone, is described.

The optimal daily dose of liquorice extract decreased from 60 g. to 3 g. in just over eighteen months.

In addition to this increased sensitivity to liquorice extract judged by the pressor response, a cumulative action was also evident.

Liquorice extract has a useful place in the long-term treatment of Addison's disease.

I am greatly indebted to Dr. John Gray for permission to undertake these investigations, to Dr. W. Walther and Dr. C. Raeburn for their co-operation in the biochemical and histological studies, to Dr. J. M. Stowers and Dr. J. D. N. Nabarro for the determinations of urinary 11-oxysteroids and of 17-ketogenic steroids, and to Mr. F. Allen for pharmaceutical advice.

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"... the study of pathology, conceived of in its widest sense, is of little value to one who is going to practise medicine unless it enables him to grasp clearly the functional changes that are produced by the anatomical changes so frequently caused by disease and seen post-mortem. For every sick person is essentially a functionally deranged organism. He may owe his symptoms to changes that are physically recognisable in his organs or to disorder in the workings of his mind or, if you prefer, of his central nervous system. A sick person is a person with morbid physiology or psychology, and the physician's business is to learn what the disorder—in its literal sense—is due to, and to apply this knowledge to remedy the defect—in other words, to 'cure' the patient. The modern trend is to use pathological knowledge to prevent disease, if that is possible, rather than to cure it. I cannot stress to you too much, therefore, the desirability of acquiring the point of view which will lead you to ask yourself in every case, 'What do the observations, of whatever nature, that I make tell me about the disease process from which my patient is suffering?' Never be intellectually satisfied with a diagnosis or a label. But it must be recognised with sadness that such an exhortation will probably affect the conduct of only the most alert students and practitioners."—Sir HOWARD FLOREY, F.R.S., in *Lectures on General Pathology*. London, 1954, p. 20.

INTRAVASCULAR HÆMOLYSIS IN CHOLERA

THE EFFECT OF OXYTETRACYCLINE

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THE observation of hæmoglobinuria in a case of cholera (De et al. 1952b) led us to wonder whether intravascular hæmolysis is a regular feature of this disease; and, if so, what may be its possible mechanism and effects. In an attempt to elucidate these points we have made a special study of some cases admitted to the cholera ward.

Materials and Methods

The patients came in with a history of vomiting and purging and with signs of shock. They may be divided into three groups:

Group 1.—23 patients were given the routine treatment of intravenous hypertonic alkaline saline solution followed by physiological saline solution. None had oxytetracycline (terramycin). In each case *Vibrio cholerae* (21 Ogawa and 2 Inaba strains) was isolated from the stools.

Group 2.—7 patients received oral oxytetracycline 1000 mg. on admission with 500 mg. after two hours and then four-hourly to a total dose of 5·0 g. They were given intravenous saline solution as in group 1. Their stools contained *V. cholerae* (Ogawa).

Group 3.—7 patients in whom *V. cholerae* could not be isolated from the stools received routine intravenous saline solution as in groups 1 and 2 and served as controls. No oxytetracycline was given.

Soon after admission 5–10 ml. of venous blood was collected: of this 2 ml. was heparinised and the rest allowed to clot. The serum-bilirubin level was estimated (one-minute and thirty-minute) by the modified Malloy and Elvyn technique (Ducci and Watson 1945) and the van den Bergh reaction was determined. Hæmoglobin percentage (Sahli), erythrocyte-count, and packed-cell volume were estimated from the heparinised fraction. The supernatant plasma from the centrifuged heparinised sample was examined for the colour of hæmoglobin, which if present was measured with a photo-electric colorimeter by the acid-hæmatin method. The deposited red cells were washed thrice in physiological saline, and the osmotic fragility was determined by the technique described by Dacie and Vaughan (1938). In the cholera cases the effect of mechanical trauma on the red cells (ninety shakes per minute for half an hour in a Kahn shaker) was also noted. Samples of heparinised and clotted blood were collected similarly on the second, fourth, and eighth days, and all the above-mentioned investigations except the fragility tests were repeated.

The first sample of urine passed after the period of anuria was collected and centrifuged, and the supernatant fraction was examined chemically and spectroscopically for methæmoglobin.

Findings

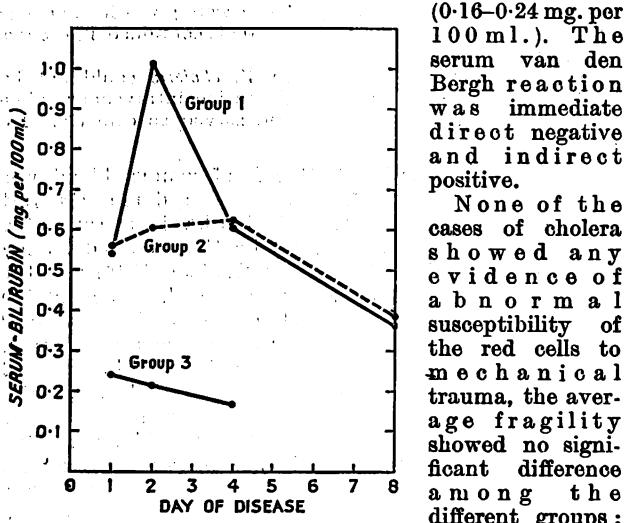
The accompanying table shows the average figures worked out from the above investigations. It will be seen that in all the groups there was considerable hæmoconcentration on the first day: the hæmoglobin percentage was much raised (112–116% Sahli) and the

BLOOD CHANGES IN CHOLERA AND NON-CHOLERIC DIARRHEA

Group	Day of disease	Hb % (Sahli)	Red cells (million per c.mm.)	Packed-cell volume (%)	Serum-bilirubin (mg. per 100 ml.)	Osmotic fragility (% NaCl)		
						Starts	Completed	M.C.F.
1	1	115	5.71	51.35	0.54	0.457	0.297	0.370
	2	95.4	4.94	42.7	1.09
	4	90.6	4.64	40.5	0.62
	8	85.2	4.38	40.2	0.38
2	1	112	5.67	49.4	0.55	0.435	0.295	0.370
	2	103	5.08	42.7	0.61
	4	91	4.44	38.3	0.63
	8	61.5	3.72	32.5	0.39
3	1	116	6.27	54.4	0.24	0.450	0.303	0.390
	2	100.7	5.26	42.6	0.22
	4	100.5	5.27	43.5	0.16
	8

Mean figures have been tabulated.

erythrocyte-count (5,670,000–6,270,000 per c.mm.) and packed-cell volume (49.4–54.4%) increased. These figures gradually came down during convalescence. The one-minute or prompt serum-bilirubin level was 0 in all the cases; but the thirty-minute serum-bilirubin varied among the different groups. The average serum-bilirubin was higher (0.54–0.55 mg. per 100 ml.) on the first day in the cholera cases (groups 1 and 2) than in the controls (0.24 mg. in group 3). Besides, the patients in group 1, who received no oxytetracycline, showed on the second day a steep rise in the serum-bilirubin level (1.09 mg. per 100 ml.), which gradually fell later (see figure). In group 2, who received oxytetracycline, this acute rise of serum-bilirubin on the second day was absent, although hyperbilirubinaemia persisted even to the fourth day (0.62–0.63 mg. per 100 ml.). In the controls in group 3 the bilirubin curve remained almost flat at a low level (0.16–0.24 mg. per 100 ml.). The serum van den Berg reaction was immediate direct negative and indirect positive.



Serum-bilirubin levels in 23 cholera patients
(group 1) not treated with oxytetracycline;
7 cholera patients (group 2) treated with
oxytetracycline; and 7 controls (group 3).

at which initial haemolysis took place (see table). Only 3 cases in group 1, 0 in group 2, and 2 in group 3 showed initial haemolysis at a saline concentration just above 0.46%, which is usually taken as normal.

3 of the patients in group 1 had haemoglobinæmia with plasma-hæmoglobin levels of 180, 180, and 138 mg. per 100 ml., and the plasma-hæmoglobin done on the second day in a 4th patient was 96 mg. per 100 ml. The haemoglobinæmia disappeared by the next day after it was discovered. Including the case reported earlier (De et al. 1952b) 5 cases of haemoglobinæmia in cholera have been reported. Of these 5 cases 3 had haemoglobinuria

also; in the 4th patient the first sample of urine voided after the period of anuria was not obtained; and the 5th patient died before passing urine. It is the first sample of urine that is likely to contain the largest amount of the abnormal pigment, which tends to disappear rapidly from the succeeding specimens. Of the 5 patients with haemoglobinæmia 3 died later of postcholeric uræmia (between the eighth and the tenth days); 1 died in the stage of shock; and 1 had an uneventful recovery.

Discussion

All the cases of cholera, whether they were treated with oxytetracycline or not, had hyperbilirubinaemia, which was greatest on the second day. The absence of a yellowish colour in the cholera stool suggests biliary obstruction as the cause of the hyperbilirubinaemia; but a negative immediate direct van den Berg reaction excludes this possibility. The hyperbilirubinaemia must therefore be due either to retention of a normal amount of bilirubin from anoxic or toxic injury to liver cells or to an excessive formation of bilirubin from abnormal breakdown of red cells, or to both causes.

The maximum rise of serum-bilirubin on the second day, and the persistence of hyperbilirubinaemia on the fourth day (when the patient has recovered from shock and haemoconcentration), together with the absence of prompt bilirubin in the serum, make it unlikely that toxic or anoxic hepatic injury is a cause of the raised serum-bilirubin. The absence of any significant histological changes in the liver of patients dying of cholera also supports this contention, although such a possibility cannot completely be ruled out. On the other hand, the occurrence of frank haemoglobinæmia and/or haemoglobinuria in 5 cases leaves no doubt about the cause of the hyperbilirubinaemia which was subsequently observed in them, and suggests that a relatively milder and slower process of haemolysis may explain the rise of serum-bilirubin in the others.

Cohnheim (1892) considered the possibility of red-cell damage, haemolysis, and haemoglobinæmia in cholera when he observed that the plasma contained potassium salts. d'Herelle et al. (1930) also emphasised the important rôle of haemolysis in cholera, though on less secure observations, and Rogers (1922) regarded haemolysis as the cause of coloured serum in some of his worst cases. Awny (1948) observed an increased icterus index in only a small proportion of cases of cholera, and attributed it to haemolysis.

A low chloride content was suggested by Rogers (1922) as the cause of haemolysis with coloured serum in cholera. Banerjee (1941) recorded very low plasma-chloride levels in cholera even after the administration of saline solution. More recently Saha and Das (1951) have reported hypochloraemia in cholera before the administration of saline solution. However, of their 22 bacteriologically proved cases 17 had plasma-chloride levels above 0.46 per 100 ml. In our study of the fragility of red cells no trace of haemolysis was seen above this concentration in most of the cholera cases. Therefore a low plasma-chloride level can hardly be held responsible for the haemolysis in cholera.

Awny (1948) believed that the fragility of the red cells was increased by cholera toxin or by the mechanical trauma resulting from dehydration and increased viscosity of the blood. We, however, have not detected any abnormal fragility of washed red cells either in hypotonic saline solution or after mechanical trauma. Moreover, Cooray and De (1949) have shown that the subcutaneous injection of hypertonic glucose solution sufficient to induce considerable haemoconcentration in rabbits does not produce any significant alteration in the red cells or any haemolysis. Further, in our controls in group 3, with equal if not greater haemoconcentration, no hyperbilirubinaemia was found. These facts suggest that dehydration with its consequences cannot explain the haemolysis noted in cholera.

OXYTETRACYCLINE

We have previously discussed the possibility that a haemolysin produced by *V. cholerae* destroys red cells (De et al. 1952b). The effect of oxytetracycline on the rise of serum-bilirubin level on the second day supports this hypothesis. Oxytetracycline has been found by De et al. (1952a) to exert both bacteriostatic and bactericidal action against *V. cholerae* in vitro, and clinical reports (Konar and Sengupta 1951, Das et al. 1951, 1953) also suggest that the stools become vibrio-negative earlier in cases treated with oxytetracycline than in controls. These reports indicate that the antibiotic may influence the serum-bilirubin level in cholera through its adverse effect on the vibrios and thus on their production of haemolysin. De et al. (1954) have also observed that *V. cholerae* produces a thermolabile haemolysin which acts on human red cells only in the presence of calcium salts, and that the typical haemolytic activity is also exhibited by samples of cholera stool yielding a pure growth of *V. cholerae*.

The present study was made at the height of a cholera epidemic, and random cases were selected for investigation; hence the incidence of haemoglobinæmia recorded here may be shown to be too high when a larger number of cases are collected throughout the season. Of the 5 patients with haemoglobinæmia 4 died, whereas only 1 of the 26 others did. It would be unwise to generalise from this limited observation, but it indicates a grave prognosis for cases with excessive haemolysis and consequent haemoglobinæmia. Further, the development of postcholeric uræmia in 3 of the 4 fatal cases of haemoglobinæmia suggests that there is a significant relation between the two conditions (see De 1953).

The effect of oxytetracycline therapy on the serum-bilirubin level in cholera is interesting. We did not start with the idea of assessing the success or otherwise of such therapy but we found incidentally that the cholera patients not exhibiting a sharp rise of serum-bilirubin on the second day had been given oxytetracycline.

The clinical reports cited above hold out very little promise of success for oxytetracycline therapy in cholera, although the vibrios in the stool disappear rather earlier. Nevertheless the present study of a small number of cases suggests this antibiotic has some definite beneficial effect on at least one, perhaps ominous, pathological process going on inside the body in cholera. Perhaps higher doses given more frequently, especially at the onset of the illness, would have more obvious clinical results.

Conclusions and Summary

30 bacteriologically proved cases of cholera, of which 23 were treated with intravenous saline solution alone and 7 with oxytetracycline also, exhibited hyperbilirubinæmia, which is ascribed to intravascular haemolysis induced by the haemolysin of *Vibrio cholerae*. Controls without cholera but with diarrhoea and a comparable degree of haemoconcentration did not show this change.

Oxytetracycline seems to prevent a rise of the serum-bilirubin level to a peak on the second day.

Haemoglobinæmia with or without haemoglobinuria was observed in 4 of these 30 cases of cholera and in 1 reported earlier (De et al. 1952b). The prognosis of such cases appears serious.

The initial haemoglobinæmia and haemoglobinuria may play an important part in the subsequent development of postcholeric uræmia.

The incidence and the effects of these haemolytic phenomena should be studied in a larger number of cholera cases.

We are indebted to Dr. A. K. Duttagupta for permission to publish, and to Dr. A. Mondal, medical officer in charge of the infectious diseases wards, for help in collecting the materials from his cases. Messrs. Chas. Pfizer supplied the oxytetracycline.

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PLASMA-INSULIN ACTIVITY IN

HYPOPITUITARISM

ASSAYED BY THE RAT-DIAPHRAGM METHOD

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The insulin activity of plasma from acromegalic patients, assayed by a modification of the rat-diaphragm technique originally described by Groen et al. (1952), has been shown to be significantly greater than the insulin activity of normal human plasma (Randle 1954).

The results of similar assays of plasma-insulin activity in three authentic cases of hypofunction of the anterior lobe of the pituitary gland are presented here.

The methods, procedure, calculation, and expression of results have been described previously (Randle 1954).

The results of these experiments are presented in the accompanying table. The insulin activity of plasma from patients with hypopituitarism was significantly

* In receipt of a full-time grant from the Medical Research Council.

INSULIN ACTIVITY OF PLASMA FROM NORMAL PEOPLE AND PATIENTS WITH HYPOPITUITARISM

Case no.	Type of subject	Blood-sugar level (mg. per 100 ml.)	Glucose uptake (mg. per g. per hr.) in the presence of			Calculated plasma-insulin activity (milliunits per ml.)	Limits of error P = 0.05	N
			Buffer	Buffer + insulin (2 milliunits per ml.)	Buffer + plasma (plasma diluted 1 : 4)			
1-7 A B C	Normal Hypopituitarism " "	80 110 77	2.41 ± 0.17 2.22 ± 0.21 2.35 ± 0.14	3.96 3.31 ± 0.20 4.01 ± 0.20 3.84 ± 0.39	4.20 2.47 ± 0.11 2.89 ± 0.18 2.82 ± 0.12	13.5 0.57 0.77	12-20 0.22-1.5 0.28-2.9	75 12 12 10

* With this single exception, all glucose uptakes in the presence of insulin and of plasma were significantly greater than the basal glucose uptake.

N, total number of hemidiaphragms used for determining the mean glucose uptake in the presence of plasma and of insulin.

The figures for normal human plasma are the mean values for seven separate determinations. The individual values have been previously published (Randle 1954).

Plasma in case A was collected 3½ hr. after oral glucose 50 g.; in the other cases it was collected 2½ hr. after oral glucose 50 g.

less than the insulin activity of plasma from normal people. This difference does not necessarily mean that the insulin content of plasma from patients with hypopituitarism is less than that of normal human plasma; for Ottaway (1953) observed that small amounts of growth hormone had an insulin-like effect in vitro on the utilisation of glucose by the rat diaphragm, and the level of growth hormone in plasma from patients with hypopituitarism is likely to be low. The nature of the material responsible for the insulin-like activity of human plasma in the rat-diaphragm assay has yet to be satisfactorily determined, but these results and the results of similar studies in acromegaly (Randle 1954) suggest that the level of this material in the plasma is influenced by the activity of the pituitary gland.

The possible use of this technique in the diagnosis of hypopituitarism and in assessing the activity of the disease process in acromegaly is being investigated further.

Park (1952) and Bornstein (1953) have attributed the insulin-like effect of normal rat plasma in the rat-diaphragm assay for insulin to non-specific effects of plasma-protein. The results presented here show clearly that this hypothesis cannot explain the insulin activity of human plasma in the rat-diaphragm assay, since plasma samples from two authentic cases of hypopituitarism showed diminished insulin activity in the rat-diaphragm assay despite their normal protein content.

I wish to thank Prof. F. G. Young for much helpful advice and criticism during these investigations; Dr. L. C. Martin, of Addenbrooke's Hospital, for permission to study cases A and C; Prof. M. L. Rosenheim and Dr. J. D. N. Nabarro, of the medical unit, University College Hospital, London, for permission to study case B and for assistance in the study of this patient; Dr. N. R. Lawrie, of the John Bonnett Clinical Laboratories, Addenbrooke's Hospital, for plasma-protein determinations in cases B and C; and Miss D. Cope for technical assistance in the assays. The cost of this work was largely defrayed by an expenses grant from the Medical Research Council. Messrs. Boots Pure Drug Co., Ltd., supplied the crystalline insulin.

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A SENSITIVE DIGITAL PLETHYSMOGRAPH

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ALTHOUGH the most frequent presenting complaint of a patient with peripheral obliterative vascular disease is intermittent claudication, the deficiency in the blood-supply to the muscles rarely leads to loss of the affected limb. It is impairment of the blood-flow to the skin of the extremity that produces at first nutritional changes, then gangrene of the digits, and finally loss of the digits or the limb by amputation.

Thus it is of the greatest practical importance to be able to assess the blood-flow in that part of the limb in which obliterative arterial disease has the most serious consequences—i.e., the digits. The greatest limiting factor to date has been the lack of sensitivity of the available plethysmographs. This limitation has been overcome largely by taking advantage of the high

sensitivity of the R.C.A. transducer tube (no. 5734). The possibilities of using this sensitive valve have been explored previously (Burton 1953, Clamann 1951), but more recently workers have felt that the electric circuits required such a high degree of stabilisation as to make them clinically unpractical (Simeone et al. 1952). Studies in this laboratory have led to the incorporation of the valve into a stable electric circuit, and the mechanical alterations produced by the pulse wave are converted into electrical changes, suitably amplified and photographed. This plethysmograph has proved stable, sensitive, and practical for the clinical study of the character and responses of the digital pulse waves in the fingers and the toes of normal people and of patients with disorders of the peripheral arteries.

Apparatus

The device is an R.C.A. 5734 transducer valve coupled to a light aluminium diaphragm 2 in. in diameter and 0.008 in. thick. The valve forms part of a valve-voltmeter circuit driven by suitably stabilised high-tension (H.T.)

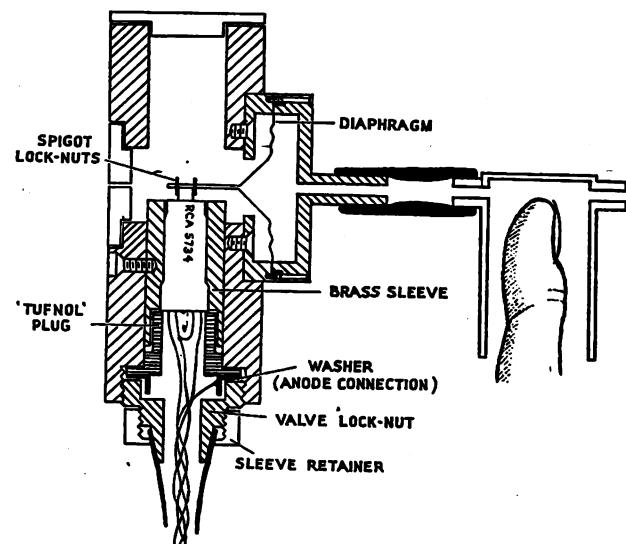


Fig. 1.—Details of pick-up assembly.

and low-tension supplies. Details of the construction of the pick-up are shown in fig. 1. Although they are simple, considerable care must be exercised in construction to secure very close tolerances between the valve and the brass sleeve, and between this sleeve and the outer case. In particular, care must be taken to avoid rotation of the valve, and the method of construction prevents this without distortion of the valve.

The valve spigot must be clamped to the diaphragm with the amplifier adjusted to maximal sensitivity and set to zero, thereby avoiding mechanical distortion. The locking nuts are sealed to the diaphragm spindle with shellac.

Since the transducer valve is essentially a miniature triode whose plate is mechanically adjustable with reference to the cathode and grid, it may be considered as a variable resistance forming with its anode load a potential divider network across the H.T. supply. With small angular movements of the anode control spigot the change in output voltage or divider network potential is substantially linear. This movement is necessarily small and does not exceed $\pm 0.5^\circ$. Under influence of this movement and with an anode load of some 75,000 ohms the output expected is ± 20 V. It will be noticed that the output is phase-sensitive. A normal valve voltmeter of cathode-follower type is used, half the circuit being directly coupled to the transducer anode, and the

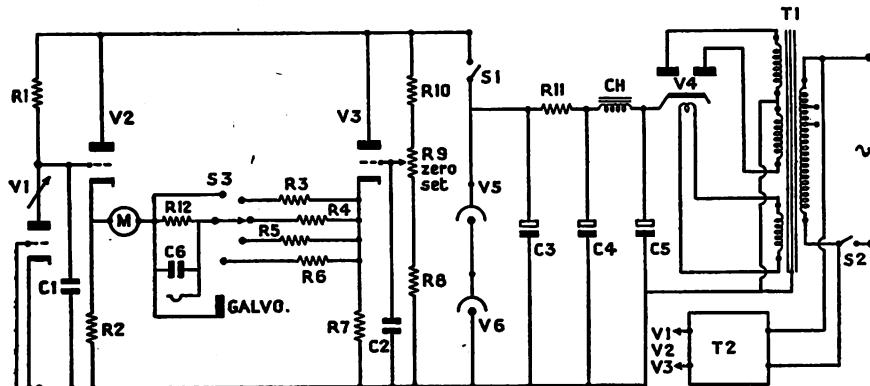


Fig. 2—Circuit diagram of valve-voltmeter, transducer, and power supply.

R1	= 100,000 ohms (H. stab.).	C1	= 0.5 μ F (tub.).
R2	= 50,000 ohms (H. stab.).	C2	= 0.5 μ F (tub.).
R3	= 680 ohms ($\frac{1}{2}$ w.).	C3	= 8 μ F (400 v. elec.).
R4	= 8200 ohms ($\frac{1}{2}$ w.).	C4	= 16 μ F (400 v. elec.).
R5	= 33,000 ohms ($\frac{1}{2}$ w.).	C5	= 8 μ F (400 v. elec.).
R6	= 150,000 ohms ($\frac{1}{2}$ w.).	C6	= 25 μ F (25 v. elec.).
R7	= 50,000 ohms (H. stab.).	CH	= Gardner's C246 (10H, 60 mA).
R8	= 75,000 ohms (H. stab.).	T1	= Gardner's R106 (250-0-250 v., 60 mA, E.T.C.).
R9	= 10,000 ohms (W. W. pot.).	T2	= 'Advance' constant voltage transformer.
R10	= 100,000 ohms (H. stab.).	S1	= H.T. on-off.
R11	= 1000 ohms (4 w.).	S2	= Mains on-off.
R12	= 680 ohms ($\frac{1}{2}$ w.).	S3	= Sensitivity switch.

other half being coupled to a balance potential obtained from the H.T. line via a variable potentiometer forming a zero control (fig. 2).

Any change of anode voltage at the transducer due to spigot deflection will cause a shift in the current distribution of the valve-voltmeter arrangement, and an out-of-balance voltage will appear at the cathodes. If the galvanometer of the recording camera is then connected between these cathodes with a suitable resistance in series, the light beam will be deflected proportionally to the out-of-balance voltage produced by the change of voltage in the transducer anode. By the use of a variable series resistance the galvanometer

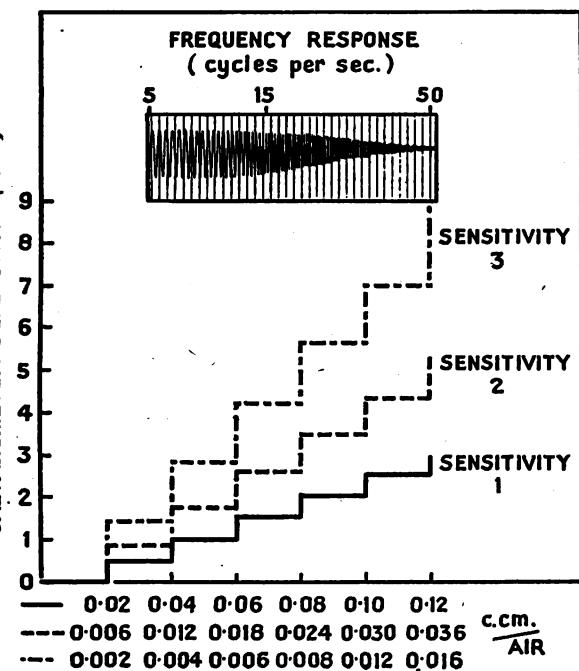


Fig. 3—Graph of response to volume displacement between 0.02 and 0.002 c.c.m. and from zero frequency to 15 cycles per second.

deflection may be set to a convenient magnitude, and the incorporation of a series of switched fixed values of resistance produces a variable sensitivity control. With the diaphragm in use and a 100,000 ohms anode load with a H.T. line of 255 V a volume displacement of 0.1 c.c.m. produced a voltage change of 1.75 V at the transducer anode.

To obtain stability of the valve-voltmeter circuit the H.T. supply is gas-tube stabilised and the heater fed from a constant-voltage transformer, because the transducer valve is particularly susceptible to variation in the heater. To facilitate adjustment of zero control a centre zero meter of 500 μ A full-scale deflection is connected in series with the galvanometer.

The apparatus is completely stable at low sensitivity—i.e., in the range of 0.25-0.001 c.c.m.—but thereafter some instability develops. Random changes of temperature of the air column

in the transducer head and connecting tubes, together with thermal drift of the valve, are partly responsible. Local alterations in the pressure of the environment are even more important, but with care these can be minimised. Calibration has been done with a Burroughs Wellcome microsyringe. Comparison with the Goetz (1949) plethysmograph indicates that the accuracy of this calibration is virtually unaffected by any build-up of pressure within the closed system. The overall response is substantially linear over a range of volume displacement between 0.25 and 0.0004 c.c.m. and from zero frequency to 15 cycles per second (fig. 3).

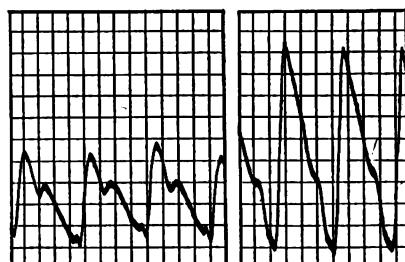


Fig. 4—Pulse volumes from finger-tip in healthy people at sensitivities 2 and 3.

Clinical Observations

The digit being studied is enclosed in a metal collecting cup sealed to the finger or the toe with 'Sealastik,'* which does not cake or constrict, and therefore does not interfere with the blood-flow. Thick-walled fine-bore rubber pressure-tubing leads to the transducer mount. When blood-flows are being calculated, a venous-occlusion collecting cuff is placed at the base of the digit being studied, or, in special circumstances, when the flow is exceedingly rapid, at the wrist or the ankle with due recognition of the error so incurred (Cranley et al. 1952, Goetz 1946, Wilkins et al. 1938). The pulse-volume deflections are expressed in c.c.m. per 10 c.c.m. of digit, and the blood-flows in ml. per 100 c.c.m. of digit a minute. Air conduction has proved quite satisfactory, and the sensitivity is such that it fails to detect a recordable pulse volume or blood-flow only in the

* Manufactured by Expandite Ltd., Cunard Road, London.

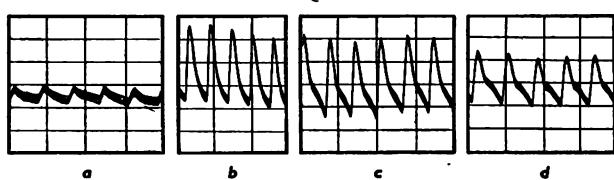


Fig. 5—Resting pulse volume in toe in patient with Buerger's disease : a, at rest before operation ; b, twenty-four hours after lumbar sympathectomy ; c, on second postoperative day ; d, on sixth post-operative day.

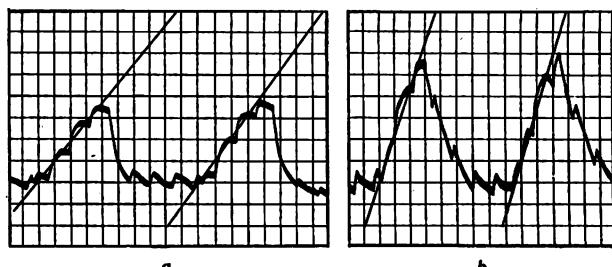


Fig. 6—Blood-flow shown by venous occlusion : a, before cervicodorsal sympathectomy in Raynaud's disease ; b, on fifth postoperative day.

presence of advanced arterial obliteration or severe arterial spasm, when a functioning circulation in the digit is, for all practical purposes, non-existent.

The pulse volume from the finger-tip of a healthy person is illustrated at two sensitivities in fig. 4, and from the toe of a patient with Buerger's disease before and after lumbar sympathectomy in fig. 5. Blood-flows obtained by the venous-occlusion method are illustrated before and five days after cervicodorsal sympathectomy for Raynaud's disease in fig. 6. The digital blood-flows and pulse volumes are plotted against each other in fig. 7 before and after ulnar-nerve block in a patient

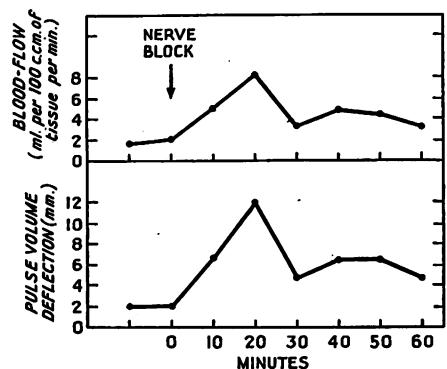


Fig. 7—Digital blood-flow and pulse volume before and after ulnar-nerve block.

with advanced sclerodactyly. The close relationship between the two is apparent—a fact that has been confirmed by Burton (1939).

The plethysmograph described here has been under study in this laboratory for more than a year, and during this time it has satisfied the requirements of stability, sensitivity, and accuracy. The same transducer valve has been in constant use in this period, which is proof of its ruggedness unless grossly mishandled. Finally, the valve is inexpensive and easily assembled, and replacements are readily obtained.

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METASTATIC CARCINOMA OF THE THYROID SUCCESSFULLY TREATED WITH THYROXINE

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THE treatment of simple goitre with thyroid has been reviewed by Greer and Astwood (1953). Shrinkage takes place, probably because the administered hormone leads to a corresponding suppression in the output of the gland. No toxic effects are observed unless doses in excess of physiological requirements are given (Riggs et al. 1945, Greer 1951, Danowski et al. 1952, Perlmutter et al. 1952).

Carcinoma of the thyroid gland is not likely to respond in the same way as simple goitre unless it is well differentiated and still depends to some extent on pituitary thyrotrophic hormone. In the case described here a highly differentiated tumour, with widespread pulmonary metastases, was shown to depend on thyrotrophic hormone and responded favourably to prolonged medication with sodium-l-thyroxine.

Case-report

A woman, now aged 40, was first seen twenty-one years ago with a painless lump in the right side of the neck, thought to be a tuberculous gland. This was treated by radiotherapy without effect. Fifteen years ago a second and smaller lump was noticed, nearer to the midline on the same side. Eleven years ago slowly increasing dyspnoea on exertion was first noticed, and eight years ago mass radiography revealed widespread mottling throughout both lung fields. This mottling has very slowly progressed during the succeeding years. Four years ago the patient was admitted to Woolwich Memorial Hospital, where the first lump was excised; on section this was found to consist of apparently normal thyroid tissue. The second lump was then excised and showed the same histology. Since it seemed probable that these represented local metastases of carcinoma of the thyroid, total thyroidectomy was done, but no neoplastic focus could be identified in the excised gland. The patient was then referred to St. Bartholomew's Hospital for radiotherapy, under the care of Mr. I. G. Williams, and a course of 5500 r was given to the neck at 250 kV in thirty days. Three years ago a third nodule was noticed in the neck and was removed; on section it was found to be composed of colloid-containing thyroid acini showing evidence of hyperplasia. Though it was impossible to diagnose thyroid carcinoma in the specimen, the cellular irregularity was greater than is usually seen in simple hyperplasia.

Radiography of the chest showed widespread mottling of innumerable small metastases throughout both lungs, but no other metastases were found elsewhere, and radiographs of the skeleton were normal.

Investigations.—A tracer dose of radioactive iodine was given; of this 43% was excreted in the urine in forty-eight hours, but the greatest uptake in the neck reached only 10%; no direct counting over the chest was attempted at this time. A second tracer dose was given five months later. The greatest accumulation of radioactivity was found in the chest, reaching 30% of the dose at twenty-four hours; the uptake in the neck reached 9% only, and it is likely that much of this was due to scatter from the chest. The test was repeated two days later with carrier iodide to simulate a therapy dose; 30% uptake in the chest and 9% in the neck were again recorded.

Respiratory function tests were kindly made by Dr. D. V. Bates. The patient was shown to have a normal mixing efficiency as regards gases in the lungs and a normal uptake of carbon monoxide, but a greatly reduced vital capacity (2190 c.cm.) and maximal breathing capacity (47 litres a minute and 42 litres a minute on two consecutive runs). These findings strongly suggested that the dyspnoea was due to interference with distensibility of the lungs and not to emphysema or to bronchospasm.

Electrocardiography.—An electrocardiogram was normal.

Screening of the chest showed no evidence of enlargement of the right ventricle, but it was felt at this time that a real danger of progressive cor pulmonale was present, although dyspnoea was not yet severe and the patient's general health was still good.

Treatment with radioactive iodine seemed indicated, and on Sept. 11, 1951, a dose of 20 mC was given by mouth. Of this 56% was excreted in forty-eight hours, the uptake in the chest reaching 35% in twenty-four hours. Two months later a fourth tracer dose showed a maximal uptake in the chest of 46% at twenty-four hours, and a second treatment dose was then given, this time of 102 mC. A fairly prolonged radiation sickness followed this, and the patient did not recover normal vitality for about two months. Transient lymphopenia developed but no dangerous depression of the marrow.

A further tracer study on June 19, 1952, nine months after this last treatment, showed that the uptake by the lungs had now risen still further, reaching 56% of the dose at twenty-four hours, with no demonstrable uptake in the neck. Calculation (Oddie 1951) showed that the therapeutic doses should have provided local irradiation of about 10,000 r.e.p. throughout the lungs. It seemed that effective ablative doses of radioactive iodine would have to be prohibitively high, and X-ray therapy also, if an adequate response were to be obtained.

Treatment with thyroxine was therefore started in the hope that the metastases might behave like nodular goitre and slowly regress. L-thyroxine was used because it contains less non-hormonal iodine than does the racemic form, and less than thyroid extract, and would not therefore interfere with any subsequent tracer studies. Sodium-L-thyroxine was started on July 16, 1952, in a dosage of 0.1 mg. daily, which was slowly increased until by Oct. 7 the patient was receiving 1.0 mg. daily, with the production of signs of mild toxicity. The dosage was reduced to 0.7 mg. daily, at which level no symptoms were produced, and the patient was then readmitted for further tracer studies. On Dec. 15, 1952, 99% of an intravenous tracer dose was excreted in forty-eight hours, without any demonstrable uptake either in the chest or in the neck. Thyroxine was then discontinued, and four weeks later, on Jan. 12, 1953, the patient was readmitted for further study. She now presented the typical appearance of hypothyroidism; the uptake of radio-iodine in the chest reached 26% of the dose at twenty-four hours, with no demonstrable concentration elsewhere.

Further Progress.—Since then she has been maintained on thyroxine, without intermission, in a dosage of 0.5 mg. daily. There has been a slow but considerable reduction in dyspnoea; the lung-function tests have been repeated and show a rise in the maximal breathing capacity, from 47 litres a minute to 79 litres a minute, although the vital capacity has remained unaltered at 2070 c.cm.; and there is now a slight but definite clearing of the X-ray shadows in the lungs.

Discussion

I am indebted to Dr. G. J. Cunningham for his report on the histology of the local recurrence in the neck. The tumour here was well differentiated, and it is likely that the pulmonary metastases are similar to it. This is confirmed by the ability of the pulmonary metastases to pick up iodide, as the tracer studies showed; and the patient's euthyroid state despite total thyroidectomy was presumably attributable to their activity.

The suppression of iodide uptake after treatment with thyroxine parallels that observed in healthy people both in its degree and in its duration (Greer 1951, Morgans et al. 1952). It was followed by a phase of rebound hypothyroidism, as in healthy people (Farquharson and Squires 1941). It is reasonable to suppose that the mechanism of this lies in the suppression, by the administered hormone, of the pituitary output of thyrotrophic hormone, as in healthy people, and the resultant diminution in activity of the thyroid gland. This would indicate the dependence of the pulmonary thyroid tissue on normal thyrotrophic stimulation from the pituitary.

Regression of the metastases after treatment with thyroxine was shown by clinical improvement, with lessening of dyspnoea subjectively and a better per-

formance of objective tests of lung function; and it has been confirmed by definite clearing of the X-ray shadows in the lungs. (I am indebted to Dr. G. Simon for the interpretation of these films.)

Summary

A case of well-differentiated thyroid carcinoma is described in which very numerous functioning deposits in the lungs proved resistant to treatment with radioactive iodine, but now appear to have been satisfactorily suppressed as a result of prolonged treatment with thyroxine.

This patient was in the first place under the care of Mr. I. G. Williams, and my thanks are due to him and to Dr. A. E. Jones for permission to publish her case. As an inpatient she was under the care of Prof. R. V. Christie, to whom I am grateful for permission to publish and for help with the preparation of this paper. The radio-iodine studies were undertaken by the Department of Physics, and I am indebted to Prof. J. Rotblat and to Mr. G. M. Owen for the great deal of careful work they have done.

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Preliminary Communication

TOXOPLASMOSIS IN CHILDHOOD

PATIENTS with unexplained pyrexia of 7-10 days' duration accompanied by generalised lymphadenopathy and sometimes by a rash and splenomegaly are commonly seen in the outpatient department of a children's hospital. A blood-count shows a leucocytosis of 10,000-15,000 per c.mm. with an increase in the proportion of polymorph cells, a threefold or fourfold increase in the absolute eosinophil-count, and no "glandular fever" cells. The Paul-Bunnell test is negative despite a reasonable clinical diagnosis of infectious mononucleosis.

Throughout the world it has been found that up to 50% of apparently normal adults have a positive dye test for toxoplasmosis, while less than 10% have complement-fixing antibodies. In toxoplasmosis the complement-fixation test is believed to become positive later, and its titre to fall more quickly, than does the dye test. Although domestic animals are presumed to be the reservoir of infection, apart from congenital toxoplasmosis little is known of how or when man becomes infected with toxoplasmas or whether the initial exposure to the parasite, leading to the production of antibodies, is invariably unassociated with symptoms.

The lack of explanation for the numbers of cases of children with pyrexia and lymphadenopathy, and their resemblance to known cases of acquired toxoplasmosis,

RESULTS OF DYE TEST AND COMPLEMENT-FIXATION TEST IN 20 CASES OF CHILDREN WITH UNEXPLAINED PYREXIA AND LYMPHADENOPATHY

Case no.	Dye test (titre)	Complement-fixation test (titre)
1	1/512	1/32
2	1/32	1/32
3	1/64	1/16
4	1/256	1/16
5	1/64	1/64
6	1/64	1/16
7	1/256	Anticomplementary
8-20	Negative	Negative

led me to wonder whether this condition might represent the first, antibody-stimulating exposure to toxoplasmosas, resembling a primary tuberculous complex.

INVESTIGATION

Sera from 20 children and young adults suspected on clinical grounds of having glandular fever were all found to give a negative Paul-Bunnell test. Toxoplasma dye and complement-fixation tests were made, and the findings are shown in the accompanying table.

COMMENT

These results were unexpected, because of both the number of positive findings and of the high titres. It is still difficult to know, in the absence of recognised signs of toxoplasmosis, what attention to pay to positive serological findings, but a titre of 1/8 for the complement-fixation test is generally regarded as of some diagnostic significance. Of the 20 cases 6 had titres in excess of this; while in a 7th case where the serum was anti-complementary the dye-test titre was 1/256—four times as high as that usually found in the symptomless adult.

These preliminary findings are far too incomplete for any firm conclusions. A much larger series of cases of glandular enlargement must be investigated, and a long follow-up is being undertaken to observe changes in antibody titre. Also the haematological findings must be accurately correlated with the serological. But the present data do lend support to the belief that some, at least, of the cases of apparently non-specific generalised lymphadenopathy with pyrexia in children may be due to toxoplasma infection, and that the positive serological tests so often found in the symptomless adult may be a residuum of such infection.

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Reviews of Books

Rh-Hr Blood Types

Applications in Clinical and Legal Medicine and Anthropology. ALEXANDER S. WIENER, M.D., F.A.C.P., senior serologist to the office of the chief medical examiner of New York City. New York: Grune & Stratton. 1954. Pp. 763. \$11.50.

An Rh-Hr Syllabus

The Types and their Applications. ALEXANDER S. WIENER. New York: Grune & Stratton. 1954. Pp. 82. \$3.75.

BETWEEN 1929 and 1953 Dr. Wiener and his co-workers published 333 papers on the Rh-Hr blood types. The first of the two volumes reviewed here gives a full list arranged in years. The papers have appeared not only in the United States but also in British, French, and Italian journals and some others. From these numerous and often important writings Dr. Wiener has selected 84 to represent his contribution to every aspect of the subject. As they have been reproduced from the originals by a photographic process, the book inevitably contains a mixture of sizes and shapes of type which makes for difficult reading; sometimes the reproduction is not too clear and some of the more complex tables need a magnifying-glass. It may be useful to have this collection under one cover, but the relatively few experts directly interested in the subject are likely to have read the principal papers already and probably possess reprints. The non-expert will hardly tackle so difficult a set of papers, and in his *Rh-Hr Syllabus* Dr. Wiener himself has in fact provided them with a much shorter and simpler account of his work.

The *Syllabus* is an excellent little monograph, containing all that anyone not actually pursuing research into blood-groups needs to know about the Rh-Hr blood-group system and the pathological conditions in which it is concerned. It begins with a series of definitions of fundamentals, and the next two chapters, on Rh antibodies and on the serology and genetics of

the Rh-Hr types, contain short didactic discussions, illustrated by clear diagrams. A fairly long and remarkably informative chapter on erythroblastosis foetalis is followed by short chapters on blood-transfusion, anthropology, and medicolegal applications. Unfortunately Dr. Wiener's views on nomenclature introduce difficulties for many of the readers who would benefit most from his book. In this country the CDE nomenclature is in everyday use; but, as is well known, Dr. Wiener regards it as misguided and misleading, and will have none of it. As things stand, the ordinary student needs the help of books that, unlike Dr. Wiener's, make a fair job of collating the two systems. But it is a measure of his skill that he makes his subject plain despite the complexity of the notation which the devotees of the theory of multiple alleles find necessary for the expression of their ideas.

Spot Diagnosis

Volume 1. Compiled by the Editors of *Medicine Illustrated*. London: Harvey & Blythe. 1954. Pp. 128. 7s. 6d.

THIS is an entertaining and teasing book. The reader is invited to examine a photograph and consider some clues; he must then make a diagnosis, and answer some questions, before turning to the right answer on the next page (rather too handy for those who readily succumb to temptation). Most of the pictures have appeared under similar examination conditions in *Medicine Illustrated*. The game is both instructive and aggravating; for the baffled diagnostician learns from his mistakes, yet complains that he would have done better, of course, in the flesh or with a coloured photograph. And he may be annoyed when a non-fluctuant swelling turns out to be a cold abscess, even though the answer generously excuses him from blame in this case. One or two of the conditions are on the rare side, but then many of the commoner diseases do not lend themselves to this form of demonstration. The answers include brief notes on diagnosis and treatment, and at the end of the book there are summaries of some recent developments in medical treatment. This volume is the first of a series.

Medical Electronics

G. E. DONOVAN, M.D., M.Sc., D.P.H. London: Butterworth. 1953. Pp. 215. 30s.

THE aim of this book is "primarily to provide a bird's eye view of the uses of electronics in medicine." The list of contents is impressive, including such subjects as X rays, radioactive isotopes, television, electron microscopy, amplifiers, phono-electrocardioscopy, electromyography, servo mechanisms, and cybernetics. But in his effort to cover so much ground so quickly the author does not always carry the reader along with him.

Much electronic terminology is used without additional or simplifying explanation: "the p-n-p junction triode," "frequency selector and clipper, pulse shaper and delay circuit," and "the usual arrangement of push-pull stages with cathode degeneration of in-phase voltages" are phrases unlikely to convey any clear idea to those not engaged in electronic work. The almost complete absence of cross-references is tiresome: thus a porous-plug transducer is mentioned on p. 88 but not in the chapter on transducers, while gas amplification is not explained in the chapter on photo-electric cells, though the reader is told earlier that gas amplification does not take place in ionisation chambers.

The illustrations are of mixed quality: some, such as those in the chapter on electron microscopy, are good, especially the comparison between the electron microscope and the optical microscope; others, showing merely the outside appearance of cabinets, are unhelpful. Dr. Donovan believes that detailed circuit diagrams are not necessary for an understanding of the principles involved in an apparatus, and that may be so; but there is still a real need for the imaginative use of block schematic diagrams.

The preface suggests that doctors who are not already familiar with the applications of electronics to medicine may find the book of interest; but those who are not well versed in electronic terminology will find much of it perplexing—though they may profit from the accounts of the various applications. Physicists, research-workers, and electronic engineers will find some useful references.

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THE LANCET

LONDON : SATURDAY, APRIL 17, 1954

The Bombs

THE terrific explosion of the hydrogen bomb last month was one of those dramatic events that display a dangerous situation and compel us to consider where we are going. Absorbed though we may be in our own affairs, we have to adjust our minds to the probability that if there is another world war this weapon will be used on our behalf. For many millions this probability means that they must examine afresh their opinions on the ethics of war.

In such an examination we may begin by noting that within almost all human groups the members are forbidden to kill each other. Man is a social animal whose success has generally depended on the support of his fellows, and, whether the group is small or large, homicide within it is regarded as a crime—often, as in our own country, as almost the gravest of crimes. On the other hand, there is no social objection to the destruction of an enemy *outside* the group: on the contrary, when two groups are at war, the very code of loyalty which prevents internal killing enjoins external killing, and the aggressive violence which is criminal at home becomes meritorious abroad. Moreover, so strongly social are mankind—so devoted to their own group—that to the large majority this apparent anomaly of conduct comes quite naturally; and they will go to equal lengths to kill their foes or to save their friends. Distinguishing thus sharply between "our side" and the others, they readily extend protection to anyone who wants to join their group—even yesterday's enemy. Indeed civilisation has been made possible only by the formation, in this way, of larger and larger groups whose members feel that in essentials they are all on the same side, and who therefore accept a code which stops them from killing each other.

In the past, fifty years this process of social coalescence has gone on much faster—so much so that in the present Cold War most of the nations belong to one or other of two opposing groups, not unevenly matched in numbers. The more hopeful among us take comfort in the thought that the creation of these two immense groups, each securing peace within its borders, may be the last stage on the way to the creation of a single world community—a community of which every human being is a member, and whose protection he enjoys. Through the centuries this goal of human unity has been set before us alike by the idealist and by the realist—the one asserting the brotherhood of man, the other demonstrating the artificiality and impermanence of the political and racial boundaries which appear so formidable. (Both in this idealism and in this realism no small part has been played by our own profession, whose members, in undertaking to do their best for any man, woman, or child at any time, have reflected, however imperfectly, the best of Christian teaching and Greek thought). Given time, there can in fact be little doubt

that these ideas will be accepted: the remaining groups will in one way or another be fused, and thenceforward only those who are outcast from the world community will feel justified in taking the lives of others of their own species. But we do not know when or how this will happen: and meanwhile the division of the world into two major groups means that though we have far more potential friends we also have far more potential enemies. Nor has our progress towards a World State in the future lessened the antagonism, or civilised the methods, with which war is waged in the present. On the contrary, our struggles have become more intense; having begun to fight, we find it harder to break off the engagement and reach an honourable settlement; and our techniques of killing, though in some ways less horrible than our ancestors' personal use of fire and sword, have a recklessness which suggests a blunting of moral values. Certainly the conventions of war have changed astonishingly within a few decades.

To the primitive member of a group, the declared enemy is always something to be destroyed, and the more thoroughly the better. We have lately witnessed dreadful examples of such barbaric warfare. But human societies have never consisted entirely of mental myopes, and even before the time of the greatest religious teachers many nations adopted conventions designed to prevent the worst atrocities of war. In Europe Christian influence increased the power of such conventions so greatly that a time came when the right to kill and the methods of doing so were strictly circumscribed by rules; and any combatant breaking these rules exposed himself to the contempt of neutrals. Those who are old enough to remember the earlier part of the first world war may recall the shocks of horror that went through this country at the report that our enemies were using dum-dum bullets, at their shooting a woman for helping prisoners to escape, at their use of poison gas, and above all at their attacks on liners conveying civilians and on hospital ships conveying the wounded. Of all the motives that inspired our nation in 1914–18 none perhaps was stronger than the determination to defeat a country which in these ways flouted the rules of war, and which openly declared that the end justified the means; and it was in the hope of preventing the triumph of such doctrine that great numbers of young men of the Allied Forces gave their lives. In 1939 the cause presented to their successors was not perhaps very different; but this time there was no surprise at our enemy's bombing of open towns, and the minds of nearly everybody were soon adjusted to the policy of retaliation which ended in the destruction of so many Continental cities and so many of the people in them. By the time the first atom bombs were dropped on Nagasaki and Hiroshima we had come a long way from the dum-dum bullet. Rightly or wrongly, we had reconciled ourselves to the annihilation of any member of an opposing group, whether old or young, man or woman, under arms or not. And to annihilation the atom bomb added the possibility that our action would so damage the genes of survivors that our enmity would reach even their descendants.

On the practical rather than the moral plane, the use of new weapons requires further thought because they are becoming so powerful that their effects may

soon be incalculable. Many will be grateful, therefore, to a member of our profession, Prof. ALEXANDER HADDOCK, both for his plain statement of the risks now developing and for his proposals for meeting them.¹ The events in the Pacific, he says, bring to an end the notion that the area of danger can have any but relative meaning, and he goes on to speak of the subtler menaces arising from the liberation of radioactive products. "We approach," he thinks, "the time when future risks must be envisaged on a terrestrial scale, with more than a hint of new kinds of catastrophe from increased physical incalculability"; and this opinion has since been given further point by the announcement² that there is now no obstacle to making "the most dreaded weapon of all"—a cobalt bomb which on explosion is transformed into a radioactive cloud that will travel thousands of miles, destroying all life in its path.

"The solution," Professor HADDOCK continues, "is one for statecraft and not for science as such. Yet the issue is so universal, and the Governments of the world are so compromised in their attitudes towards it, that we must despair whether there exists in fact either the mechanism or the will. . . . If all solution is beyond the present means, the question must be raised whether the representatives of world science itself, imbued by some sense of humane responsibility, can assist in the judgment."

"While the crisis is unlikely to be affected by the endeavour of any single individual today, such would not necessarily be so were the issue transferred, under the aegis of the United Nations, to a concilium of world science, representing especially physics, chemistry, biology, and medicine, representative also of their nationalities, yet supranational in outlook, of an authority transcending that of the politician, and with an unimpeachable primary loyalty to humanity as a whole. From such a body, and possibly from such a body alone, might we expect a factual appraisal and an advocacy of policy of such overwhelming weight as to command itself to the whole of the civilized world."

"International relations is clearly not a discipline susceptible to the scientific method, yet it could perhaps be affected by the outlook of science, and some approximation made towards an analysis of the contemporary situation, more objective than those monumental travesties to which, from one side or the other, we are sufficiently accustomed."

Three months ago we suggested that in facing this further year of peril the chief need was to keep a sense of proportion. That need remains; but a sense of proportion is not maintained by pretending that very big things are really quite small. In the discussions of the past few weeks some have argued that an unnecessary fuss is being made about a weapon which is only the latest in a long series of lethal developments in the art of warfare—from the bow and arrow to the bacterial toxin. To this the answer is that in this process of development there are certain profoundly significant points, of which one was the agreement to the mass bombing of cities, another was the first use of atomic fission for the same purpose, and a third is the possibility that we are moving from the indiscriminate to the incalculable. At any such point a pause for thought is proper; and before we teach ourselves to regard the hydrogen bomb as a legitimate means of protecting our civilisation we should consider what effect such protection is having on the civilisation itself. Man often kills the things he loves; and if by civilisation we mean freedom of speech and belief, a good conscience towards others,

and a respect for human life and personality, we may find that it is being sacrificed in its own defence. There are indeed already signs of our acquiring a barbarity of thought that makes us unfit to be its defenders.

The moralists say that if an end can be reached only by evil means, that end must itself be evil; and few of us can have any real doubts about the wrongness of wiping out a city or a nation with a bomb. On the other hand the mere existence of this invention is not necessarily an evil, and it may even prove our salvation if it induces the leaders on both sides to consider objectively whether the differences between us really justify and necessitate the continuance of an undeclared war carrying such risks for everybody. At present both sides are strong in armaments but nevertheless afraid; and the reason for their fear is largely that neither ceases for a moment its efforts to undermine the position of the other. Is it too much to ask that, as a first step towards the return of human relations, both should call a truce to this aggressive propaganda? Profoundly though we may disapprove of the Eastern régimes, we should remember that their citizens think they have reasons for no less disapproval of the West; and in trying to preserve a sense of proportion we should not forget that half the nations of the Free World were once our own enemies, either because we hated their tyrannies or because they hated ours. If by curbing our fears and restraining our threats we can avert a conflict which will ruin both worlds, the two different civilisations may be able to live side by side and eventually absorb what is best in each other. On a historical view such coalescence of rival groups is very far from being impossible; and its attainment must be the aim of all who recognise that, for survival, all men must come to regard themselves as members of a single group—in which homicide, by any method, is forbidden.

Detection of Tuberculous Contacts

BURIED beneath the mortality-rate and the notification-rate lies the epidemic pattern of tuberculosis, as secret and tenuous as the mycelium of a mushroom-bed. Neither rate gives a reliable map of its ramifications: the deaths have fallen fast in the last five years, the notifications hardly at all, as Dr. TATTERSALL¹ has pointed out in our correspondence columns; indeed in Scotland in 1953 they were slightly higher than in 1952. Nevertheless, the greater the proportion of cases detected, the more informative the notification-rate will become. The situation is complicated by the fact that patients with advanced disease are now living longer and perhaps adding to the risk to other people. Our greater success in making the tuberculous sputum-negative may not offset this as much as we hope if, as Dr. STEWART and Dr. VAN ZWANENBERG suggest in their letter this week, we cannot rely on bacteriology in determining the infectiousness of a particular patient. As things stand, it is still very hard to assess either prevalence or risks. But our lack of a perfect map need not prevent our doing much more than we are doing to contain this disease.

A memorandum from the Ministry of Health,² designed to help medical officers of health to review

1. *Times*, March 30, 1954, p. 7.

2. *Ibid.*, April 8, 1954, p. 5.

1. Tattersall, W. H. *Lancet*, April 3, 1954, p. 730.
2. Prevention of Tuberculosis. Circular H.M.(54)30.

their own programmes of control, rightly insists that the chief cause of primary infection is close contact of a susceptible subject with an infected person. Spread from other causes—from inhalation of infected dust, for instance—is nothing like so important. The first job of the preventive team, then, is to find every infected person and notify him. Notification of every case discovered, indeed, is an essential contribution to prevention which all clinicians, in or out of hospital, ought to make. For only when a case has been notified can the M.O.H. set about finding out where the patient got his infection and whether he has infected others. The Ministry thinks that if as much effort were put into tracing sources and contacts of tuberculosis as is put into tracing sources of typhoid or contacts of smallpox, we should make faster progress. Contacts should not only be examined : they should be kept under observation for a time to see whether they are incubating the disease, or whether, in common with the index case, they are exposed to a source of infection not yet detected. Children, adolescents, and young adults naturally need the closest supervision ; and all tuberculin-negative contacts, of whatever age, should be given whatever protection B.C.G. vaccination confers. Local health authorities are now at liberty to give this vaccine to children about to leave school, and the Ministry has published a circular³ and memorandum⁴ on the subject.

In tracing sources of infection, skin tests can be very useful, and they could be applied much more widely than at present to investigate the family contacts of an infected child, and so to trace the person by whom he was infected, or even the source of infected milk. Surveys of the family contacts of tuberculin-positive school entrants have yielded a high proportion of infected adults ; and the Ministry thinks that further studies of this kind would be valuable. Skin testing at other ages may also be informative : thus when a child seen at a chest clinic is found to have a primary infection or adult-type tuberculosis, the skin testing of his class and teachers at school may reveal an unknown case in another child or an adult. Indeed, skin tests could be used, STEWART and VAN ZWANENBERG believe, to map the incidence of infection in various age-groups, and in different schools, throughout the country. This would give us a picture of the black spots, and, as the years go by, a measure by which to judge the success or failure of our attempts to control the disease. In areas where not all milk is pasteurised the discovery of a high proportion of tuberculin-positive children may reinforce a campaign to get rid of bovine infection. Repeated radiographic examination of school staff seems a reasonable precaution, and one to which no teacher ought to object—though it is not always easy to be enthusiastic about an investigation when one's livelihood depends on the result. The Ministry favours the selective use of mass radiography rather than the examination and re-examination of large groups. Patients referred by their general practitioners, and patients attending hospital, give a relatively high yield of positive findings, and it is often useful to radiograph the work group of a patient newly diagnosed at a chest clinic. Similarly the

appearance of several cases in one village is a good argument for a survey of the whole population by radiography and skin testing. The Ministry also holds that all pregnant women should be radiographed as part of routine antenatal care.

In short it believes that the M.O.H., the chest physician, the family doctor, and the mass-radiography unit, working together and consulting often, can apply the traditional methods of epidemiology, and the newer techniques of radiology and skin testing, to the detection of the epidemic pattern of tuberculosis in their area. It is particularly important, the memorandum adds, that the general practitioner should be fully informed about what is going on ; for without his support the campaign cannot succeed : and indeed its complete success depends on the active collaboration of everyone concerned in the detective work.

The Sardinian Campaign

IN 1945, when the destructive consumption of war mercifully ceased, the Allied nations diverted their geared-up production and surplus stores to beneficent uses under the direction of UNRRA ; in addition, the United States provided dollars to aid recovery in Europe under E.R.P. In the Italian sphere the first call on these materials and funds was for emergency work, such as controlling malaria and other epidemic diseases. But members of the UNRRA mission were anxious to invest some of the funds in work of lasting value. Dr. F. L. SOPER, of the Rockefeller Foundation, proposed a mosquito eradication campaign ; and Sardinia was chosen because, being an island, it is a relatively isolated unit and because it was the most malarious part of Italy. Members of the Rockefeller International Health Division had behind them successful eradication campaigns in Brazil and Egypt. They had established that, at least in some circumstances, extensive and vigorous eradication work could obviate the trouble and expense of routine control measures. With this background, it was intended to plunge directly into a similar campaign in Sardinia, relying on administrative experience gained in earlier schemes and on existing knowledge of the Sardinian malaria vector, *Anopheles labranchiae*.

In October, 1945, UNRRA agreed in principle to the project, which was to be carried out jointly by the Italian government, UNRRA, and the Rockefeller Foundation (which supplied technical staff and extra funds). A special agency known as ERLAAS (Ente Regionale per la Lotta Anti-Anofelica in Sardegna) was set up to conduct the campaign. Delays in assembling staff and equipment deferred the start of eradication work until early in 1947 ; but this was no misfortune, since it gave time for a survey of the island by a malarialogist and an entomologist. By 1947 it was realised that this campaign, aimed at the extermination of indigenous mosquitoes, would be much more difficult than the earlier campaigns, which had dealt with mosquitoes intruding into new territory. Furthermore, the Brazilian schemes had attacked highly domestic strains of mosquitoes which were never found breeding far from man ; whereas *A. labranchiae*, though a man-biter, will readily breed in remote places and feed on wild animals. To offset these difficulties, there was the new weapon of

3. Circular 22/53.

4. Memorandum 324/B.C.G.

dicophane (D.D.T.), for attacking both larval and adult mosquitoes. Dicophane house-spraying programmes had substantially reduced malaria in continental Italy and elsewhere; but in these regions the behaviour of the anopheline vectors was very different from that of *A. labranchiae* in Sardinia. Thus, in the potentially malarious Roman Campagna this mosquito inhabits a relatively crowded agricultural area. The adults readily enter houses to feed and rest, and a high proportion of the mosquito population soon encounters dicophane. In Sardinia, on the other hand, the people live in few compact villages surrounded by wild territory; and most of the adult mosquitoes rest in caves and other natural shelters, safe from residues of dicophane. Accordingly, though the campaign against *A. labranchiae* in Sardinia included several island-wide house-spraying operations, the main attack consisted in tracing and treating all breeding-places; and in 1948 this attack was extended throughout the island. When it was found that many breeding-places were inaccessible, an enormous army of workmen, numbering up to 30,000, was recruited to clear vegetation and drain swamps so that the 6000 larviciiders could treat all sites. A large force of scouts was employed to check the work. Despite all this effort, positive foci of *A. labranchiae* were found in many places in 1949, and attempts were made to eliminate these by vigorous local attacks. Yet almost as many breeding-sites were discovered in 1950, and when the campaign

finally closed in the autumn of that year it had failed in its object.

An ill-natured or ill-informed critic might dwell on the fact that, over a period of four and a half years, some 6700 million lire (about £3 million) had been spent without achieving eradication. But a great deal has been gained; for whereas in 1946 there were 10,000 primary cases of malaria and 75,000 relapses, the disease is now reduced to the vanishing-point. This is no mean gain; for the disease, as well as impairing the health of Sardinians, hindered colonisation of their under-developed island. Perhaps malaria could have been eliminated more cheaply; but in 1945 eradication of the mosquito seemed feasible, and no-one could then predict the outcome. It now seems probable that *A. labranchiae* cannot be exterminated without quite disproportionate effort and expense, and the Organisation were wise to cut their losses and stop in 1950. The final act of the Rockefeller Foundation has been to produce an account of the campaign, written by Dr. LOGAN,¹ who directed the work for most of the period. It is well that the lessons so hardly learned should be on record, for guidance of the many further anti-mosquito programmes that are afoot.

1. The Sardinian Project: An Experiment in the Eradication of an Indigenous Malarious Vector. By JOHN A. LOGAN, with the collaboration of Thomas H. G. Aitken, Guido V. Casini, Frederick W. Knipe, John Maier, and Athol J. Patterson. Baltimore: Johns Hopkins Press. 1953. Pp. 415.

Annotations

CHOLECYSTOGRAPHY AND CHOLANGIOGRAPHY

SINCE cholecystography was introduced by Graham and Cole in 1924, the radiographic examination of the gall-bladder with opaque media has been a routine and invaluable aid to the clinician in the diagnosis of gall-bladder disease. The contrast medium first used—tetrabromphenolphthalein—was soon replaced by the corresponding iodine derivative. Administration was at first intravenous, but later the oral route was adopted to avoid the systemic reactions which occasionally followed injection into a vein and the danger of sloughing of tissue from inadvertent local injection into the tissues. For some time there was doubt about the significance of failure to obtain any gall-bladder shadow. Experience, however, proved that the radiological finding of a "non-functioning gall-bladder" was fairly reliable evidence of disease; and Gordon¹ concludes that this finding is significant in about 94% of cases. Such a degree of reliability compares favourably with that of many other investigations which we regard as valuable.

In 1940 Dohrn and Diedrich² introduced an iodine-containing derivative of phenylpropionic acid which has been widely used (as pheniodol). It has the advantages that reactions to its oral administration are less common and absorption is more consistent. Moreover, since it is freely excreted also by the kidneys, it can be given without danger to patients with impaired liver function or even jaundice. Latterly it has been claimed that 'Telepaque,' a derivative of ethylpropanoic acid, causes even less alimentary upset and gives a denser shadow because its iodine content (66%) is 15% greater than that of pheniodol.³

The usefulness of these media depends on their concentration in the gall-bladder. They do not permit distinction between obstruction of the cystic duct and

failure of concentration due to disease of the gall-bladder wall; and they do not display the bile-ducts except in the rare event of radiography coinciding with the secondary filling of the ducts with concentrated dye from the contracting gall-bladder. What is required is a substance that will display the biliary passages without concentration in the gall-bladder. This property is claimed for a new agent, 'Biligrain Intravenous,' which is the disodium salt of adipic-di-(3-carboxy-2 : 4 : 6-triiodoanilide). It contains 64% of iodine, and after intravenous injection is excreted so rapidly into the bile-ducts that these are shown on radiographs taken 20–30 minutes after injection. The gall-bladder fills more slowly and is seen on films exposed about 2 hours after the injection. The practicability of cholangiography with biligrain intravenous is confirmed by Hornykiewytsch and Stender,⁴ Pahl,⁵ and other German workers. It is said to be well tolerated when injected intravenously; accidental paravenous injection results in transient burning pain but no necrosis of tissue. The extrahepatic and even the intrahepatic ducts are nearly always shown, provided liver function is not seriously impaired and the sphincter of Oddi is competent; stones in the common duct are demonstrated even with jaundice of recent onset.

If these claims are confirmed, biligrain intravenous should prove most valuable in the investigation of diseases of the biliary tract. It may prove particularly useful in the diagnosis of functional disturbances of the biliary tract both before and after cholecystectomy.

ANÆSTHETIC EXPLOSIONS

THE Ministry of Health's Working Party on Anæsthetic Explosions is expected to report soon on its investigations and to propose lines of research. Meanwhile Dr. Bullough describes on p. 798 of this issue a method of preventing the collection of explosive gases in the theatre by withdrawing them into the outer air. This method, which calls for a leakproof apparatus, does not reduce the risk of

1. Gordon, I. R. S. *Quart. J. Med.* 1953, 22, 261.

2. Dohrn, M., Diedrich, P. *Dtsch. med. Wschr.* 1940, 66, 1133.

3. See *Lancet*, 1953, i, 432.

4. Hornykiewytsch, T., Stender, H. St. *Fortschr. Röntgenstr.* 1953, 79, 293.

5. Pahl, R. *Dtsch. med. Wschr.* 1954, 79, 363.

explosion arising within the anaesthetic machine; but it will, as Dr. Bullough suggests, prevent explosions caused by ignition of a pool of gases outside the machine. A not inconsiderable advantage of Dr. Bullough's arrangement is greater purity of the theatre atmosphere. At the end of a long day anaesthetists, despite their acquired tolerance, are sometimes more noticeably sedated than at the outset.

In this week's issue of the *British Medical Journal*, Dr. J. G. Bourne draws attention to a danger of cyclopropane anaesthesia for dental extractions. A spark may be given off when forceps slip on a tooth; and Dr. Bourne finds that after administration of a mixture of 50% cyclopropane and 50% oxygen, the expired gases may be ignited by a spark up to the sixth exhalation after the anaesthetic is withdrawn. Cyclopropane, he says, should not at present be used for dental extractions.

CONTROL OF TRICHINOSIS

FROM time to time outbreaks of trichinosis in Britain draw renewed attention to the need for improved control of this serious and not infrequently fatal disease. Man is infected by eating trichinosed pork, while the pig is thought to become infected usually by eating scraps of raw pork. In other countries certain other mammals have recently been shown to spread the disease; in Germany fox trichinosis is apparently widespread, and cases in domestic pigs may largely arise from ingestion of infected fox flesh. During a series of outbreaks of trichinosis in Greenland in 1947, examination of muscles of the mammalian fauna showed that nearly 70% of the sledge dogs and about 30% of the Polar bears were infected.

One way of countering the risk of trichinosis in man is to examine samples of the muscle of all carcasses of pork slaughtered for human consumption; and this method is followed routinely in Germany, Denmark, and other Continental countries. In British abattoirs no such routine examination is made; but isolated examinations from time to time have suggested that the prevalence of the disease in the pig population is low. In the U.S.A., on the other hand, trichinosis is a serious problem. Gould et al.¹ believe that, as a result of eating trichinosed pork, "about 25% of all Americans during their lifetime will harbour parasites in their muscles"; and 1·5% of the pigs slaughtered are infected with trichinosis. Only a small proportion of the pork is processed, under government regulations, by heating, freezing, or other methods.

Gould et al. have now described their investigations into gamma radiation of raw pork as a method of controlling the disease. They find that a dose of gamma radiation of Co⁶⁰ applied to infected raw pork will render sterile any adult worms which may develop in man's intestine after a meal of such pork, while a slightly larger dose will render the encysted larvae in the pork non-viable and prevent their development into adult forms. A preliminary study of irradiation with waste fission material contained in old nuclear fuel rods suggests that this may prove a suitable substitute for Co⁶⁰. It seems that the flavour of pork exposed to irradiation is unaffected, and no known harmful effect would ensue in a person who consumed it.

Further research on these lines will be followed with interest in this country, for the lack of data on the prevalence of the disease in our indigenous pig population must cause some concern. This gap should be filled by a country-wide survey. Another measure which would commend itself to public-health authorities is intensive propaganda drawing attention to the danger of pork products—particularly sausage—unless these are thoroughly cooked before they are consumed.

1. Gould, S. E., Gomberg, H. J., Bethell, F. H. *J. Amer. med. Ass.* 1954, 154, 653.

PERIPHERAL ARTERIAL EMBOLISM

THE events that follow impaction of an embolus in a peripheral artery are fairly clear. The soft mass of blood-clot is subjected, after its initial arrest, to the hammer-like blows of the pulse wave, which may cause its disintegration and further migration. Where the embolus is finally impacted the artery may be moderately distended, with reactive oedema and cellular infiltration in its wall. Shepherd¹ has shown that occlusion of the femoral artery over a short segment caused a sharp fall of intraluminal pressure distal to the block, but that, owing to the collateral circulation, within a few minutes the peripheral blood-flow approximates to a normal resting level, although the amplitude of the pulse wave is impaired.

After embolic occlusion the expected restoration of blood-flow through collateral channels may not occur. The reason for this has been much debated; and Richards² has marshalled much of the evidence in a review of 52 closely studied patients. The patient with a severe cardiac lesion may not have a high enough blood-pressure effectively to open up collateral circulation. Moreover the embolus may lodge at a bifurcation, such as the division of the femoral artery, obstructing both the main vessel and the major collateral pathway. Some³⁻⁵ believe that widespread arterial spasm, such as develops in traumatic lesions,⁶ follows lodgment of an embolus. But many would agree with Pickering⁷ that the idea of "vascular spasm, occurring in the absence of a recognisable stimulus is entertained too freely and uncritically in current thought and writing." The diminution in arterial diameter distal to the occlusion is probably quite often due to diminished arterial pressure; and Burton⁸ suggests that blood-vessels, being distensible tubes, have a "critical closing pressure." Thrombosis probably always extends beyond the site of embolism.

Richards concludes that the clinical onset of embolic impaction is usually sudden and dramatic. Pain, if present, is of two types: an initial pain most severe at the onset and localised to the site of embolic occlusion; and a delayed ischaemic pain felt more peripherally, which becomes so intense that it dominates the clinical picture. Absence of peripheral pulses, changes in colour and temperature of the skin, and muscle and nerve lesions are evident on examination.

Enthusiasm for embolectomy has decreased in recent years.⁹ Collective results published by Strömbeck¹⁰ showed that two-thirds of patients so treated died in hospital, and only 19% were discharged with adequate circulation in the affected limb. The case for embolectomy is perhaps strongest where the embolus straddles the aortic bifurcation. Milwidsky et al.¹¹ state that most patients with an embolus at this point die from shock or heart-failure shortly after the onset of symptoms, and those who survive the first day usually die from limb gangrene and infection. Albright and Leonard¹² cited 26 reported cases in which an aortic saddle embolus had been successfully removed by embolectomy. Milwidsky et al.,¹¹ however, describe 2 cases in which the patients

1. Shepherd, J. T. *Clin. Sci.* 1950, 9, 355.
2. Richards, R. L. *Quart. J. Med.* 1954, 23, 73.
3. Reynolds, J. T., Jirka, F. J. *Surgery*, 1944, 16, 485.
4. Holden, W. D. *Aacute Peripheral Arterial Occlusion*. Springfield, Ill., 1952.
5. Nystrom, G. *Lectures on Embolism and other Surgical Subjects*. Baltimore, 1936.
6. Griffiths, D. L. *Bril. J. Surg.* 1940, 28, 239.
7. Pickering, G. W. *Lancet*, 1951, ii, 845.
8. Burton, A. C. *In Visceral Circulation*. Edited by G. E. W. Wolstenholme. London, 1953.
9. See *Lancet*, 1953, ii, 1194.
10. Strömbeck, J. P. *Acta chir. scand.* 1935, 77, 229.
11. Milwidsky, H., Ehrenfeld, E. N., de Vries, A. *Angiology*, 1952, 3, 275.
12. Albright, H. L., Leonard, F. C. *New Engl. J. Med.* 1950, 242, 271.

recovered with conservative therapy; and such experience is probably not exceptional. In the arteries of the arm and the smaller peripheral arteries of the leg embolectomy has no place. Richards² agrees with Veal and Dugan¹² that embolectomy is indicated when the embolus has lodged in the femoral arteries if conservative measures have not brought about distinct improvement within a few hours. Under conservative treatment morphine is given for the relief of pain, and the leg is kept horizontal in an environmental temperature of 20°–25°C. The body is warmed by a heat cradle or electric blanket, in an attempt to open up the peripheral circulation; and sympathetic constrictor fibres are interrupted by a paravertebral block of procaine hydrochloride or 8% phenol. Heparin should be given, to control secondary extension of the thrombus. There seems to be no advantage in intra-arterial injection of vasodilator drugs. Should both patient and limb survive—as in 24 of Richards's 52 cases—symptoms of arterial deficiency ensue. Claudication, nerve palsies, and nutritional changes are common, and few patients are symptom-free.

The correct treatment for peripheral embolism is still undecided. For a balanced evaluation it is important that further well-documented series like that of Richards—and not only reports of cases successfully treated—should be published.

OXFORD UNIVERSITY AND THE RADCLIFFE

THE future of the clinical medical school at Oxford is again under discussion. Ever since the establishment some twenty years ago of the Nuffield professorial units at the Radcliffe Infirmary, the practical service of a large county hospital has been supplemented by these specialised departments to which postgraduates from all over the world have come for training. These units have worked out their respective spheres of action more or less amicably with the established services, but a difficulty here as elsewhere has been the scarcity of beds. After the late war the Radcliffe Infirmary developed from a large county hospital to become the centre of the regional hospital organisation under the National Health Service.

In 1939 the teaching facilities in the Radcliffe were extended to allow for a complete medical course to be taken in Oxford, and in 1943 in the Goodenough report Oxford was envisaged as a small medical school of carefully selected students, taught under the tutorial system, the stress lying on the scientific aspects of medicine. On this suggestion medical opinion in the university is sharply divided: some feel that the pre-clinical and clinical departments could work closely together to this end, while others favour a wider training for a putative specialist, and doubt (as we do) whether he should be selected so early in his career. Certainly the clinical school will have to attract a number of candidates of a high intellectual calibre, which may not be easy for a young school competing with the prestige of the older hospitals in both medicine and sport.

Oxford University has now written to the Minister of Health asking for a controlling voice in the management of the Radcliffe Infirmary, so that it can develop as a teaching school on the lines of the Goodenough report, with the Nuffield professors of medicine, surgery, and obstetrics and gynaecology in full control of their departments, as regards finance, appointments, beds, and laboratory space. On this plan cases deemed unsuitable for teaching would presumably be admitted to such hospitals as the Churchill, a munificent present from the American Armed Forces to the City of Oxford. At present the allocation of cases between the two depends both on the facilities available and on their relative sites, the Churchill standing high above Oxford on the slopes of Shotover; and an artificial division of ill people into

teaching or non-teaching cases would not be universally approved. The university says that its dissatisfaction with the present teaching arrangements was apparent to the hospital board when an application for the quinquennial grant was made in 1951 to the University Grants Committee; but the board state that they have never been informed exactly what changes the university desires in the teaching facilities, and express regret that they were not asked to comment on this letter to the Ministry until after the decision had been taken to send it. They are clearly anxious to fulfil their two great responsibilities in the Radcliffe Infirmary—to keep up its great tradition of service to the surrounding district, and to contain a thriving young medical school backed by the old-established preclinical departments. We should expect from Oxford a statesmanlike solution to this problem.

EGGS AND RHEUMATIC FEVER

FEW would now dispute that infection with β-haemolytic streptococci plays an important part in the aetiology of rheumatic fever; but the absence of these organisms from the rheumatic lesions themselves has led to the view that the true cause is some circulating toxic product of the organism; and since a first attack of rheumatic fever does not usually become manifest until 2–3 weeks after the streptococcal infection, the rheumatic lesions are usually regarded as the result, not of direct action of streptococcal toxin, but of an allergic reaction between the toxin and its specific antibody.

In epidemics of streptococcal sore throat, the incidence of rheumatic fever is usually about 3%.¹ Apart from some genetic predisposition little is known of the factors that lead to this complication. Nutrition has long been regarded as a possibly important factor, especially as the incidence of the disease is higher in the poorer members of the community. Coburn² showed that a supplement of egg-yolk powder equivalent to 8 eggs per day apparently had a significant protective effect in a small group of children known to be susceptible to rheumatic relapse after a streptococcal infection. Moreover, of 14 rheumatic children of wealthy families, only 1 ate a normal diet and 10 did not eat eggs at all. The mechanism of this protection was obscure, but Coburn was inclined to associate it with the rise in the serum-cholesterol level induced by eggs.

Wallis³ has again drawn attention to the apparent protection afforded by this food. His evidence is based on the results of questioning 184 patients with rheumatic heart-disease and 1380 normal controls. Despite the undoubtedly errors that must mar such an investigation, the results are suggestive. 40·6% of all the cardiac patients asserted that they ate few eggs in childhood, and 10·2% expressed dislike for eggs; the comparable figures in the control group were 16·3% and 4·6%. In an attempt to explain this observation, Wallis and Viergiver⁴ concentrate particularly on the level of the serum inhibitor of the serum extractable haemolysin of β-haemolytic streptococci—the so-called streptolysin S. It is now established that this naturally occurring inhibitor is, or is closely related to, plasma-phospholipid, and Wallis and Viergiver seek to correlate the protective value of eggs with their stimulating effect on plasma-phospholipid synthesis. They rightly point out that choline, an essential constituent of most of these phospholipids, is present in unusually rich amounts in egg-yolk; but they err in classing choline among the indispensable dietary constituents, since the body can readily synthesise all the choline it requires provided the intake of labile methyl

1. Rammelkamp, C. H., Denny, F. W., Wannerman, L. W. *In Rheumatic Fever*. Minneapolis, 1952.
2. Coburn, A. F., Moore, L. V. *Amer. J. Dis. Child.* 1943, 65, 744.
3. Wallis, A. D. *Amer. J. med. Sci.* 1954, 227, 167.
4. Wallis, A. D., Viergiver, E. *Ibid.* p. 171.

13. Veal, J. R., Dugan, T. J. *Ann. Surg.* 1951, 133, 603.

groups from other sources (e.g., methionine) is adequate. That choline is not deficient in rheumatic fever is confirmed by the absence of any signs of undue fat accumulation in the liver of patients with the disease. Furthermore, dietary deficiency of choline, while certainly affecting the phospholipid turnover in the liver, may nevertheless be associated with a rise in the plasma-phospholipids secondary to diminished intrahepatic utilisation.^{5,6} Since, therefore, there is no real evidence that a diet deficient in eggs leads to deficiency of plasma-phospholipid, and hence of the serum inhibitor of streptolysin S, and since, moreover, there is no experimental evidence that this lysis produces any lesions resembling those of rheumatic fever,⁷ the protection, if any, afforded by eggs cannot be explained on Wallis's hypothesis.

THE FEVER NURSE

The General Nursing Council's proposal to ask the Minister of Health to close the infectious-diseases register has disquieted both doctors and matrons, who predicted that such a step would gravely damage the service.⁸ The Minister of Health has now decided that the obligations of the council to maintain the register and to provide for admissions to it are to "remain in force for the time being".⁹

The G.N.C. suggested that training for the register was often unsatisfactory because of dearth of clinical material; and that, many of the training-schools being small, the services of sister-tutors were being used uneconomically. The council believed that the fever register might be discontinued without detriment, provided that suitable infectious-diseases hospitals were included in group schemes of training for the general part of the register. The Minister, though refusing to accept the council's proposal, is impressed by its reasoning. Training for the fever register, he says, should be concentrated in the larger units, and the smaller units should abandon the attempt to provide this training. Small hospitals are advised to take one or other of the following courses:

- (a) To seek to become part of a group training-school training nurses for the general register.
- (b) To seek approval as training-schools for assistant nurses in association with other suitable hospitals.
- (c) To form their nursing establishment on the basis of a nucleus of registered fever nurses assisted by enrolled assistant nurses and/or nursing auxiliaries.

In the Minister's view the needs of the infectious-diseases hospitals for specially trained staff can best be met by general-trained nurses with additional training and experience. Such nurses can be admitted to the fever register after a year's post-registration training; but the G.N.C. has approved several experimental courses of training whereby general-trained nurses can qualify for admission to the fever register after nine months' additional training. The council is also ready to consider approving experimental courses of integrated training for admission to both the general and the infectious-diseases parts of the register.

The Ministry strongly advises the management committees of the hospitals which continue to train for the infectious-diseases register to try to attract general-trained nurses to take the special training; and to give such applicants preference over untrained applicants seeking to take the two-year course. It would be interesting to know, however, in what the attraction is to consist. The vulgar subject of money is not mentioned in this circular; but the fact remains that a general-trained nurse who seeks a further qualification in infectious

diseases drops, on starting, some £15 per annum on the salary she has been getting as a staff nurse in a general hospital—a somewhat negative attraction.

HÆMOLYSIS AND ECLAMPSIA

Pritchard et al.¹ have described three cases of eclampsia complicated by severe intravascular haemolysis, thrombocytopenia, and deficiency of some clotting factor which was present in fresh normal plasma. Plasma-fibrinogen levels were normal; the patients' blood contained no auto-agglutinins or haemolysins, and in only one case was there rhesus incompatibility with positive direct and indirect Coombs tests. Corticotrophin (A.C.T.H.) was given to each of these patients, and in two, who died, the platelet-counts increased; but in the third, who survived, the platelets increased spontaneously, and Pritchard et al. believe that corticotrophin did not influence the course of the disease.

Although pigment casts are found in the collecting tubules of the kidney in fatal eclampsia,² such gross haemolytic episodes as those described by Pritchard et al. are uncommon. Young and McMichael³ described the "crush syndrome" in two women who had difficult labours; and Young⁴ reported several such cases, from which he concluded that this syndrome arose in obstetrics only with trauma to the maternal tissues or premature separation of the placenta. Paxson et al.⁵ reported a case of eclampsia with clinical and pathological features of this type.

Clotting defects due to fibrinogenopenia, and histological changes superficially similar to those of toxæmia of pregnancy, have been induced in animals by injections of thromboplastin⁶ and trauma to the placenta⁷; and fibrinogenopenia has been demonstrated in patients with eclampsia and retroplacental haematomas,⁸ in whom incidentally the plasma showed traces of haemolysis. Although fibrinogenopenia was not a feature in Pritchard's cases a derangement of normal haemostasis, which was not fully understood, was detected in both series, and a common aetiology may reasonably be suspected. Pritchard and his colleagues conclude that some immunological reaction was responsible for the condition they describe; and, if it cannot be explained in terms of the crush syndrome, at least the trend of their thought is shared by another group, who have likened the manifestations of eclampsia to a generalised Shwartzman phenomenon.⁹

Dr. J. GREENWOOD WILSON has been appointed medical officer of health of the Port of London.

1. Pritchard, J. A., Weisman, R., Ratnoff, O. D., Vosburgh, G. J. *New Engl. J. Med.* 1954, 250, 89.
2. Sheehan, H. L. In Ciba Foundation Symposium on Toxæmias of Pregnancy. London, 1950.
3. Young, J., McMichael, J. *Brit. med. J.* 1941, ii, 887.
4. Young, J. *Ibid.* 1942, ii, 715.
5. Paxson, N. F., Golub, L. J., Hunter, R. M. *J. Amer. med. Ass.* 1946, 131, 500.
6. Schneider, C. L. *Proc. Soc. exp. Biol., N.Y.* 1946, 62, 322.
7. Schneider, C. L. *Surg. Gynec. Obstet.* 1950, 90, 613.
8. Schneider, C. L. *Ibid.* 1951, 92, 27.
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⁵. Balfour, W. M. *Gastroenterology*, 1947, 9, 686.
⁶. Zilversmit, D. B., Entenman, C., Chalkoff, I. L. *J. biol. Chem.* 1948, 176, 193.
⁷. Barnard, W. G., Todd, E. W. *J. Path. Bact.* 1940, 51, 43.
⁸. See *Lancet*, 1953, i, 683.
⁹. H.M. (54) 34.

Special Articles

THE MENTAL HEALTH OF UNDERGRADUATES IN ENGLAND

A report on the first 18 months of a psychiatric service for students at the London School of Economics.

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In the major American universities the mental health of the students has for some years had systematic attention. The fullest reports have come from Yale and Michigan. In 1942 Fry and Rostow² gave a very readable account of a decade's experience at Yale, and Raphael⁹⁻¹³ has provided data of all kinds on the mental health of the students at Michigan University since the opening of a full-time service in 1930. Other valuable papers have come from Harvard,¹⁸ Minnesota,⁴ Oakland,¹⁴ and some of the medical schools.^{5 15 16 18 20} But in this country little information has been available. Parnell in 1947 drew attention to his finding at routine examinations that minor psychological disturbances are common⁷; but more interest was generally taken in his indictment in 1951 of mental illness as the most important cause of a loss of a term or more of residence at Oxford.⁸ A similar finding in a report for 1949-50 made to the University of Wales was noted by the *British Medical Journal*,¹ and *The Lancet*⁶ drew attention to Macklin's two-year study at Aberdeen which pointed out the bad effect of an overfilled curriculum. Other annotations in 1951 in both these journals refer to the unusual strains of undergraduate life and their effect on mental health. In the same year Verney¹⁹ commented on the influence of National Service on Edinburgh medical students, and Swainson¹⁷ described a project carried out by a lay therapist at University College, Leicester. But very little on the subject has appeared since then.

At the third Conference on Student Health in British Universities and Medical Schools, held under the auspices of the Nuffield Provincial Hospitals Trust at Cambridge in 1951, mental health was a good deal discussed. Of the many papers presented at that gathering the only one published is that of Henn,³ dealing with failure in examinations; but the privately circulated transcripts contained much interesting material and showed that at various universities special provision had been made for students needing psychiatric help. In London, however, little had been done except at University College, where psychiatric advice was provided by the student health centre.

AN EXPERIMENTAL SERVICE

In January, 1952, on the initiative of the Institute of Psychiatry, an experimental psychiatric service was established for students of the London School of Economics.

At this school there is no routine medical examination of new students, and it was thought inexpedient to try to discover the prevalence of nervous troubles by circulating questionnaires. To find out who would come for psychiatric advice, and for what kind of problem, a purely clinical approach seemed to be the right one. The only publicity given to the service, to launch it, was a meeting between the students' welfare committee and the psychiatrist, and a letter sent individually to the students inviting them to come for consultation if they were worried about their work or their personal life. The confidential nature of the service was emphasised, and the fact that no fees would be payable. The staff, also, were informed by letter of the purpose of the service.

The plan was to interview all who sought advice, and, after making sure they were not already in a doctor's hands, to take as complete a history as possible and, where it seemed proper, undertake treatment. It was arranged that in cases of serious breakdown the patient could be referred to the Maudsley Hospital. Six sessions weekly were held at the school, but those who preferred greater privacy could be seen at other times at the Institute of Psychiatry.

During the remainder of the 1951-52 session, 68 students came for advice and treatment. In the 1952-53 session, 63 new cases presented themselves. Thus the total for the whole period from Jan. 24, 1952, to June 30, 1953, was 131. Of these, in the first session 64 were full-time students (out of a total of 1743), and 4 were part-time students (out of a total of 402). In the second session 59 were full-time students (out of a total of 1753), and 4 part-time (out of a total of 434). 20 students first seen in 1951-52 were carried into 1952-53 which made the total dealt with in this session 83.

Because so many attended, patients were rarely seen more frequently than once a week. The usual length of an interview was fifty minutes, but the first usually lasted an hour. The number of times any one student was seen varied between 1 and 53, the average being 9. Ages ranged between 18 and 40 years (average 24½).

DIAGNOSES

The diagnoses were:

1. SEVERE CASES		
Affective breakdown
Mixed depression and anxiety
Acute anxiety attacks
Chronic anxiety state
Anxiety with disorder of physical function
Mixed anxiety and obsessional state
Obsessional state
Hypochondriasis
Conversion hysteria
Personality disturbances with marked social consequences
		27
2. MODERATE CASES		
Depression
Anxiety state
Anxiety with disorder of physical function
Emotional outbursts
Hypochondriasis
Asthma and dermatitis
Paranoid state
Obsessional state
Speech difficulties
Personality disturbances (inferiority feelings, study difficulties, &c.)
Marital and other family problems
Psychosexual difficulties
		44
3. MILD CASES		
Depression
Anxiety state
Emotional outbursts
Obsessional state
Hypochondriasis
Physical symptoms of functional origin
Personality disturbances (inferiority feelings, study difficulties, &c.)
Marital and family problems
Psychosexual difficulties
Other problems
		60

The allocation of these cases to one of the three categories of severity is necessarily imprecise. It depends either on the acuteness of the disturbance at first presentation or the degree to which the patient's nervous condition affected his social adjustment.

As examples of those put into the first group may be cited students with affective disorders who needed hospital care, those suffering from acute anxiety attacks so severe that they were physically ill, and those whose symptoms were so severe that it was obvious to their

teachers that they needed treatment and perhaps advice whether or not to continue with their studies. 11 of the patients allotted to this group had had psychiatric advice on some previous occasion and 5 of them had had frank breakdowns.

The patients placed in the second category are those whose symptoms were evidence of a considerable degree of disturbance but whose social adjustment was good enough for their distress to have remained to a large extent a private matter. In this group perhaps the clearest signs of improvement due to treatment are shown.

The third group is similar to the second but milder.

RESULTS

The table shows the result of treatment in those who came for more than one interview.

RESULTS OF TREATMENT

Category	Case complete or student left L.S.E.	Still having treatment
Severe :		
Much improved ..	4	1
Some improvement ..	7	8
No change ..	1	2
Moderate :		
Much improved ..	5	2
Some improvement ..	10	8
No change ..	11	7
Mild :		
Much improved ..	16	—
Some improvement ..	12	1
No change ..	8	2
Total :		
Much improved ..	25	3
Some improvement ..	29	17
No change ..	20	11

11 students terminated their treatment by default.

In 53 cases the emotional disturbance was affecting the student's studies in an obvious manner; in 15 of these treatment led to a definite improvement in this respect.

The therapeutic effects of the clinic are difficult to assess with any accuracy. So much else goes on in the lives of students, and so many of them are at a period of great change in their personal development, that such evaluations are even more hazardous than with the average series of results of psychotherapy. It can, however, be said that their symptoms improve and that the students connect this with their interviews and themselves suggest discontinuing as soon as they feel fit to do so.

The diagnoses of the 12 cases in the first two groups which showed a marked improvement are:

Acute anxiety attacks	3
Anxiety state	1
Anxiety with disorder of physical function	2
Obsessional state	2
Hypochondriasis	1
Personality disturbance affecting relations with others	2
Personality disturbance mainly revealed in study difficulty	1

To achieve this improvement the various types of anxiety required between 5 and 37 interviews; obsessional states 13 and 20; the case of hypochondriasis 30, and the personality disturbances 15, 23, and 41.

An effort was made to make the clinic self-contained and not to regard it as a stepping-stone on the way to treatment elsewhere, except for the few patients who were ill enough to need hospital care. Treatment at weekly intervals is not intensive, but patients of this age and intelligence seem definitely able to benefit from it. It is an advantage that the small amount of time

required interferes little with other commitments, an important consideration in view of the fullness of the present-day undergraduate time-table.

That the students in the first two groups can be successfully dealt with in such circumstances goes far to justify such a clinic as this; and there is reason to believe that some of them might have hesitated dangerously to seek help if it had been more difficult to obtain. All those in the third group, whose condition might be described as a neurotic reaction to a situation of temporary strain, would hardly be accepted for treatment elsewhere and yet undoubtedly need help. The undergraduate is living under conditions of special strain—intellectual, financial, and cultural. The healthy student will withstand this strain and may even benefit from it, but the more vulnerable individual gives way and begins to exhibit weaknesses and abnormalities which in less exacting circumstances would have remained latent. Such in varying degree is the situation of the students whose cases are enumerated above.

These emotional disturbances, unless severe, may pass unrecognised. This is illustrated to some extent by the fact that only 27 of the 131 students came for advice at the suggestion of their teachers; in the remainder there were only 20 of whom it could be gathered from the school records that they were in any way unstable. A psychiatric service of this kind permits the quickest contact and disposal for the severe cases, and the others have assistance which they would not find easy to obtain elsewhere.

CONCLUSION

From this eighteen months' experience it is clear that a service of this kind at a school or university has great advantages: teachers and administrators find it helpful to have a close contact with a psychiatrist in the case of need; and there is no doubt that students are prepared to seek advice when they feel themselves to be emotionally disturbed. None come frivolously and few show any inclination to prolong their attendance unduly: they have too much else to do. As they have the insight to seek help and the ability to use it when it is provided, a psychiatric service for students appears to meet a real need and deserves to become an integral part of a university school. It is justified by the immediate gain for certain students and the probable good effect on their future well-being; and over a number of years such a service would be a valuable source of information about the mental health of the community, because of the high intelligence and ability to communicate of its patients, who are drawn from a very wide range of the population.

Thanks are due first and foremost to Prof. Aubrey Lewis, of the Institute of Psychiatry, who conceived the idea of this service, gave it the opportunity to develop, and has supported it throughout with his advice and kindness; to the Board of Governors of Bethlem Royal Hospital and the Maudsley Hospital for financial support; and also to Sir Alexander Carr-Saunders, and the staff and students of the London School of Economics, for their hospitality to the experiment and their co-operation in running it.

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THE DISTRESSED STUDENT

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THE occupational hazards of a student are principally psychiatric. In its most specialised aspect, the work of a doctor in charge of a student health service concerns mental distress. Recently in this country there has been a considerable amount of publicity about mental ill health in the universities, and in particular about its tragic highlight—suicide. A general discussion of the topic may, therefore, be in order.

THE SIZE OF THE PROBLEM

How prevalent is student distress? What, in the unsatisfactory analogy of disease, is the morbidity-rate? It is almost impossible to answer this; for, except by an objective and dramatic action, like abandoning an examination, assaulting a professor, or committing suicide, the student only registers his distress if he comes and tells you. By no means all distressed people tell their troubles to others. Even when they do, it may not be to the university physician, but to a friend, or an academic supervisor, or even a doctor outside. Their unhappiness is then statistically non-existent. Again, the degree of distress which a person will suffer before coming to the consulting-room varies greatly. In America, where psychiatry is respectable almost to the point of being de rigueur, the number of people going to psychiatrists is higher than in this country, but one would hesitate to conclude that the sufferings are greater. At Oxford Parnell¹ was able to trace 9 suicides among 18,500 student years, whereas at University College, London, I am able to find only 2 suicides in 12,000 student years. Even as a Cambridge man, I find it hard to believe that the differences are due to the more heinous conditions at Oxford. They must reflect differences in the students' cultural backgrounds. Despite the difficulties, one must try to compose some sort of estimates.

At University College, London, there are about 2800 full-time students and about 600 part-time. Only a small proportion of the part-timers are likely to use the health service, so it might be fair to say the population at risk is about 3000. About 75 new cases of distress present themselves every year. Assuming an average stay at college of three years, there would be 225 students who had suffered, were suffering, or were going to suffer distress that would bring them to the consulting-rooms. This would represent something like 7½% of the total population. About half the students come from homes in the London area and live at home during their course; about half of these apparently do not use the health service. It seems probable that if, and when, they suffer distress and seek help, they go to their family doctor, or perhaps their priest, rather than come to us. If these few are included in our estimate, the prevalence goes up to 10%.

It is difficult to compare this estimate with the incidence of distress in other institutions because circumstances are

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always different. In the University of Michigan, which has a well-developed mental-hygiene service, 10% of the student body—the same proportion—had sought help at one time or another during their course. Most other American mental-health services have a similar attendance. In England comparisons are more difficult, but most of my colleagues would accept this general estimate. The round figure of 10%, then, is probably as close as one can get. It is a considerable figure and in practice must have considerable implications.

In this country, about 10% of the students who start at university do not finish the course. Most of these failures occur at the end of the first or second year. A small number repeatedly fail their final examinations. Since everyone who comes to university has presumably shown adequate intellectual ability in the entrance examinations, it seems more than probable that distress, as one meets it clinically, is a major element in this failure.

THE QUALITY OF THE PROBLEM

Psychiatric classification is an inaccurate necessity. The following has a rough utility:

Serious mental illness.—In this group are the psychoses (of which schizophrenia is far and away the most common), the melancholias, the confusional states, and those psychoneurotic disturbances that are so severe as to constitute an almost total disability. At University College over the last four years about 5% of distressed students fall into this category. In general this tallies with figures from many American universities and is similar to figures from other English universities.

Severe adjustment problems.—This empirical category covers those cases where distress is a major obstacle to the student's university career or personal happiness. Dealing with his distress is, therefore, his primary concern, for it compromises the possibilities of university success. Most of the students in this category have a definitely psychoneurotic personality and my clinical impression is that they will suffer psychiatric symptoms off and on throughout their life. At University College, about 30% of the distressed students can be classified here.

Mild adjustment problems.—In this equally empirical category are all those students who suffer distress which is a disability to them, yet not one of overriding severity. Such people may be successful in the university, both in their examinations and in their social life. Nevertheless, they are suffering unhappiness, and usually some diminished efficiency, and they come to the consulting-room in the hope of amelioration. At University College about half of the distressed students belong to this group.

Miscellaneous.—One is left, as always, with a mixed bag of cases—i.e., those referred by the departments for administrative reasons, and so forth.

HOW THE DOCTOR CAN HELP

For the university physician, the severe cases, paradoxically enough, are fairly easy to manage. Treatment is primarily for the qualified psychiatrist and it almost always involves interruption of studies and admission to hospital. It is the adjustment problems, serious or mild, that are the headache of university practice. Not only are they numerically the greatest, but their management, as a rule, falls to the physician himself.

The first step is to take a full history. This must cover not only such obvious things as the family relationships, social life, sexual life, and previous periods of unhappiness, but it must also go thoroughly into the student's academic record, his way of work, his hours of work, and all his particular studying difficulties. If there is any question in the patient's mind as to whether there could be any physical basis to his symptoms, a full medical examination must be undertaken. In my view, this full know-

ledge of the patient, and the personal rapport that is made in getting it, is the basis of effective help.

The simplest help one can give is by medication. A little judicious sedation with the ordinary barbiturates is a relief to most unhappy people. Sometimes a stimulant is more effective. Occasionally something a little more bizarre is indicated. Doubtless the psychological effect of bottles and pills is often as important as the pharmaceutical—no matter, it helps. All clinical work is empirical.

Advice is next in the clinical armamentarium. Simple study advice is often needed. Many students, particularly anxious students, overwork themselves greatly. They study till late at night, and when exhaustion impairs their efficiency they are overcome by mortifications and anxiety. If one can impress them sufficiently with one's own confidence, they may be prevailed upon to work more regular hours and stop before the point of tiredness. They may be persuaded to take up games or other social activities which, in their anxiety, they have cut out of their life to make way for work. They have not realised that the mind does not rest; it is refreshed only by variety. Simple physiological advice, even with reference to Kinsey, may be valuable. It is surprising how many young men in this enlightened age have not realised that masturbation, or even simple nocturnal emission, is an ordinary event, and not a hideous perversion. Sometimes a little straight advice about a love affair that has gone on too long works wonders. Sometimes financial problems have to be discussed so that a bursary can be arranged. Sometimes loneliness or homesickness can be countered by getting an all too scarce place in a university hostel. All these things, many of them in essence hardly medical at all, have a prominent place in the treatment of student distress, particularly in the treatment of the milder adjustment problems.

Support, by which I mean simply keeping in touch, seeing the patient again in a week or a fortnight, is also an essential part of treatment. It may not always be necessary to fix appointments in advance, but it is essential to impress upon the student that he has immediate and easy access to you and that you are pleased to see him and not bothered by him. Not to have to carry one's problem quite alone lightens it a lot, and many a student will be helped by being able to see one repeatedly, even, as it were, only to gossip.

There is no doubt in my mind that a fair proportion of students with severe adjustment problems cannot be helped without formal *psychotherapy*. Any university doctor is bound either to undertake some such treatment himself, or to refer cases for treatment elsewhere. Only a minority of distressed students need psychotherapy, but for them it is irreplaceable.

For a student to begin a course of psychotherapy, particularly a course of psycho-analysis, brings its own problems. Not only is it time-consuming, but it takes a great deal of mental energy. Its immediate aim is not to establish a day-to-day working compromise, but to bring to the surface difficult emotional problems, forcing them into prominence so that they can be grasped and dealt with, however painfully. Often the student, held into the trammels of an academic course requiring regular and repeated effort, finds it difficult to manage the two things at once. In general the simpler procedures of medication, advice, and support, all that is sometimes called "counselling," are the most appropriate to treating distress among students. Supportive therapy, which cannot be continued indefinitely, has been criticised as a transient and palliative procedure whose benefits will fade once the patient is discharged. But the circumstances and difficulties of the student are themselves transient, and in this work supportive therapy has a place of election.

CAUSES OF DISTRESS

Most of us, having in mind some vague image of summer punting on the backs, think of a university as inherently pleasant. When we realise that many young people are far from happy there, we instinctively feel that there must be something, or some combination of things, superimposed to prevent its natural joy.

Many factors have been invoked as such malign influences. The syllabus is overloaded. Games and recreational facilities are inadequate. There is a dreadful lack of hostels and halls of residence. Social contact between students and dons is less than it used to be. Interest in religion is waning. The grants system sometimes brings up students unsuited for the university as it is, particularly when there are great discrepancies between the cultural backgrounds of home and college. All these things are important and all take their toll. But there is more to it than that. Difficulties, of one sort and another, are the common stock of life, but they do not usually make such havoc of happiness and achievement. More and more I come to feel that for many people there must be some element of severe emotional strain implicit in the process of higher education itself.

But why should university life be difficult? I should say that learning—taking in—absorbing—is essentially a faculty of the young, of the prepubertal. On reaching physical maturity, an animal—or man in the more natural state—becomes independent, fends for himself, takes a mate, produces offspring, initiates rather than copies, acts rather than learns. His modus operandi becomes out-going rather than in-taking. In society, however, we block the simple course of Nature. The physically mature is still socially immature. By enjoining a further long period of education, we impose a period of psychological childhood on the physiological adult. For however courteous and sophisticated a university may be, being an undergraduate involves, in essence, a childhood situation. It means a greater or less period of celibacy; a greater or less period of dependence, either on the parents or on a benign parental government; and essentially a period of intensive learning—of in-taking rather than out-putting. It is this discordance, inevitable in a modern society, which I suggest is the implicit difficulty of the student. Many can cope with it and come through their university career with happiness and vigour. Many, even sturdy people, patently cannot.

It may be, then, that the present casualty-list, great as it seems, is nearly as low as we can get it under the present conditions. Any radical improvement might involve really radical changes in the form of higher education. Good universities are soaked in tradition, as good Stiltons are soaked in port; they might find it hard.

Even assuming a preparedness for radical change, it is hard to know what could be done. The fact is nobody now knows where, how, or why the student comes unstuck. The university after all is a productive machine. Time and again we have scrutinised the raw material. Volumes have been written on student selection and thousands of pounds have been spent on selection research. Time and again we have scrutinised the finished product. Industry, the Civil Service, and the Armed Forces—all have advised us about the material they want, and what they in fact receive. Now we are beginning to scrutinise the rejects, the mental breakdowns, and the failures. I fancy the next step should be to scrutinise the machine. It is not sacrosanct, it was made by man, not sent by God. A very small part of the cost of the failures would support a full-scale study of the university, its students, and their mutual impact. Then, but surely only then, we could all make some really sensible suggestions.

DOUBLY HANDICAPPED CHILDREN

RAYNERS SCHOOL, PENN

ANY deaf child, if he is to learn to communicate with his world, needs his wits about him. But when his wits, like his hearing, are defective, then he is handicapped indeed : in a losing race, he falls steadily farther and farther behind his age-group. Yet his mental defect may not be great : he may well be merely feeble-minded ; or a high-grade imbecile, able to respond well to appropriate education. Rayners School, at Penn, in Buckinghamshire, caters for just such children, as well as for others who are deaf and mentally normal but handicapped in other ways.

FULL HOUSE

This boarding-school, now belonging to the London County Council, was first opened by the London School Board in 1900, in Hackney ; and for many years it was unique in providing education, training, and care of deaf or partially deaf children with additional handicaps. The school was moved from London to the comfortable Victorian house, "Rayners," in 1921. Here it is set in beautiful surroundings, in an old and famous village, with twenty-three acres of gardens and playing-fields about it. With 62 children in residence it is full—even too full. The big pleasantly coloured bedrooms which have become dormitories contain rather too many beds, the dining-tables are rather too crowded, the classrooms have had to be subdivided, the rooms are not quite light enough, and there is no school hall. The reason for this elbow-jostling is that Rayners—which takes children not only from London (though these have preference) but from all parts of the country—has a waiting-list longer than its roll-call. And so far there have never been any serious epidemics. All the same the work of the school would probably benefit, and the roll could certainly be increased if two or three modern classrooms rose up on the foundations of the old stables, lying near the house.

WORD AND SIGN

Meanwhile, it is a lively and cheerful place, and doing remarkably good work.

Of the 62 boys and girls between the ages of 5 and 16 now in residence, 34 are deaf and educationally subnormal, 17 are partially deaf and educationally subnormal, 2 are deaf and partially sighted, 2 are partially deaf and partially sighted ; and 7 have three handicaps apiece, 3 being deaf, educationally subnormal, and physically handicapped, 3 deaf, educationally subnormal, and partially sighted, and 1 partially deaf, educationally subnormal, and physically handicapped.

The fact that some have residual hearing raises an educational problem, as Mr. John H. Blount, the headmaster, has explained elsewhere.¹ For those who can hear a little, the oral system of training—speech and lip-reading—is the method of choice ; but when a child is both deaf and dull the great need is to get into touch with him—to establish some precise means of communication—so that his understimulated mind has a chance to respond and develop. In teaching such children Mr. Blount has no hesitation in using finger-spelling. The difficulty comes, as he says, from having children of both types working side by side. It would be better to have them in separate schools ; but he does the best he can by keeping them as far as possible in different classes. All the partially deaf children have hearing-aids, and every effort is made to get them to learn to lip-read and to speak. The generous staffing of the school—there are only about 8 children in each class—makes much individual teaching possible. However, when a deaf child finds it impossible to comprehend language (and lip-reading must follow and depend on the comprehension of language), he is taught finger-spelling. A remarkable development in his educability often follows.

It is generally held that once a child has been allowed

to learn finger-spelling he will never take the trouble to learn to speak ; and this is probably the case with most mentally normal children. Mr. Blount, however, does not join in the general condemnation of finger-spelling. His own parents, intelligent people, were both deaf, and had both learnt to lip-read and speak ; nevertheless, they agreed that in talking to other deaf people finger-spelling was often useful, because it was precise : if they wished to make absolutely sure that a message was understood they used finger-spelling. This is a practical point which deserves reasonable attention.

Mr. Blount would like to be able to segregate not only the deaf from those with partial hearing but also the educationally normal from the educationally subnormal children ; for, as he says, if it is thought undesirable to mix these two groups among children who can hear, how much less desirable it is to mix them when the children are handicapped by deafness. He estimates that there are, in England and Wales, about 240 children who need special education as deaf—or partially deaf—with additional handicaps. We need, he thinks, four schools : one, taking about 100 children, for the deaf and educationally subnormal ; another for about 60 partially deaf and educationally subnormal children ; and two others, each taking about 40—one for mentally normal deaf children with some other handicap, the other for mentally normal partially deaf children with some other handicap. A thorough examination of children in ordinary schools for the deaf would, he believes, bring to light quite 100 educationally subnormal children who had failed to profit by the oral method ; and these could be taught far more adequately in a separate school by finger-spelling.

SOME RESULTS

The children in the classrooms at Rayners are certainly alert and responsive, for the most part, especially to finger-spelling. The seniors, even if they do not choose to speak much, are not bad at lip-reading ; and the standard of school work (as judged by exercise books) is remarkably high : the best group of children—at present chiefly boys approaching leaving age—can read, write a neat hand, compose a good informative letter, and do quite advanced sums. They are also well-mannered, cheerful, attentive and friendly. In recreation time they play football or cricket on their own playing-fields, help the gardeners, or otherwise enjoy themselves in the grounds and countryside. Those who are normal mentally—and even some who are not—can hope to earn their own living : aftercare records show that 61% find satisfactory employment and become self-supporting, and a further 14%, though not entirely self-supporting, are also in satisfactory employment ; 14% prove to be unemployable, and end up in institutions, and 11% have either died or cannot be traced. This seems a record of useful work.

Medicine and the Law

Spinal Anæsthesia

A JUDGMENT¹ in the Court of Appeal has upheld the decision² of Mr. Justice McNair in an action alleging negligence in the administration of spinal anæsthetics. Both plaintiffs had had intrathecal injections of 'Nupercaine' in the same hospital on the same day in 1947, and both had later become paralysed. The judge found that the damage was caused by contamination by the phenol in which the apparently intact ampoules were stored, and he held that the anæsthetist was not negligent in failing to appreciate this risk in 1947. Their Lordships in the Court of Appeal agreed ; and Lord Justice Denning added : "We must not condemn as negligence that which is only a misadventure."

1. *Times*, April 9, 1954.

2. See *Lancet*, 1953, ii, 1089.

Reconstruction

THE AUSTRALIAN HEALTH SERVICE

UNLIKE our own health service, which began on the appointed day "all at once and nothing first," the Australian health service is being introduced in two parts and by easy stages. Long-term plans for capital expenditure on universities, medical schools, and hospitals will form the second part. The first part tackles the prevention and treatment of disease by the provision of free drugs, tuberculosis allowances, and medical and hospital benefits. A basic principle of the scheme is that eligibility for a large part of the benefits depends on voluntary insurance rather than compulsory contributions. The introduction last July of the scheme for medical benefits completed the first part, and offers a convenient opportunity to review the whole scheme.

The first moves were exercises in preventive medicine.

ANTI-TUBERCULOSIS CAMPAIGN

In July, 1950, generous tuberculosis allowances were introduced to ensure that people who were infected would not hesitate to accept treatment. Over 6000 new cases have been discovered since the allowances were introduced. The weekly allowances are :

	£ s. d.
Patient with dependant wife	9 0 0
Each dependant child	10 0
Patient without dependants receiving inpatient treatment free of charge	3 7 6
Patient without dependants not receiving free inpatient treatment	5 10 0

These allowances are subject to a means test which has regard to income but not to property. Thus a patient may have an income of up to £2 (£4 for a married couple) a week without affecting his allowance. Patients who receive these allowances must give up work temporarily and accept treatment and examination in an institution or at home according to medical advice.

The Commonwealth has also entered into an agreement with each State to carry out an anti-tuberculosis campaign. The Commonwealth has agreed to reimburse the States for all approved capital expenditure incurred after July 1, 1948, and all maintenance expenditure above the 1947-48 figure. As part of this national campaign each State has made compulsory the notification of all cases of tuberculosis. Everyone over the age of 14 must have his lungs radiographed. Anyone with tuberculosis and all contacts must accept any medical, X-ray, or bacteriological examination thought necessary. The States have also taken power to restrain recalcitrant patients (such as the tuberculous patient who is a chronic alcoholic) who are a menace to themselves and to the community.

FREE MILK

Another preventive measure introduced in 1950 was the provision of free milk for children. The Commonwealth now provides one-third of a pint of milk free on each school day in the year for 750,000 children under 13. All the States are taking part in this service.

PHARMACEUTICAL BENEFIT

In September, 1950, a limited number of "life-saving and disease-preventing drugs" were made available free of charge to everyone on a doctor's prescription. In the first three years 20 million prescriptions have been made up. At first the list, on which there were no compounds, contained 139 items, and by March, 1951, there were 185 items. The cost of the scheme for the first full year, 1951-52, was about £7½ million. Owing to excessive prescribing of some scarce and expensive drugs, notably the antibiotics, a measure of control has been introduced.¹

1. Dampney, M. J. *Lancet*, 1952, ii, 879.

By 1951 a doctor before prescribing streptomycin or chloramphenicol had to obtain a numbered authority from his State director-general of health. The minister of health may declare by regulation that a drug may only be prescribed in the treatment of a disease specified by him.

The list of drugs was prepared by an expert committee which from time to time advises the minister on the inclusion or exclusion of drugs. A research organisation has been set up in the pharmaceutical departments of the Universities of Sydney and Melbourne to test the purity and standard of the drugs supplied.

MEDICAL SERVICE FOR PENSIONERS

Early in 1951 a free family-doctor service, including free drugs, was made available for pensioners and their dependants. This includes everyone who gets an age, invalid, widow's, or Service pension (but not a war pension), or a tuberculosis allowance. The service does not include specialist treatment.

The doctor may make a small charge (not exceeding 5s.) for treatment outside the ordinary hours of his practice. The pensioner and his dependants are entitled, free of charge, not only to approved life-saving and disease-preventing drugs but also to almost all the drugs and preparations in the *British Pharmacopoeia* and any combinations of these, but not to proprietary preparations and medicinal or industrial gases.

The scope of medical services and the terms, conditions, and fee schedules of the doctors who provide them have been agreed by the minister of health and the Federal council of the British Medical Association.

HOSPITAL BENEFITS

These were introduced at the beginning of 1951 and are the first section of the scheme to be bound up with voluntary insurance.

There are two forms of hospital benefit. The first, usually called the "ordinary benefit," of 8s. a day, is paid by the Commonwealth to any approved hospital, public or private, in respect of each inpatient, whether or not he is a member of an insurance organisation.

An additional benefit of 4s. a day, called the Commonwealth benefit, is available only to members (or dependants of members) of a registered hospital insurance organisation. It is also available to pensioners.

Most organisations have waiting periods and do not pay benefit for diseases existing when the member joins. But a member, even when he is not eligible for benefit from his own organisation, can claim the Commonwealth benefit.

It is a condition of registration of the hospital insurance organisation that it should be prepared to pay a benefit of at least 6s. a day. A member of a registered organisation can thus count on a hospital benefit of at least 18s. a day (8s. ordinary benefit, 4s. Commonwealth benefit, 6s. private insurance benefit). These benefits are intended to cover only hospital board and nursing care. The cost of medical care is covered by the scheme of medical benefits.

The time of stay in hospital covered for benefit is at least 10 weeks for general treatment, and up to 15 days for maternity care. Doctors may recommend extensions.

MEDICAL BENEFITS

These latest benefits, which began in July of this year, are available only to members (or dependants of members) of an approved medical insurance organisation. But here again members are eligible for a government benefit even when they are not eligible for benefits from their private organisation—e.g., during a waiting period before qualifying for benefit and for chronic or pre-existing illness.

The medical benefit, which is paid directly to the insurance organisation, takes the form of a subsidy towards the cost of treatment. The government's aim is that their subsidy, plus the payment from the patient's own insurance organisation, should "cover the major portion of the doctor's bill."

The government subsidy varies according to the nature of the service. It remains the same whatever fee the doctor charges and whether the service is rendered by general practitioner or consultant. The government have compiled a table of their subsidies which has been divided into two schedules. The first (or minimum) schedule covers consultations and visits and the common medical, surgical, and obstetrical service; the second (or optional) schedule covers specialised services such as radiological, laboratory, and the less common medical and surgical services. An insurance organisation will not be approved by the government unless it provides benefits, at least equal to the government's subsidy, for all the services included in the minimum schedule. The following are examples of the subsidies offered:

Type of service	Commonwealth benefit	Commonwealth plus minimum private benefit
	s. d.	s. d.
Professional attendance, non-specialist (at rooms, surgery, or hospital) ..	6 0	12 0
Specialist attendance :		
(a) Referred by another doctor— first attendance ..	1 0 0	2 0 0
(b) Referred by another doctor— subsequent attendance ..	10 0	1 0 0
(c) Not referred by another doctor ..	6 0	12 0
Appendicectomy ..	5 12 6	11 5 0
Exploratory laparotomy ..	5 12 6	11 5 0
Cholecystectomy ..	11 5 0	22 10 0
Antenatal care—seven or less attend- ances (each) ..	6 0	12 0
More than seven attendances ..	2 2 0	4 4 0
Confinement and postnatal care ..	2 5 0	4 10 0
Antenatal, confinement, postnatal ..	3 15 0	7 10 0

An insurance organisation need not pay benefits for the services in the optional schedule, but its members are still entitled to claim the government subsidy. The government hope that with the backing of the new scheme the insurance organisations will extend their benefits, and members their insurance, to cover the optional schedule. The combined government and private benefits should, they believe, then "largely meet the cost of specialist services."

The government believe that most people who are barred by age and illness from joining a voluntary insurance society will probably be receiving an age, invalid, or widow's pension which will entitle them to free general-practitioner treatment under the pensioner medical service scheme. The Commonwealth subsidy will also be paid to indigent people who are not pensioners.

PROFESSIONAL REPRESENTATION

In his address to the World Medical Association last September, Sir Earle Page, F.R.C.S., F.R.A.C.S., who as minister of health for Australia is chief architect of the scheme, affirmed his belief that its most important feature was that the professions took their place as active partners, and helped to control and implement it through committees chosen from their own ranks. Disciplinary and advisory committees for medicine, pharmacy, and insurance have accordingly been set up.

In Australia, on financial and political matters the whole medical profession speaks through the Federal council of the B.M.A. The Royal Australasian Colleges of Physicians and Surgeons, whose fellows are all members of the Australian division of the B.M.A., have delegated discussions on these topics to the council. From this body the Federal government have been able to get a "representative opinion on all vital matters in a reasonable time."

Other professional committees include the advisory committee which determines which drugs should be on

the free list. It consists of four doctors appointed by the minister from a panel of six nominated by the Federal council of the B.M.A., a pharmaceutical chemist, and a pharmacologist, together with the director-general of the Commonwealth department of health, who is by law a doctor, or his nominee, and a secretary, who is a pharmacist belonging to the department of health. The committee recommends to the minister from time to time the drugs and medicinal preparations to be made available as pharmaceutical benefits, and advises on other matters referred to it by the minister. In the future, drugs or medicinal preparations additional to those already in use may not be prescribed except in accordance with the recommendation made by the committee to the minister.

Medical and pharmaceutical committees of inquiry have also been set up, on a Federal and State basis, to deal with professional misconduct in the pensioner and pharmaceutical services. All the members of the medical committee of inquiry are doctors—the Federal committee consisting of the director-general of the Commonwealth department of health and four members. The State committees consist of the deputy-director of health and four doctors nominated by the organised profession. Appeal to a supreme court against the report of the committee and the decision of the minister is allowed. In cases of obvious fraud and dishonesty, the government may act independently of the committees directly through their own legal department, though even these cases are usually submitted to the committee for report before action.

Public Health

Scotland in 1953

In a preliminary return for 1953 the Registrar-General for Scotland¹ reports that the birth-rate has risen for the first time since the late war. The rate for 1953 was 17.8 per 1000 population, which is 0.1 more than in 1952 but 0.4 below the average for the preceding five years. The death-rate fell by 0.5 to 11.5 per 1000 population. Deaths from all forms of tuberculosis numbered 0.26 per 1000 population, compared with 0.32 in 1952. The infant-mortality rate decreased from 35 to 31 per 1000 live births (the lowest figure yet recorded), and the stillbirth-rate from 26 to 25 per 1000 total births.

Infection from Telephones

Transfer of infection by telephone instruments has often been suspected, but no very serious instances of this have been disclosed by various bacteriological surveys. Williams² has found that the risk is apparently very slight.

Bacterial flora were counted in 153 examinations of telephones in central London street kiosks, in a large City office where no "disinfection" routine was followed, and in another office where weekly disinfection was practised. Swabs moistened in saline were inoculated on to blood-agar and into nutrient broth. *Staphylococcus aureus* was cultured from 7.2% of mouthpieces and 17.6% of earpieces; and one pneumococcus was found. Otherwise no pathogenic bacteria were isolated.

Laboratory experiments showed that *Staph. aureus* and *Streptococcus pyogenes* could survive for several days on the instrument, but suspended particles artificially inoculated on to it were not dislodged by an air current considerably stronger than that emitted in normal conversation. It therefore seems improbable that organisms in saliva or sputum can be dislodged by talking into the mouthpiece, or that there is any appreciable risk of its transmitting respiratory infection.

1. Quarterly Return of the Registrar-General, Scotland, for the Quarter ended Dec. 31, 1952. H.M. Stationery Office. Pp. 40. 2s. 6d.

2. Williams, R. E. O. Mon. Bull. Minist. Hlth Lab. Serv. 1954, 13, 52.

In England Now

A Running Commentary by Peripatetic Correspondents

They had applied for an indoor invalid chair and, to ensure that the need was genuine, they had been asked to attend my outpatient clinic. The patient was the husband, who told me how muscular dystrophy had begun in his right arm when he was 18. Now he was 49 and both arms, both legs, and his back were affected. Until lately, he had been able to walk a few steps, enough to allow him to get from room to room, but this was no longer possible. His wife, a plain little body with thick-lensed glasses, explained "Now I have to carry him about the flat, Doctor, and it is rather too much for me. That's why we want the indoor chair."

Undressing looked like being a tedious job requiring the help of two nurses. But the wife, bustling round like a hen with one chick, had the job finished in less than five minutes. Naked he was a pathetic sight—the great proximal muscle-masses melted away, thighs and upper arms like match-sticks, the grotesque hypertrophy of the calves unable to conceal the gross weakness of his foot-movements. Apart from his face, the only movements left to him were pronation and supination, a fair grip in both hands, and the ability to maintain, but not assume, a sitting posture. But here was no self-pity. As we talked, I learned that he managed to feed himself by having his arms placed on the table when, by supporting one elbow with one hand, he was able to convey food to his mouth with the other. He had traced the other members of his family who were affected and offered to lend me the genealogical tree. He willingly agreed to appear at a clinical meeting. At this stage something dawned on me.

"If this affliction began when you were eighteen, did you ever do any work?"

"I worked until I was twenty-one."

"When did you get married then?"

"Only a few years ago. You see my father and mother looked after me till then, but they weren't able to do so any longer. Then this lady, who was a good friend of ours, said I wasn't going to be sent away, and we got married, so she could look after me."

With a sense of unworthiness, I filled in the appropriate form. Another wheel-chair may ease their burden a little; but nothing can adequately reward this unknown heroine.

* * *

Beauty seems to be spreading. I am a peripatetic physician and journeys from one hospital to another can be varied. In the spring I always pick my way through a village which has the nicest green I know. Last month it was a mass of crocuses—purple, white, and yellow. What a poor description yellow is for that brilliant sheen in the sunshine. This month there are daffodils under the chestnut and elms. But, as so often, beauty is not effortless. I have discovered that many of the villagers subscribe half a crown a year to the upkeep of their green. Every year a few more flowers are scattered here and there in what was once unkempt grass. What is even better, other villages have imitated their neighbours. Lawns are now stocked with bulbs which will soon have their leaves braided so that the mower can do its work.

* * *

During a cocktail party the administrator of our hospital for mental defectives told me that if I needed any help in the garden of my new house he would gladly send me down a few of his "higher grades" to give me a hand.

The garden is a meadow-field stretching in gentle undulations to the still, mirrored waters of the canal. My intention is to convert it into a fine, smooth, shaven lawn on the style of the great château gardens which grace the banks of the Loire—or even those flawless, velvet lawns which hem the higher reaches of the Thames. I visualise a lawn so perfect that the sparrows would glance at their feet before alighting on it. With these ideas in my mind I grasped the administrator's offer and asked him to send me four of his best boys on the morrow.

When they arrived I selected one who looked as though he had a less elusive hold on his faculties than his colleagues. I appointed him foreman and he seemed well

satisfied with his early promotion. He said I would not regret my decision. He said he had always wanted to be a foreman and that he was a liberal and believed in free enterprise. This last remark was obscure, but I did not feel it necessary to follow it up.

I told him to get his men to take six inches of the top soil away from a restricted area next the house and then to level the ground with ashes. After watching them take away a few sods to make sure they had understood my simple instructions I went to work.

When I came home for lunch I was amazed to see only one figure in the field. This was my foreman. The other three were lost in an enormous hole and spadefuls of red clay were being ejected high into the sky like the debris from some nuclear explosion. The scene was apocalyptic. The foreman was shouting frenzied orders from the brink of the crater. Ever and anon he fired a fistful of clay at a flagging colleague. This was greeted from the belly of the earth with gales of ungovernable laughter. The hole was so near the house I feared for its foundations and rushed to the garage for a hose-pipe. It was clear the men had gone berserk and a sudden drenching might, I hoped, bring them back to a sense of their responsibilities.

I was assembling the pipe as fast as I could when my wife joined me and explained that she had striven valiantly to hold up the excavations, and, when she had failed in this, to deflect them away from the house and towards the canal. But the foreman was inflexible and told her I had given him instructions to dig a six-foot hole for an ash-pit, and that he had been a foreman far too long to take advice from a woman.

* * *

At our staff meeting last week a consultant complained bitterly that much of his work could be done at registrar level. His remark is not unjustified; but raises the fresh difficulty of defining the upper limits of the houseman's lowliness and the lower limits of the consultant's elevation.

For instance, the level of the surgical registrar, with his tail-end operating-lists for haemorrhoids and hernia, lies on a distinctly inguino-perineal plane, while that of his orthopaedic colleague is governed by centrifugal force, for his endeavours are confined almost exclusively to the big toe or the little finger. In the E.N.T. terrain the pillars of the fauces form convenient landmarks, golden gates beyond which a registrar rarely trespasses. In gynaecology and anaesthetics the level is not so much a matter of height as of depth, varying in direct proportion to seniority in gynaecology, and inverse proportion in anaesthetics. Classification of the psychiatric registrar is not feasible, for one can never be certain whether his level lies above or below the id.

What about the medical registrar? Why, I see all the patients over ninety.

* * *

When Uncle Arthur, home from the East, feels an attack of malaria coming on, he retires to his room with large quantities of whisky and hot milk. This prophylactic, he finds, never fails to abort the attack. Uncle Arthur has found it necessary to take these precautionary measures more often of late and it has strained his resources, both financial and diplomatic, to maintain an adequate supply of whisky. He might be expected therefore to welcome Professor Maegraith's discovery that a milk diet is protective against malaria and that, instead of being a mere innocuous vehicle for conveying the rare and expensive active principle, the milk itself is the specific agent in Uncle Arthur's prophylactic mixture. But Uncle Arthur is not convinced. He agrees, however, that there is a strong case for a properly controlled clinical trial and he is willing, in fact anxious, to participate. With a rare public spirit he is prepared to volunteer as one of the controls receiving the prophylactic mixture from which the milk has been omitted.

* * *

We were delighted to read¹ that the opossum, *Didelphis virginiana*, has at last come into its own and is to be used in psychiatric research. We can just imagine our psycho-analytical friend conning his appointments for the day: 9 A.M., the manic; 10 A.M., the anxiety; 11 A.M., the depressive; 12 noon, the opossum. Do you think he will hang upside down from the branch of a tree during his analysis?

1. Wiedorn, W. S. *Science*, March 19, 1954, p. 360.

Letters to the Editor

TREATMENT OF HYPERTHYROIDISM

SIR.—I should like to express my appreciation of your excellent leading article last week.

There is one point, however, which is open to criticism—namely, the care of the hyperthyroid patient after operation. You imply that thyroideectomy is very similar to appendicectomy, an incident in the patient's lifetime, and that after a fortnight in hospital and a fortnight's convalescence, she returns to work cured. This is not true of the great majority of cases. The postoperative thyroid convalescence consists in two stages: the primary stage starts immediately after operation, goes on for a few weeks, and brings a great improvement in the patient's health; but very often residual symptoms, especially fatigue and nervous phenomena, linger. The complete recovery may be long delayed, and the secondary advance may occur after nine, twelve, or fifteen months. The patient may, especially if she is debilitated and the disease is of long standing, improve more during the second year than during the first. It is possible for a careful clinical observer to foresee in which cases complete recovery will be slow, and such patients are very grateful if they are told beforehand that this slow progress is no reason for despondency.

If a patient is not progressing satisfactorily three or four months after operation, the following questions should be considered. Firstly, was the original diagnosis correct? Secondly, was the amount of thyroid tissue left at operation (estimated and recorded in the notes of the operation) what the surgeon judged to be the optimum amount? Thirdly, is there any concomitant condition hindering recovery? Fourthly, is there any adverse influence in the patient's life? The last question is most important. If, for example, a woman is living alone with a sister and constantly quarrelling, or if she is harassed by a dominating and interfering mother-in-law, or if she dreads return to work because she fears an overseer who has got a hold over her, it is most unlikely (however perfect the operation) that she will recover from her nervous phenomena until the exciting cause has been removed. If all these questions can be satisfactorily answered, the patient can be told with confidence that complete recovery will occur in due time.

Treatment with thiouracil is considered to act in the same way as thyroideectomy, only more slowly. This is not quite correct, for a patient who remains uncured under full treatment with thiouracil may quickly and dramatically respond to operation. Nevertheless, the parallel is close enough to suggest that these factors, which are borne in mind by the careful surgeon during the convalescence of his hyperthyroid patients, should also be kept in mind by the physician using one or other of the modern methods of medical treatment.

Bradford.

PETER MC EWAN.

KWASHIORKOR

SIR.—We agree with Professor Moncrieff¹ that discussions of the etymology of "kwashiorkor" are making heavy weather. If his suggestion were accepted that the word means "the deprived child" it would simplify the issue and fit in excellently with the concept of "protein malnutrition" in weanlings which has now been clearly defined.² It would also meet the criticism of Dr. Kahn³ that the concept of redness attached to the word is preventing people from diagnosing the

syndrome when the characteristic pigmentation of skin or hair is lacking.

In defence of the position which we took in our monograph,⁴ we must point out that we were concerned solely with the syndrome as seen in Africa, and we were urging what we thought to be a correct etymological use of the word kwashiorkor. We are dealing with the etymology of the word in another place, but there is no doubt that when the monograph was written the accepted meaning of "kwashiorkor" was "red boy," and there seems no doubt that the native names *mbuaki* and *diboba* do refer to the special pigmentation of hair and skin. The word kwashiorkor is derived from the Ga language of the Gold Coast, and scholars of this language assure us now that it did not refer to pigmentation but apparently to the psychological state which arises when the child is deposed from the breast at the time of a second pregnancy or birth. We therefore like Professor Moncrieff's suggestion that it should be regarded as meaning "the deprived child"; this would obviate further mental gymnastics on this subject, and would fit in well with the decision of the F.A.O./W.H.O. Committee to apply the name to similar or related syndromes throughout the world.² A decision to abandon the concept of redness would apparently have the support of Dr. Cicely Williams⁵ who introduced the word into European medical literature.

Turning to more practical considerations, we suggest that the term kwashiorkor should be used, at least in Africa, to denote protein malnutrition (subacute as well as acute), occurring during the late breast-feeding, weaning, and postweaning phase of life in regions or under conditions in which starchy paps are used as supplementary or postweaning feeds to the virtual exclusion of protein-rich foods (such as cow's milk, goat's milk, and mushes prepared from legumes, nuts, or fish). Since in Africa and many other underprivileged parts of the world the child is retained at the mother's breast until displaced by the next succeeding child, the syndrome comes to be one of the "displaced" or "deprived" child. In our monograph we confined our description to young children, although we recognised that a similar if not identical syndrome was seen at all ages in childhood, and even occasionally in adults. The new interpretations of the etymology of the word would apparently preclude its use in older children and in adults, but we leave this question open.

It is not yet clear how many of the considerable variety of physical signs and laboratory abnormalities must be present before it is legitimate to use the term kwashiorkor. The answer to this must await further knowledge of the pathogenesis of the disease. We agree that dyspigmentation of the skin and hair is not essential to the diagnosis, and that *mehlnährschaden* differed from kwashiorkor as we saw it in Africa only in the absence of the dyspigmentation of the skin and hair which is so often a striking feature of the African cases.

Dermatoses is certainly not necessary for the diagnosis, and the term *infantile pellagra* is misleading when applied to this syndrome. Pellagrous or pellagroid dermatosis occurs particularly in those children fed on a starchy pap prepared from maize (corn). Other types of dermatosis or no dermatosis at all may be found in those consuming other types of starchy pap. Some at least of the dermatoses are due to associated vitamin deficiency.

We agree with Dr. Kahn that this form of malnutrition may be primary or secondary, and that the syndrome may take a variety of clinical forms, but we do not

1. Moncrieff, A. *Lancet*, 1953, i, 1204.

2. Joint F.A.O./W.H.O. Expert Committee on Nutrition. *World Health Org. Techn. Rep. Ser.* 1953, no. 72.

3. Kahn, E. *Lancet*, 1953, i, 496.

4. Brock, J. F., Autret, M. Kwashiorkor in Africa. W.H.O. monograph series, no. 8. Geneva, 1952; *Bull. World Health Org.* 1952, 5, 1.

5. Williams, C. D. *Brit. med. J.* 1952, ii, 1360.

think it necessary to coin such terms as " malnutrition with fatty liver " and " malnutrition with kwashiorkor." The problem of terminology is simplified if it is accepted that the term kwashiorkor may be used to denote a spectrum of clinical states of " protein malnutrition " as defined by the F.A.O./W.H.O. Committee.² Each protein food differs in its amino-acid composition and is also the vehicle for other nutrients in varying combinations, the deficiency of which might, apart from amino-acids, play a part in the production of different features seen in this syndrome.

As long as the precise aetiology of the syndrome is no better defined, the name " kwashiorkor " seems to us, at least when applied to weanlings, to be as good as, or better than, any of the others in the list given in an appendix to the report.²

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M. AUTRET

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HOSPITAL BEDS FOR CHILDREN

SIR.—The estimate made by Sir James Spence and Dr. Mary Taylor (April 3) that 50 beds for children are needed for each 100,000 of population raises interesting issues in relation to the provision of children's beds in London. Comparable figures for London in 1950 are not readily available, but the following statistics of population and hospital discharges or deaths in the Administrative County of London for 1952 seem a reasonable basis for comparison :

	Newcastle 1950	London County 1952
Total population	294,800	3,343,000
No. of children under 15 years of age .. .	66,130	656,000
Children as % of total population .. .	22.4	19.6
No. of children under 15 admitted or discharged	4240	65,201
Children admitted or discharged as % of all children	6.4	9.9

The number of children discharged from London hospitals in 1952 is taken from the SH 3 returns submitted to the Ministry for that year. If anything, it is an underestimate, since only children discharged from children's hospitals or children's wards of adult hospitals are included ; children discharged from tuberculosis, infectious-diseases, and mental institutions are excluded, and some hospitals did not differentiate between adult and child discharges in their returns. The proportion of children treated in hospital in London is higher than in Newcastle. Why this should be so is hard to explain, but one reason may be that many children from the Outer Ring of Greater London and elsewhere are treated in the hospitals in London County. Again, since seven of the ten general children's hospitals in the county are teaching hospitals, more beds are needed in them to meet both teaching and regional needs, and the same applies to the children's departments of the other teaching hospitals in London.

According to Spence and Taylor's estimate, at least 1675 children's beds are needed in the County of London. Exact figures of the actual number provided are not readily available, but according to the SH 3 returns for 1952, 25,070 children were discharged from the ten general children's hospitals, with a total bed complement of just over 1000 beds, and 40,131 children were discharged from the children's wards of other hospitals in the rest of the county ; if the number of discharges bears any relation to the number of beds, these figures suggest that there are possibly over 2600 children's beds in London County. This figure can only be a rough approximation, since the method of calculation is not fully reliable, but it lends some strength to the argument that there may be more beds for children in

London than are really needed. The occupancy-rate (averaging 83% of the beds available in 1952) and the waiting-lists (over 4300 for E.N.T. admissions and over 1700 for other reasons) of the children's hospitals do not wholly support this argument, but it would be dangerous to draw dogmatic conclusions without information about children's wards in adult hospitals and about many other variable factors.

There seems to be a case for an investigation of this kind, leading to a consideration of general policy. If either now or in the future there should prove to be more children's beds than are needed in London County, or in Greater London, should the children's hospitals be developed as centres of paediatric treatment and education, and beds reduced elsewhere ? Or should the children's departments in adult hospitals be retained and the children's hospitals be reduced in number or size ? Or should children's hospitals and children's departments in adult hospitals alike be gradually whittled down by each governing body as it thinks fair ?

At present these questions, and the dependent issues of medical staffing and the training of nurses, are dealt with by a variety of bodies. Patients in London County are drawn from the areas of four regional hospital boards ; the ten general children's hospitals are controlled by six different boards of governors and two hospital management committees, and the children's departments of adult hospitals are controlled by over twenty-five other boards and management committees. Local-health authorities are also concerned. With so many interested authorities there is a danger that the problem, which is in many ways a regional one for London County and Greater London as a whole, may not be viewed as a whole. It perhaps merits more concentrated and coördinated attention than it has hitherto received.

London, S.W.5.

M. C. HARDIE.

THE FACE IN DIAGNOSIS

SIR.—I have read and re-read the interesting article by Pierrhos StKatsareas.¹ I should like to add to his long list a few more conditions in which the face carries stigmata of disease.

(a) In pellagra, the face, neck, and a V-shaped portion of the front of the chest show characteristic dermatitis. On the face this is often symmetrical and butterfly-shaped.

(b) In Egypt, it is common to see patients who have a pale face and chronic enlargement of the parotid glands—so-called endemic parotitis—a condition often found in patients with ankylostoma anaemia, although the connection between the two conditions is not clear.

(c) The face of the patient with liver abscess has a typical earthy colour.

(d) The patient with advanced carcinoma of the urinary bladder, cystitis, and ascending pyelonephritis has a typical appearance, though this is difficult to describe.

(e) The child with cervical Pott's disease is easily recognised because he is continually supporting his chin with his hand.

(f) In gargoyleism the face and the skull show characteristic features. The face has a peculiarly unchild-like look reminiscent of Tenniel's illustrations of the Duchess in " Alice in Wonderland." Whereas the hair is often fair and silky, the eyebrows are almost invariably dark and coarse. The eyelids, nose, and lips are grossly thickened. Deep creases run from the nose to the angles of the mouth. The bridge of the nose is depressed. In some cases, there is a moderate degree of hypertelorism. Distension of the skull veins has been described, the frontal veins lying in deep gutters. A characteristic feature is clouding of the cornea by multiple opacities. The skull varies considerably in size and shape, and is commonly enlarged. It has been described in different instances as hydrocephalic, scaphocephalic, and acrocephalic.

1. StKatsareas, P. *Lancet*, 1953, ii, 929.

StKatsareas's article included mumps, facial erysipelas, and labial chancre, so this may justify the mention of some other conditions in which the face is involved:

Rodent ulcer; epithelioma; leishmaniasis; lupus; dermoid cyst; sebaceous cyst; sebaceous adenoma; sebaceous adenocarcinoma; the various swellings connected with the parotid gland, including Mikulicz's syndrome and uveoparotitis; reticulosis (including Boeck's sarcoid); the various swellings of the upper and lower jaws; pachydermatocele and the café-au-lait patches of von Recklinghausen's neurofibromatosis; secondaries in the face, scalp, and skull from a malignant primary elsewhere; the various angiomas, cirrhotic and arteriovenous aneurysms; prognathism and congenital recession of the mandible; and proptosis, unilateral or bilateral, pulsating or non-pulsating.

The face may also bear stigmata of past trauma, surgical or otherwise:

Burns and Horner's syndrome (mentioned by St. Katsareas) auriculotemporal syndrome (mentioned by Dr. Parkes Weber²); drooping of the angle of the mouth following damage to the cervical branch of the facial nerve after operations high up in the neck; complete or partial paralysis of the facial nerve after operations on the parotid gland; deformity of the jaw after dislocation of the temporomandibular joint or operations on the joint or the mandible; and deformity due to depressed fracture of the zygomatic arch, fractured maxilla or mandible.

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THE CURABILITY OF CANCER

SIR.—I have read with great interest your leading article of April 3, which includes references to cancer education and early diagnosis. The value or otherwise of such education, even in the case of the breast, has not been proved, and still less for the other accessible cancers. Surely this part of the problem is of sufficient importance to justify further intensive research, which should be carried out "step by step," as indeed is being done on a small scale by the Yorkshire Council of the British Empire Cancer Campaign. Another experiment, I understand, is being carried out under the auspices of the Manchester Radiotherapy Centre, but there is room for much more investigation.

There are 5 fundamental questions to which answers are needed, in the following order:

(1) Will intensive education cut down the delay in reporting certain symptoms (about seven in number), whatever the cause may be, but which may suggest the presence of an accessible cancer in the breast, uterus, rectum, tongue and mouth, larynx, lip, and skin? Probably this is the only question likely to be answered by the small Yorkshire experiment.

(2) If the delay is cut down, will it result in an appreciably greater number of clinically early-stage accessible cancers being treated in hospital?

(3) If a greater number of early-stage accessible cancers are treated at hospital, will the "five-year cure-rate" of these accessible cancers be increased?

(4) If the "five-year cure-rate" is increased, will it result in a lower mortality from these accessible cancers?

(5) Will cancer education increase the apprehension, which at present exists in almost 100% of the population, or increase real fear, which happily exists in only a small proportion of the public? If it was proved that apprehension and fear were increased, this would be a very serious objection to public education, even if this could save a few thousand lives.

It would seem that Professor McKinnon believes the answers to (1) and (2) in cancer of the breast are in the affirmative, although exact critical figures published are few; and that the answer to (3) may be in the affirmative owing to the inclusion of a large number of non-metastasising, "non-lethal cancers." He seems convinced

2. Parkes Weber, F. W. *Ibid.*, p. 995.

that the answer to (4) is in the negative. The 5th question is very difficult to answer. In my opinion, after giving about 120 lectures within the last year to several thousand lay people, the psychological effect of such education is good; and the votes taken at the end of some of those lectures are overwhelmingly in favour—3348 in favour and 10 against. One thing is quite certain: if cancer education increases fear and apprehension, it will defeat its own purpose—namely, to get early diagnosis.

Everybody will agree that the most important factor governing the mortality from cancer is the type of tumour; but the question still remains, Are there a sufficient number of late metastasising but still "lethal" cancers to justify every effort to get the earliest possible diagnosis and treatment? Only a large-scale experiment on the lines suggested above can prove or disprove this.

British Empire
Cancer Campaign, York.

MALCOLM DONALDSON
Director of Cancer Survey.

BENZATHINE PENICILLIN IN YAWS

SIR.—Much attention has lately been given in the British medical press to the side-effects of antibiotics. Although penicillin has been used for a longer period than other antibiotics, its side-effects have only recently been appraised more thoroughly. Efforts have been made to develop penicillin-derivatives, such as allylmercaptomethyl penicillin, causing fewer sensitivity-reactions, and clinical trials have been undertaken in search of salts of penicillin with repository effect which would obviate the use of procaine or oily components now contained in repository preparations—e.g., procaine penicillin G in water or in oil with aluminium monostearate (P.A.M.). Thus, benzathine penicillin (N'N' dibenzylethylene-diamine dipenicillin G), also known as diamine penicillin, 'Penidural,' 'Bicillin,' 'Tardocillin,' &c., and benethamine penicillin (N'benzylphenylethylene-amine penicillin G), also known as 'Benapen,' have been described for oral and parenteral use in various infections.

The treponemacidal serum-levels obtainable with benzathine penicillin—a penicillinaemia of 2–3 weeks' duration follows a single injection—has made it an even more promising drug than P.A.M. in the treatment of syphilis. Recently this salt has also been tried in the yaws programme of the Thailand health administration. Among 236 yaws patients, some with early infectious yaws and others with palmar and plantar hyperkeratosis, side-effects were recorded in 11.2% of cases: 2.5% of the patients said they had been feverish for 2–5 days after the injection; another 5.6% had fever plus pain at the site of injection; and 3.1% had local pain only. On the other hand, there were no local or general skin-reactions or allergic responses in this series. Admittedly the reactions were assessed from the patient's own stories (no temperature measurements were taken), but their incidence was considerably higher than that reported (1%) with benzathine penicillin (and with P.A.M.) in the treatment of early syphilis in American patients. On the other hand, it is remarkable that the types of local and general skin-reactions and allergic responses which were commonest during the treatment of syphilis in the U.S.A. were not recorded at all among the yaws patients in rural Thailand. This suggests the importance of sensitisation by the widespread use (and misuse) of penicillin in industrial areas where the antibiotic is freely available, as contrasted with areas where the population has had no penicillin. There is also the possibility of a different underlying general tissue-response to stimuli of this kind.

In Thailand, two treatment schedules were used—namely, 0.6 and 1.2 mega-units of benzathine penicillin, given in a single injection. No difference in results between the two schedules was observed in either of the

two groups of patients. The clinical and serological effects after six months were excellent: complete healing of lesions took place in 98.0% and 89.7% of the early infectious yaws and the hyperkeratosis group respectively. While 14.3% of the patients in the former group became serologically negative, no case of hyperkeratosis showed complete reversal after six months. There was significant improvement in serum titres (quantitative V.D.R.L. tests) in both groups, the average improvement in titre representing 2.83 and 2.34 tubes in the two series. These results were better than those given by 2.4 mega-units of P.A.M. under similar circumstances in the same rural areas of Thailand.

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E. I. GRIN
T. GUTHÉ.

DOSAGE OF MEPHENESIN

SIR.—In his letter of Dec. 19 Dr. Peckover discusses the dosage of mephenesin necessary for the effective treatment of various "rheumatic" complaints encountered in general practice.

I have found that mephenesin, administered in the single doses suggested by Peckover and Nesbitt, gives rise to troublesome side-effects, especially nausea and, less frequently, vertigo. Thus, when I obtained some compound tablets in which mephenesin did not exceed gr. 1 per tablet, I tried them and was impressed by their equal if not superior effectiveness, quite apart from their undoubtedly lower toxicity. By cutting down the single dose and combining it with other drugs, the daily amount of mephenesin could even be stepped up with advantage to a total of gr. 9–12 plus the other effective drugs, such as salicylates. This suggests that compound tablets have a useful effect on the pain and spasm, and that side-effects are rarer. The promising future of mephenesin in antirheumatic therapy may lie in its combination with other drugs rather than in its use alone.

Miller Bay Hospital,
Prince Rupert,
British Columbia, Canada.

D. F. CROSS.

ON CREDULITY

SIR.—As a nurse and a member of a family of doctors, I have been brought up on orthodox views of medical science. Like many people, I have seen the failures of medicine, but I have also seen the brilliant results of team-work. So it was with interest that I read Lord Moran's story (Jan. 23) about his friend's experience of osteopathy.

I recall some years ago saying to a friend that I firmly believed that orthodox medicine could offer all that the unorthodox approach to healing could do, especially in orthopaedic surgery and physical medicine. Little did I know how my faith was to be tried.

Some 18 months later I had an acute attack of sciatica, and the pain was very bad. I was told that the cause was a prolapsed intervertebral disc, and I was treated with rest and drugs. I was able to get about for a while, but the acute pain soon returned. A specialist advised me that manipulation under anaesthesia was needed, but it only made the pain worse.

In the weeks that followed I received various forms of treatment, including spinal traction, a plaster jacket, and further rest in bed, but I was still in acute pain and unable to carry out my duties. Even so, my faith was not shaken: I must be, I told myself, a very resistant case. So when, some 7 months after the pain began, a nursing sister suggested a visit to an osteopath, I was not keen at first, but the pain made me change my mind.

Unlike Lord Moran's friend, I found that my initial consultation included a very thorough history-taking, and a careful physical examination. Treatment was delayed until radiological confirmation was obtained. The osteopath told me that the manipulation under anaesthesia had been a bad mistake, which I quite believe. Treatment was not in any

way forceful, and after the fourth visit the pain had gone from my leg, and with a further four treatments it had disappeared altogether.

I have talked to many of this osteopath's patients, most of them with a similar history to my own, and I have come to the conclusion that a lot of suffering could be eased, if not cured, by immediately seeking the advice of an osteopath.

Banstead.

C. THOMAS.

TUBO-OVARIAN TORSION AND TORSION OF HYDROSALPINX IN CHILDHOOD

SIR.—The following two cases seem worth reporting because, although it is mentioned in some standard textbooks, acute tubo-ovarian torsion in childhood does not appear to be common. The clinical picture resembles that of acute appendicitis, and its true nature is disclosed only by laparotomy. Moreover, although torsion of ovarian cysts in infancy and childhood is not uncommon, I can find no record in the standard works of torsion of hydrosalpinx in a child. Most authorities state that this condition occurs only in adults and as the end-result of long-standing pyosalpinx in which the pus has long been resolved and clear fluid left. In the second case there was no history of long-standing pelvic disease and no evidence at operation of any prior pelvic disease.

CASE 1.—A girl, aged 7, was admitted to hospital on Dec. 6, 1953. Forty-eight hours before admission, she felt sick and vomited several times during the evening and the night, and apparently had generalised colicky pain. Twenty-four hours later, the pain settled in the right side and persisted until admission, keeping her awake at night. Her bowels had not been open since the onset of pain. There was some increased frequency of micturition and dysuria during the twelve hours before admission.

She was a healthy-looking youngster. Her temperature was 100.2°F. There was tenderness and rigidity in the right iliac fossa. Laparotomy was performed on the night of admission. A right transverse gridiron incision was made; there was some free fluid in the peritoneal cavity. The appendix was normal. There was torsion of the right ovary and tube, both of which were gangrenous. The right ovary was filled with blood-clot, and was about 3 in. by 2 in. in size. The right tube was $\frac{3}{8}$ in. in diameter, and gangrenous to within $\frac{1}{4}$ in. of the uterus. Right salpingo-oophorectomy and appendicectomy were performed. Postoperative convalescence was uneventful.

The pathologist reported haemorrhagic infarction of the ovary and fallopian tube.

CASE 2.—A girl, aged 13, was admitted on Dec. 6, 1952. Three days earlier she had had intermittent pain in her back, and she had vomited once. The pain had recurred in the left loin, and for the past twenty-four hours had been constant in the lower abdomen. During the past twelve hours micturition had been painful. The bowel action had been normal, but there had been some frequency of micturition during the past two days. Her periods had started two months ago.

She looked healthy. Her temperature was 100.8°F. There was some tenderness in the left lower quadrant and the hypogastrium, and in the pouch of Douglas on rectal examination. Laparotomy was performed on the day of admission, using a right transverse gridiron incision. There was blood-stained fluid in the peritoneal cavity and a normal appendix. Torsion of the distal two-thirds of the left fallopian tube had made it purple and gangrenous, and it was distended with blood to a diameter of 2 in. The left ovary was normal. The right ovary contained a small cyst filled with blood. The right tube was normal. Left salpingectomy and appendicectomy were performed.

Postoperative progress was uneventful and the patient was discharged on Dec. 16, 1952. When seen at outpatients on Jan. 8, 1953, she was quite well.

The pathological report described haemorrhagic infarction, suggesting torsion of a hydrosalpinx.

Hackney Hospital,
London, E.9.

R. F. READ.

TREATMENT OF VARICOSE ULCERS

SIR.—It appears to me that, in his letter of April 3, Mr. Lee is only adding to the "multitude of treatments" and "maze of medicaments and bandages" to no advantage by the injection of tolazoline and hyaluronidase in the treatment of varicose ulcers.

The ulcer which results from the presence of varicose veins is a common one and is easily cured by the removal of the varicose veins. Injections alone play no part in this treatment, and the correct treatment is a Tredelenburg operation plus ligation of all incompetent communicating veins.

The ulcer arising as a post-thrombotic incident is probably even more common. It is wrong to imagine that arterial spasm plays any part in the onset or the chronicity of these ulcers in the ordinary case. I have performed very many arteriograms on these cases and have never found arterial spasm to be present. The post-thrombotic leg may indeed be an "inverted Guinness bottle," and in these cases a supporting bandage is of no value whatsoever, for there is no oedema of the foot or lower leg. A more common type of post-thrombotic leg is one with chronic hypostatic oedema, and in these cases supporting bandages are invaluable, for it is to prevent the accumulation of oedema that the bandages are required and not to get rid of "accumulated metabolites."

It is again incorrect to state that "ligation of the communicating vein does not have any effect"; in most cases it has a very dramatic effect, but to perform the ligation the ulcer has usually to be excised.

Varicose ulcers and post-thrombotic ulcers may be healed and prevented from recurring in most cases by Bisgaard treatment and supportive bandages. A cure can be effected, however, by adequate surgical elimination of incompetent varicose veins in both types of ulcers—plus the ligation of incompetent deep communicators (the "ankle blow-out syndrome"). A chronic ulcer may have a base of fibrous tissue at least an inch thick, and I have excised many like this. Surely the best treatment is to get rid of this thick avascular fibrous tissue, and a graft will then have some chance of remaining alive with a healthy blood-supply.

For the really bad cases, lumbar sympathectomy is invaluable to improve the nutrition of the skin. I can see little reason to support repeated intra-arterial injections with their very temporary effect, nor can I subscribe to the repeated needling for the purpose of injecting hyaluronidase which will only spread the oedema over a wider area—in an area which is very susceptible to infection and ulceration at the best of times. Neither of these two methods appears to me to "attack the underlying condition."

Essex County Hospital,
Colchester.

ROLAND N. JONES.

SIR.—Has not Mr. Lee succeeded only in misting a little further the windscreens of varicose-ulcer treatment? To use his own words, we are bogged down already with "a multitude of treatments" and a "maze of medicaments"; but he has no compunction in thrusting intra-arterial tolazoline injections and hyaluronidase ionisations into our already bulging knapsacks.

To me it has always been a source of mystery why the treatment of gravitational ulcers should be so fraught with difficulty, when all that is necessary is to read *The Lancet* of Feb. 28, 1931—and act accordingly. Particularly in these days when the introduction of 'Poroplast' flexible adhesive bandages has virtually banished the bogey of skin sensitivity. May I hasten to add, however, that poroplast is to my mind a most misleading name: the porosity of the bandage matters not two hoots.

What is important is the new plaster spread, which seemingly contains no irritant substances.

I have, up till now, steadfastly maintained that all gravitational ulcers (except in bedridden patients and those over ninety years of age) can be healed with elastic adhesive bandages—unless the skin is sensitive, when they must go to bed. With this latest development in the adhesive spread, I withdraw my *italics*.

London, W.1.

STANLEY RIVLIN.

* * * Our issue of Feb. 28, 1931, contained an article by Mr. Dickson Wright on the Treatment of Indolent Ulcer of the Leg.—ED. L.

BLINDNESS AND OXYGEN

SIR.—In your leading article of Jan. 9 you mention the interesting experimental work by Ashton et al. and Patz et al., who produced evidence incriminating oxygen in the development of retrobulbar fibroplasia.

We published in 1952 a preliminary report¹ in which we described changes occurring in newborn mice that had been intermittently exposed to an atmosphere of 100% oxygen. These changes consisted of haemorrhages into the vitreous body and behind the iris, persistence and hyperplasia of the tunica vasculosa lentis, and detachment and folding of the inner layer of the retina. These studies are continuing.

Karolinska,
Mediko-Kirurgiska Institutet,
Stockholm.

LARS GYLLENSTEN
BO HELLSTRÖM.

TUBERCULOSIS YARDSTICKS

SIR.—The success of modern advances in the treatment and diagnosis of tuberculosis is reflected in the rapidly falling mortality and the persistently high level of new notifications, but, as Dr. Tattersall points out in his letter of April 3, these rates are of no value in assessing the success or otherwise of our attempts to lessen the frequency of tuberculous infection or even bring about the eradication of the disease.

Dr. Tattersall and his colleagues² have shown us the most useful yardstick for this purpose: it is the incidence of tuberculous infection in the school-child as measured by the tuberculin skin-test. This test in its various forms is being more widely used, as part of the routine school medical examination, to discover children infected with tuberculosis so that their contacts can be examined and the source of the infection traced.

It would therefore be a simple matter for the school medical officer to publish the incidence of infection in the various age-groups and in different schools. From these figures it would be possible to compare the incidence of infection area by area and school by school for the whole country. Efforts to discover the sources of infection could then be concentrated in those areas showing a high incidence of infection, particularly in the younger age-groups. Yearly changes in the incidence would indicate the success or failure of our efforts to control the disease.

Dr. Tattersall suggests a list of "active cases" as another yardstick. All would agree with the value of such a list, particularly if plotted on a street or parish map of the area and related to the incidence of childhood infection and the tuberculous morbidity of the area. An "active case" is difficult to define and must depend largely on the result of bacteriological examination of sputum and laryngeal swabs. Even more difficult will it be to say when a case ceases to be active; must there be one, two, or three negative sputum or laryngeal swab cultures and at what intervals?

1. *Acta paediat., Stockh.* 1952, 41, 577.

2. MacDougall, I. A., Mikhall, J. R., Tattersall, W. H. *Brit. med. J.* 1953, i, 64.

An investigation (unpublished as yet), recently made at the Ipswich chest clinic, has shown that child contacts of patients with radiological evidence of tuberculosis but repeatedly negative sputum cultures have a significantly higher rate of infection than do normal school-children in this area. This suggests that we cannot rely upon bacteriology in determining the infectiousness of a particular patient, and it is just these patients that should be included in the "active case" list; but by what criteria?

Chest Clinic,
St. Helen's Hospital, Ipswich.

CHARLES J. STEWART
D. VAN ZWANENBERG.

HOSPITAL, DOCTOR, AND PATIENT

SIR.—Your correspondent, "Parent" (April 3), has indeed been unfortunate in her experience of reticence and silence on the part of the hospital concerned. Any parent or relative can interview me or my assistant merely by asking the ward sister for an appointment (or by writing to request one). Under no circumstances is such an interview refused.

Similar practices apply in most of the hospitals I know.

Orthopaedic and Accident Department,
Oldchurch Hospital,
Romford, Essex.

R. A. KING.

NEW TANK RESPIRATORS

SIR.—In your annotation of April 3 you suggest that the dome system incorporated in the Bristol respirator, described in the same issue, is of such a complex design that construction is a difficult matter.

In actual fact the design of the dome system is very simple and uses the pump unit on its positive stroke, the pressure being regulated by a simple "blow-off" valve. The use of this dome is so easy that it can be learned in a few minutes by an intelligent nurse, and the switch-over from negative pressure in the tank to positive pressure in the dome is so smooth that patients hardly notice it has happened.

In my experience positive pressure maintained through a face-mask is uncomfortable for the patient, who requires education in the use of this method, and it is a difficult technique which cannot be readily left in the hands of nurses.

Ham Green Hospital,
near Bristol.

JAMES MACRAE.

SPONDYLOYSIS

SIR.—I would not venture to criticise Sir Russell Brain's oration, published in your issue of April 3, had it been confined to the clinical aspects of his subject, but some of his statements are on radiological matters and may mislead those who look to him for guidance.

Sir Russell states: "Look back for a moment and recall that it is just twenty years since sciatica was first attributed to an intervertebral disc protrusion." Though the clinicians may not have noticed it, radiologists have been drawing attention to disc lesions for much more than twenty years. He will find evidence of this in my Robert Jones lecture,¹ written in 1926.

Radiologists are well aware that radiographs may show extensive changes of the nature of spondylosis and yet the patient at the time may exhibit few or no clinical signs; and that there may be prominent clinical signs in cases with little or no radiographic evidence. The radiographic signs are the end-result of a series of changes and not the cause, and, as I have shown, there is a long latent negative radiographic period between symptoms and radiographic signs. Why then does Sir Russell

urge multiple views of the spine to show the lesser signs? Surely it is the clinical manifestations which matter.

He says "without the flexed and extended lateral views it may be impossible to detect spondylolisthesis (fig. 4)." Surely an ordinary lateral radiograph would have revealed the lesion shown in fig. 4? I fear that his advice will lead to very considerable waste in time and material to get that which contributes little. And is not this use of the term spondylolisthesis unjustified in such a case? The term was introduced by Killian in 1852 to denote progressive gliding of an unstable vertebra; but fig. 4 gives no indication of this.

Some may find it hard to understand Sir Russell's advice that "it is important to bear in mind the following points in the interpretation of the X-ray appearances . . . the absence of posterior osteophytes, which are radiographically visible, does not necessarily mean the absence of a disc protrusion" (my italics). I rather fear that this may tempt the surgeon to interfere, leaving the patient worse than before.

Sir Russell Brain concludes his article with the statement: "How much we have learnt since then!" I suggest it would be better to ask: "How much have we learnt since then?" My answer would be that apparently nearly everything remains to be discovered, for have we not overlooked the common causes for the acute signs when radiographic changes are absent or minimal? And have we not neglected the preventive measures of disciplined rest and elimination of metabolic and infective toxins which bring degeneration of the discs?

Birmingham.

JAMES F. BRAILSFORD.

SIR.—Thanks to Sir Russell Brain, the neurological symptoms of spondylosis are being more often recognised and better understood. It is less widely known that the protean manifestations of this disease may comprise dysphagia and recurrent laryngeal nerve palsy, which bring the patient to the laryngologist.¹

The patient, middle-aged or elderly, complains of the feeling of a foreign body in the throat, "like a crust,"

which makes him want to swallow. Radiography shows the typical appearances of cervical spondylosis in the postcricoid region, involving C5, C6, and C7 (see figure). The dysphagia is not due to a mechanical obstacle caused by the presence of osteophytes, but to reactive changes in the areolar parapharyngeal and paraesophageal tissue, resulting in fixation and impaired mobility of the pharyngeal wall. One or both recurrent laryngeal nerves, which are surrounded by this tissue, may

become involved. Esophagoscopy must be performed in order to exclude postcricoid carcinoma, but cervical spondylosis undoubtedly accounts for a number of cases which are wrongly dismissed as "hysterical" dysphagia or "idiopathic" recurrent laryngeal palsy.

FRANCIS BAUER.

1. Brit. J. Surg. 1929, 16, 594.

1. Bauer, F. J. Laryng. Otol. 1953, 67, 615.

Parliament

The Budget

ON April 6 Mr. R. A. BUTLER, the Chancellor of the Exchequer, presented what he described as a carry-on budget. He made only minor changes in the existing basis of taxation. For the social services in 1954-55 he has set aside £1327 million, and he pointed out that it takes the whole of the taxes from tobacco, beer, spirits, and purchase-tax to provide this sum. The National Health Service's share has gone up from £411 million for last year to £430 million. Progress in social reform, Mr. Butler believed, had been well maintained. Such progress carried heavy obligations from which there was no miraculous and painless escape. "We cannot," he said, "in good conscience, put the clock back; but we must make sure that in the administration of this vast outlay humanity goes hand in hand with economy."

Health and Welfare

In the House of Lords on April 7, Lord SALTOUN moved

"That in the opinion of this House a large proportion of the failures in the welfare and health services are due to imperfect coöordination between the various authorities concerned, that local resolution of difficulties is essential to an efficient service, and that in many cases greater local discretion, financial and administrative, would result in better service at less cost."

He began by reading a list of some of the departments and authorities concerned with the functions of the Welfare State. If all these bodies acted in complete harmony it would be little short of a miracle. But the field of exercise of their functions was the body of one unfortunate man, woman, or child who suffered when these august parties were dilatory or disagreed. Division of responsibility often aggravated shortages of accommodation; and many hospital administrators and welfare workers were convinced that there was an urgent need to have someone with the power of commanding an emergency bed in a hospital and deciding on the spot how any urgent case should be dealt with. Old people, in particular, fell into the gaps between National Assistance, local-authority welfare, national hospital, and local-authority sociomedical services. If the Government could not accept the motion, Lord Saltoun hoped they would appoint a small committee to find how better coöordination of these services could be achieved.

Lord BEVERIDGE welcomed Lord Saltoun's motion, but deprecated the use of the word "failure" about a great service. But he agreed that there were things which could be improved, largely by coöordination. One way in which the National Health Service Act had tried to correct discoöordination was by the institution of health centres. But up to the present the dream of establishing those centres had failed nearly everywhere. In the intention of all who framed the National Health Service, health centres were an essential measure for coöordinating the different regional authorities. Their development was stopped in 1948 owing to the need to limit building. In his view, health, and the proper provision of health, were as important as houses. Would the Government remove the restrictions that prevented health centres from coming into being? He also asked the Government to release the regional hospital boards from some financial controls. The Treasury rule of annual budgets was inappropriate, and more freedom of capital expenditure was needed to replace out-of-date buildings and equipment. Our only chance to save on pensions for the aged was to lengthen the average working life; and that depended, among other things, on health. When the Government received the report of the Guillebaud Committee he hoped they would take the opportunity to consider the administration as well as the finances of the N.H.S. Would they ask themselves whether a Minister with an ordinary central department of ordinary Civil Servants was the right organisation for running a great national industry to secure for the people of this country the means to health?

The Earl of CRANBROOK, who is chairman of the East Anglian Regional Hospital Board, thought that it would

be unreasonable to allow hospital authorities to carry over unspent balances of funds provided for running expenses, but he would like to see a carry-forward allowed for capital expenditure and ordinary maintenance expenditure on buildings. Constant pressure was brought on the Minister to provide more hospital beds, but Lord Cranbrook thought that the existing number of beds, certainly for acute cases, was sufficient to meet the need if proper use was made of them and there was a more rapid turnover. That could only be done if there were more home helps and home nurses. There must also be constant coöperation between the responsible authorities. An extraordinarily untidy machine had grown up, he thought quite fortuitously. The machine could be made to work by constant care and effort, but he thought the effort would be better spent if it were directed into making one machine instead of trying to make three work in together. As he saw it there were two possible solutions: the first was to hand the hospitals over to the local-health authorities and the second to hand the domiciliary services over to the hospital authorities. To hand the hospitals over to the local authorities would only be useful if the local authorities were to bear part of the cost on local rates. He was surprised to see a former Minister of Health¹ suggesting that local authorities should act as the Minister's agents in administering the hospitals while the Minister continued to pay the cost. An agent, he felt, could not publicly oppose the Minister. An agent could only resign, and as local authorities were run on party lines he felt the position would be untenable. For the same reason he disliked the suggestion that members of hospital boards and committees should be elected.

Lord AMULREE thought that elderly people suffered most from the lack of coöordination between the health and welfare services. The National Health Service and National Assistance were two parallel lines, and like parallel lines they never met. The people who fell between the lines were those not strong enough to stand on either side—frail, infirm, and elderly people. There might be a good deal to be said for compulsory power to admit people to hospital, but there was also something to be said against it. As things were now the hospitals might become overfull, and overcrowded wards led to overworked staffs, and lack of proper treatment and nursing. If elderly people were treated properly in hospital and then discharged, beds would be available for all and emergencies would rarely arise. What he thought was needed was free exchange between welfare institutions and hospitals. Local authorities should provide more free accommodation for the frail and infirm and encourage the provision of domiciliary services. There was another reason why he pressed for coöperation. In 1901 the total number of people in the medical and auxiliary services was about 3000 per million of the population. In 1951 it had gone up to nearly 10,000 per million of the population. That was rather alarming, because it showed that the supply of staff was going to dry up. He had no wish to cut down the amount of work done; on the contrary, he was in favour of expanding it. But he would like to see whether something could not be done to prevent overlapping.

Lord MANCROFT, replying for the Government, could not accept Lord Saltoun's motion as it was worded, but he was prepared to accept it in spirit. There was no complacency about the health and welfare services in the minds of Ministers charged with administering them. Coöordination was one of the greatest single problems of the service. Over 50,000 people were engaged in it and it was the third biggest concern in the country. At present coöordination was secured by the interlocking membership of statutory bodies and joint standing committees. Like so many other problems it really resolved itself into one of human relationships. The suggestion that there should be all-purpose local authorities for all parts of the health and welfare services presented difficulties. Few local authorities had areas large enough for the planning, and perhaps operation, of a comprehensive hospital service. Nor was he convinced that all-purpose authorities would resolve the problem. In an authority of that size coöordination of its different departments would not in practice be a great deal easier than the coöordination of different authorities. In such a large

¹ Municipal Journal, March 12, 1954; see *Lancet*, April 3, 1954, p. 72 i.

service there must be some central control, but the Minister was anxious that the spirit of the National Health Service Act should be generously interpreted and that local bodies with local initiative and responsibility should run the service in the way which best suited the needs of their locality.

Turning to the question of the aged; he suggested that we must make certain that they were not demanding of the State higher services than their needs really required. In 1911 there were 2 $\frac{1}{4}$ million people over pensionable age; in 1947 the figure had risen to 6 $\frac{1}{2}$ million, and in 1977 there would be 9 $\frac{1}{2}$ million. In England and Wales there were 54,000 staffed beds for the chronic sick and 3600 of those were empty for lack of nursing staff. But it was the turn-over of beds which really mattered. In 1951 the number of beds increased by 3·3%, while the number of patients treated increased by 10·1%. In 1952 comparable figures were 1% and 9%. Outpatient attendances had risen from 7000 in 1950 to 14,000 in 1952, inpatients rose from nearly 85,000 in 1950 to 103,000 in 1952, and the waiting-list had been kept fairly steady at about 9700. In residential accommodation provided by local authorities there were now some 66,000 places in England and Wales, and since the end of the war about 600 homes, with accommodation for about 18,000 persons, had been provided. Health centres, of which there were now four—in London, Bristol, Nottingham, and Faringdon—must, he admitted, still be regarded as experimental. They were expensive to build and had not been as popular either with patients or doctors as had been expected. An alternative was the establishment of group practices, and executive councils could now offer interest-free loans to groups of doctors to acquire or convert buildings for this purpose.

In his view, Lord Mancroft ended, the trouble with the Welfare State was that too many people worried about what they could get out of it and never bothered to think about what they could put into it. If the Good Samaritan on the road between Jerusalem and Jericho had stopped to look at the battered body of the wayfarer he would (if he had thought the way some people did now) have thought to himself, "Now I wonder whether it is the medical officer of health for Jericho whose job it is to look after that chap, or that of the Jerusalem City Council"; and he would have gone on his way.

QUESTION TIME

Distribution of Welfare Foods

Replying to a question, Major GWILYNN LLOYD GEORGE, Minister of Food, said that the local health authorities had been invited to take over the responsibility for the distribution of welfare foods, other than liquid milk, when the local food offices were closed later in the year, as part of their duty under the National Health Service Acts to provide for the care of expectant and nursing mothers and young children. The associations of authorities covering England and Wales had already agreed to do so.

Contamination of Citrus Fruits by Thiourea

Replying to questions on the possible toxic effects arising from the contamination of citrus fruits by the use of thiourea Major LLOYD GEORGE said that he was advised that the sale and importation of any article of food containing thiourea contravened the Preservatives in Food Regulations or the Imported Food Regulations respectively and that such sale and importation were therefore prohibited. Food and drugs authorities and port health authorities were so informed last January. The matter had been brought to the attention of the governments of the exporting countries.

Mr. A. W. J. LEWIS: Will the Minister consult the President of the Board of Trade with a view to taking some action? In the East End of London, and particularly in West Ham, these oranges are being sold at the moment and children are sucking the orange skins, which he will agree is very dangerous. I am informed that, unless he and his right hon. Friend implement the banning of these articles, the local authorities have not the powers to take action. Will he implement the banning? Major LLOYD GEORGE: At the moment the local authorities and the health authorities have full powers to deal with this because thiourea is a preservative which is not allowed. Therefore it is a matter for the courts to decide whether an offence has been committed. The prohibition on

imports is an important matter, and I am looking into it urgently to see what can be done if these regulations are not sufficient. I circularised all local and health authorities on Jan. 25, pointing out the danger of this particular spray. They have full powers to deal with it. All information which I have received from various parts of the country has come from local authorities.

Obituary

THOMAS CARNWATH D.S.O., M.B. R.U.I., D.Sc.Belf., D.P.H.

Dr. Carnwath, whose death on April 2 we announced last week, was deputy chief medical officer of the Ministry of Health in the anxious years that preceded the late war. His wide knowledge of medical administration went back to the days of the Local Government Board, and after his retirement in 1940 he accepted the charge of reviewing Belfast's health services.

He was born in 1878, the son of J. Carnwath of Tyrone, and he was educated at Foyle's College, Londonderry, and Queen's University, Belfast. After he graduated as M.B. in 1900 he continued his studies at the University of Berlin. His early experience of public health was gained as an assistant at the Hamburg Institute of Hygiene and later at the Reichsgesundheitsamt in Berlin, and his first papers were written in German on such subjects as Hühner Diphtherie und Geflügel-pocken and the Technik der biologischen Untersuchung kleinstter Blutspuren. He returned to this country to take the D.P.H. in 1906 and to become the assistant M.O.H. for Manchester, and later M.O.H. for Withington. He continued his biological studies, but his papers now dealt with such topics as a Bacteriological Survey of Belfast Lough and an Experiment on Quarantine of Shell Fish from Polluted Areas.



(Elliott & Fry)

From Manchester he moved to London to take up an appointment as medical inspector under the Local Government Board, but his work there was interrupted by his war service. His cheerful gallantry in the early days in France in 1914 is described in the regimental history of the Honourable Artillery Company, to which he was attached as a surgeon captain. Later he served in the Balkans, and in 1918 he was awarded the D.S.O.

After the war he joined the staff of the newly formed Ministry of Health in the section of general epidemiology, where he was second in command to Sir George Buchanan. J. A. G., whose "early efforts" at the Ministry were in the main directed by Carnwath, recalls him as "genial, handsome, and debonair. He had great charm as well as great ability and wise judgment. For nine years I served under him; and he was always kind and ever cheerful."

After 1928 Dr. Carnwath was responsible for the complicated and technical work of administering the Therapeutic Substances Act, which controls the sale of biological products such as vaccines, sera, antigens, and insulin. During the immediate pre-war years he also took an important share in the Ministry's preparations for stockpiling medical supplies and creating a bacteriological service to meet an emergency. For both these tasks he was peculiarly fitted by his experience of laboratory work at Berlin and Hamburg. Besides these heavy official tasks he fulfilled many outside commitments. He was for a time lecturer on public health at St. Thomas's Hospital and an examiner for the Universities of London, Manchester, Birmingham, and Belfast. Many committees drew upon his experience, judgment, and common sense, and he was a member of the Army Hygiene Advisory Committee, the managing committee of the Bureau of Hygiene and Public Health

of the Colonial Office, of the board of studies in hygiene and public health of the University of London, and of the National Radium Commission.

In 1935, the year in which the University of Belfast conferred on him an honorary degree, he was appointed deputy to Sir Arthur MacNalty, who writes: "My appreciation of Carnwath's wide knowledge of public-health problems and of his sterling qualities only increased with the years. In the strenuous years of preparation preceding the second world war and in the early months of the war itself, his help was ever forthcoming, and I felt it greatly when ill health compelled him to retire early in 1940. He went back to Northern Ireland; but I met him occasionally at the Athenæum, and I was glad to know his health had improved and that he was helping Northern Ireland's work in public health as an elder statesman."

W. D.-C., who succeeded Carnwath at the Ministry, also pays tribute to his qualities: "Soon after I joined the Ministry of Health in 1927 I became Tom Carnwath's assistant, and his kindness, helpfulness, and good advice quickly made us the firm friends that we always remained. He had all the finest characteristics of the Northern Irish: quiet determination, cheerful acceptance of responsibility, and a hatred of humbug. His quiet almost casual manner cloaked a shrewd intellect, thoroughness in all he undertook, invariable consideration for others, and a keen sense of humour. He had the happy knack, so valuable to an administrator, of quickly seeing the most practical solution of any problem. His philosophical outlook enabled him to bear the disappointments of life with equanimity and to enjoy his retirement in his beloved County Antrim."

Dr. Carnwath married in 1908 Margaret M'Kee of Belfast, who survives him with two sons.

HENRY WILLIAM MARETT TIMS O.B.E., M.A. Camb., M.D. Edin.

DURING the early years of the century Dr. Marett Tims was well known at many London colleges and medical schools as a teacher and examiner in anatomy and biology.

He was born in Calcutta, the son of Dr. T. Lamb Tims, and was educated at Reading School. After graduating at Edinburgh University in 1887 as M.B., with honours in almost every subject, he held demonstratorships in anatomy and physiology in Edinburgh before he came to England in 1889 to continue his postgraduate studies at St. Thomas's Hospital and the University of Cambridge. In 1890 he took his M.D. with commendation, and two years later he was appointed lecturer in biology and comparative anatomy at Westminster Hospital Medical School. Soon afterwards he was appointed reader in zoology at Bedford College for Women. About this time he became an examiner in physiology and biology for the Society of Apothecaries and in elementary biology for the Conjoint Board. He also held a demonstratorship in human morphology in the University of Cambridge, and in 1901 he took his B.A. (research) at King's College, Cambridge. In the same year he was appointed lecturer in comparative anatomy and biology at Charing Cross Hospital Medical School, and in 1908 he joined the staff of the Royal Veterinary College as professor of biology. During the 1914-18 war he left these multifarious duties to serve in the R.A.M.C. with the rank of lieut.-colonel. For his work in these years he was appointed O.B.E. in 1919, and in 1920 he was awarded the order of St. Sava of Yugoslavia.

As his career suggests, Dr. Tims's experience was varied and wide. He was a recorder and vice-president of section D of the British Association, and his papers to the association included one on the development, structure, and morphology of the scales in teleostean fishes. But no aspect of comparative anatomy held his interest so greatly as that of the teeth and their homologies, which had been his main preoccupation since the 'nineties when he had read papers before the Linnean Society on tooth genesis in the Canidæ and the Cavidæ. It was therefore appropriate that after the war he was appointed lecturer in comparative dental anatomy at the Royal Dental Hospital and was chosen as scientific editor of *Tomes's Dental Anatomy*. He was responsible for the 7th and 8th editions, and C. B. H., who shared in this task, writes: "Marett Tims entered with zest,

and effectively, into the arguments about polyphyodontism and tooth-vestiges and the evolution of the forms of teeth. While rejecting Kukenthal's idea that molars represent the fusion of teeth belonging to two successive series, he expressed his opinion that fusion of two teeth anteroposteriorly in the same series may occur. He was absorbed in the evolution of dentition, and no other authority was in the same rich position to re-edit Tomes's manual, which was first published in 1876. No further edition has been published, and no new publication has supplanted his eighth edition which remains the standard work of reference in comparative dental anatomy."

In 1888 he married Alice Maud Mary, the daughter of Lieut.-Colonel Alexander Findlay, acting governor of Sierra Leone and the Gambia. Dr. Marett Tims survived her by four years and died on March 4, a few days before his 91st birthday. They leave a son and a daughter.

Diary of the Week

APRIL 18 TO 24

Tuesday, 20th

SOCIETY FOR THE STUDY OF ADDICTION

8 P.M. (11, Chandos Street, W.1.) Mr. Derek Curtis-Bennett, Q.C.: Alcoholism and the Law.

Wednesday, 21st

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1

5 P.M. Section of Comparative Medicine. Prof. L. P. Garrod: Effects of Antibiotics on Body Functions of Man and Animals. Prof. Alan Kekwick: Pharmacology of Some Commonly Used Antibiotics. Dr. W. S. Gordon, Mr. J. H. Taylor: Growth-Promoting Effect of Antibiotics—their Possible Modes of Action. Mr. S. K. Kon, D.Sc.: Function of Antibiotics in Animal Nutrition.

8.15 P.M. Section of General Practice. Dr. Oliver Plowright, Dr. Wilfrid Sheldon, Mr. R. J. Cann: Tonsils and Adenoids.

Thursday, 22nd

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2

5 P.M. Mr. D. J. Browne: Principle of Controlled Movement in Orthopaedics. (Hunterian lecture.)

ROYAL SOCIETY OF MEDICINE

8 P.M. Section of Urology. Mr. F. G. Smiddy: Hyaluronidase and Urinary Stone. Mr. A. W. Badenoch, Mr. A. G. Dingley: Influence of Hyaluronidase on Renal Lithiasis. Mr. Basil Page, Mr. Ashton Miller, Mr. D. T. H. Paine: Vasotomy. Mr. D. St. Clair Henderson: Vesico-ureteral Reflex.

8.15 P.M. Section of Obstetrics and Gynaecology. Mr. C. M. Gwillim, Dr. H. J. Wallace, Dr. Magnus Haines: Leucoplakia and Allied Conditions.

CHADWICK LECTURE

5.30 P.M. (26, Portland Place, W.1.) Dr. C. Banning (Netherlands): Antenatal, Natal, and Postnatal Care in the Netherlands.

UNIVERSITY OF ST. ANDREWS

5 P.M. (Medical School, Small's Wynd, Dundee.) Mr. J. Bruce: Surgery of Small Intestine.

Friday, 23rd

OSIER CLUB OF LONDON

7.45 P.M. (11, Chandos Street, W.1.) Mrs. Marie Stopes, D.Sc.: History of Contraception.

Appointments

BARNES, JOSEPHINE, D.M., Oxf., M.R.C.P., F.R.C.O.G.: part-time asst. obstetrician and gynaecologist, Charing Cross Hospital, London.

BURNS, J. P. J., M.C., M.B. Belf., D.P.H.: senior asst. M.O., area No. 6, Middlesex

DONELAN, M. J., M.B., N.U.I., D.P.H.: M.O., area No. 1 (Tredegar and Rhymney urban districts), Monmouthshire.

EDMONDSION, MARGARET M., M.B. Edin.: asst. M.O.H. and school M.O., Grimsby.

FOURACRE, A. J., M.R.C.S.: factory doctor, Withernsea, Yorks. FOWLER, P. B. S., D.M. Oxf., M.R.C.P.: part-time asst. physician, Charing Cross Hospital, London.

PICKLES, A. N., M.B. Leeds, D.P.H.: district M.O.H. and asst. county M.O., Kettering.

LIVERPOOL REGIONAL HOSPITAL BOARD:

BRYSON, J. R., M.B. Glasg., F.F.A.R.C.S.: consultant anaesthetist, Clatterbridge General Hospital.

PRINSLEY, D. M., M.D. Durh.: senior R.M.O., Barrowmore Hospital.

THORP, EDITH M., M.B., R.S.C. Manc., D.P.M.: whole-time asst. psychiatrist, Winwick Hospital.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD:

BRAMLEY, P. A., M.B., R.D.S. Birm., F.D.S. R.C.S.: consultant dental surgeon (part-time), Plymouth clinical area.

TROBRIDGE, G. F., M.B. Birm.: registrar in diseases of the chest, Hawkmoor Chest Hospital, Bovey Tracey, S. Devon.

TULLOCH, L. G., M.D. Aberg.: senior registrar in dermatology, Bristol clinical area.

Notes and News

WORLD HEALTH ORGANISATION

THE fifth year of W.H.O. is described by the Director-General, Dr. M. G. Candau,¹ as a period of "growth, adjustment, and consolidation" but also of "extremely serious and prolonged financial crises." The cut in the proposed United Nations Technical Assistance funds from an expected \$9 million to an eventual \$4.5 million resulted in curtailment or cancellation of many projects. Nevertheless, there were many substantial achievements. More than 330 health projects were helped in seventy-four countries; and 106 of these were completed during 1953. The campaign against communicable disease was extended; campaigns for control of malaria were carried on in twenty-one countries; 15 million persons were examined and 4 million treated for yaws and venereal diseases; and in twenty-four countries assistance was given for anti-tuberculosis measures. Health education has continued to be one of the major activities of W.H.O., in accordance with its consistent policy of helping underdeveloped countries to become self-supporting in medical services. 894 fellowships for study abroad were granted to health workers, in addition to those granted for local studies; the exchange of scientific information was encouraged by provision of teams of visiting medical experts, by regional or international medical conferences, and by supplying teachers or equipment to medical schools.

The World Health Day, on April 7, was this year devoted to the theme The Nurse, Pioneer of Health. Speaking in London on this occasion, Dr. Candau said that the basic aim of W.H.O. was to help countries to strengthen their national health services so that they might take the next feasible step forward in their development. It could be said, with some justice, that W.H.O. was, in the end, a self-liquidating organisation in that its task was to remove, in the largest possible measure, the need for its services. In the Western world the habit had become rather widespread of referring to certain countries as "underdeveloped." "There is always a danger in simplification; and the particular danger in this case is that it can lead to those feelings, and consequently expressions, of national superiority which can make international co-operative action well-nigh impossible. It is true that the Western communities are farther ahead along the road to national health and well-being than are, for instance, their brothers in Asia; but it is a chastening experience to consider just how short is the distance which divides them. . . . Everybody in this great city takes the existence of a supply of safe drinking-water for granted. Yet exactly one hundred years ago—that is, within the lifetime of the grandfathers of many now listening to me here—London possessed no general water-supply. One small section . . . was served by a pump which brought up water from a well in Broad Street . . . in 1854 this well, polluted by leakages from a neighbouring cesspool, brought death, in the form of cholera, to six hundred and sixteen people within the short space of two months."

Dr. Candau concluded by saying that the World Health Assembly next month would be asked to increase the effective working budget of the Organisation from the previous year's figure of \$8½ million to \$10,300,000. The United Kingdom was the second largest contributor, after the U.S.A.; and the proposed increase would raise the annual contribution per head of population in the United Kingdom from 1½d. to 2d.

HUNTERIAN INFLUENCE IN EXETER

At a meeting of the Devon and Exeter Medico-Chirurgical Society on March 18, Mr. Norman Capener, the president, spoke of the Hunterian Influence in Exeter, relating his talk particularly to the medical school which flourished there during the first half of the 19th century. The school failed to survive the Medical Act of 1858, but while it lasted it included among its teachers outstanding figures, many of whose portraits are displayed in the board room of the Royal Devon and Exeter Hospital. As a background to the Hunterian tradition, the President discussed the influence of Cullen, Cheseldon, and Pott, and the impact of the Hunters upon their pupils, and their pupils' pupils. Nurtured in the Hunterian tradition was John Haddy James, a favourite pupil of John Abernethy. He was born in Exeter and with Samuel Barnes, another Exeter Barts man, he was a leader in the

development of the Exeter school of medicine. He joined the staff of the Devon and Exeter Hospital after serving with Wellington at Waterloo, and two years later won the Jacksonian prize for an essay on inflammation. He invented many interesting mechanical devices and is noteworthy for having introduced continuous traction in the treatment of fractures. He was one of those who assisted Charles Hastings, of Worcester, in the foundation of the Provincial Surgical and Medical Association which later became the British Medical Association. James became its president in 1842, and the next year was one of the original fellows of the Royal College of Surgeons of England under its new charter. By 1854 the medical school had a close liaison with the Royal College of Surgeons. It had its museum, lecture-room, dissecting room, and laboratory and a magnificent library.

A HOME FOR BACKWARD CHILDREN

St. Christopher's Trust, formed by the parents of mentally handicapped children in 1951, has opened a home at Glossop in Derbyshire. The house, which is called Redcourt, is a large one, with extensive grounds; and though at present there are only six children (aged 8-14), it will be able to take about fifty receiving residential training. The trust is running Redcourt unaided for 12 months, after which time it should be eligible for grants from local authorities.

N.H.S. AMBULANCE SERVICES

THE demands on these services continue to rise¹ and a recent memorandum (H.M.(54)33) from the Ministry of Health announces that local health authorities and hospitals are being asked to co-operate in local surveys to be undertaken by an ambulance adviser and a medical officer for the Ministry. Ways of securing better co-ordination and more economy in the use of ambulances are to be sought.

The Minister suggests that local authorities, when replacing vehicles, should bear in mind the advantages of ambulances for sitting patients which will accommodate a stretcher case if need be. They should also remember that travel by rail is not only cheaper but often more suitable for both types of case, and that stretchers suitable for transfer direct from ambulance to train are now available. Greater operational efficiency and economy in use of vehicles and staff is usually possible if all calls for ambulances go through ambulance control stations, especially where there is radio communication between these and individual ambulances. The duplication of ambulance services and inequalities between charges of various ambulance authorities should be reduced by closer co-operation between them.

ALUMINIUM HOSPITAL BUILDINGS

At the British Industries Fair to be held at Earls Court, London, from May 3 to 14, the Bristol Aeroplane Company (Weston) Ltd. are showing a 'Bristol' permanent aluminium hospital building. This consists of a reception lounge 24 ft. square by 9 ft. high flanked by a complete operating-suite 48 ft. long, 32 ft. wide, and 12 ft. high, comprising a theatre and four ancillary rooms. The company has already built over twenty hospitals and nurses' homes in Australia, including the largest prefabricated hospital in the world, the Manly District Hospital, Sydney. The advantages claimed for this method of unit construction include speed of erection, saving in site labour and designing time, dry construction, and easier installation of services.

STANDARD FOR TRANSFUSION EQUIPMENT

THE new British Standard for transfusion equipment (B.S. 2463 : 1954) has been prepared to cover the requirements of the National Blood Transfusion Service and the Armed Services. The design of the bottle is that of the M.R.C. bottle, but without the "waist," which, though useful in providing a firm grip, has proved undesirable during freeze-drying operations. Attention has been paid to the need for interchangeability with similar equipment in other countries. Certain essential dimensions, such as those of the neck of the bottle, of rubber tubing, and of olive mounts, have been arrived at, and cognisance has been taken of discussions at a meeting of the transfusion equipment technical committee of the International Organisation for Standardisation held in London in 1952. In certain items—namely, the drip-counter, the filter-chamber, and the rubber closure—the design has not been specified but performance requirements are given instead. Only tubing made from natural rubber has been

1. The Work of W.H.O., 1953 : Annual Report of the Director-General. H.M. Stationery Office, 1954. Pp. 190. 10s.

1. See *Lancet*, 1953, i, 1316.

included in the standard since it is considered premature to include plastic tubing in the specification at this stage. Copies of this standard (3s. each) may be obtained from the British Standards Institution, Sales Branch, 2, Park Street, London, W.1.

OPERATION ON CONJOINED TWINS

The *Conjoined Twins of Kano* (16 mm., sound, colour, 40 minutes) is a film record of the operation at Hammersmith, at the end of last year, to divide conjoined twins. A brief history of the birth of the twins is followed by details of the examination of them, with special reference to the linking bridge and the structures it may contain. In this sequence there is a methodical development of thought from the examination by inspection and palpation to the more complex investigations by radiography and radioactive-isotope circulation tests, including a summary of the calculations by which the circulatory interchange between the twins was estimated. The operation itself is shown in great detail, including the instruments; skin preparation, anaesthesia, and intubation of the two infants; incision; operative technique; and precautions taken. Intelligent camera-work and skilful editing make clear every feature. The film ends with shots of the surviving child with his mother and of the necropsy specimen from the other. The bulk of the exposition is carried by the commentary, expertly delivered by Alvar Liddell, while the picture illustrates and often supplements what is said. The production, by Stanley Schofield, is of high standard. The medical adviser was Prof. Ian Aird.¹

University of London

Dr. F. E. Camps, lecturer at the London Hospital Medical College, has been appointed to the part-time university readership in forensic medicine at the college.

Mr. G. E. Francis, Ph.D., senior lecturer at St. Bartholomew's Hospital Medical College, has been appointed to the university readership in biochemistry at the college.

University of Leeds

Dr. Alfred Blalock, surgeon in chief to the Johns Hopkins Hospital, Baltimore, will deliver the Moynihan lecture at the University Union on Friday, May 14, at 3.30 p.m. He has chosen as his subject the Expanding Scope of Cardiovascular Surgery.

University of Edinburgh

On May 5 Prof. H. K. Beecher (Harvard Medical School) will deliver a Macarthur postgraduate lecture on Resuscitation and Other Early Care of the Severely Wounded Man. On May 6 Prof. Gerhard Domagk, director of the research laboratories for pathology and bacteriology of Farbenfabriken Bayer, is to give a Cameron lecture on Chemotherapy in Tuberculosis. On May 11 Dr. Ewart A. Graham, chairman of board of regents, American College of Surgeons, is to deliver the second Sir John Fraser lecture on Cancer of the Lung. All these lectures will be held at 5 p.m. at the University New Buildings, Teviot Row.

Royal Society

Sir Howard Florey, F.R.S., will deliver the Croonian lecture on Thursday, May 27, at the society's rooms, Burlington House, Piccadilly, London, W.1, at 4.30 p.m. He will speak on Mucins and the Protection of the Body.

Society of Medical Officers of Health

Dr. Frederick Hall has become part-time medical secretary of this society. Mr. G. L. C. Elliston has given up his post as secretary to give all his time to the editorship of *Public Health and the Medical Officer*.

Naval Medical Compassionate Fund

A meeting of the subscribers of this fund will be held at 2.30 p.m. on April 30 at the Medical Department of the Navy, Queen Anne's Mansions, St. James's Park, London, S.W.1, to elect six directors.

St. John Ambulance Brigade

A conference for surgeons, nursing officers, and non-medical officers of the brigade is to be held at the Cairn Hotel, Harrogate, from Friday to Sunday, April 23 to 25. The speakers will include: Major A. C. White Knox, the surgeon-in-chief, Dr. A. D. D. Broughton, M.P., Prof. Cyril Polson, and Dr. C. C. Boley.

1. See Aird, I. *Brit. med. J.* April 10, 1954, p. 831.

Royal College of Surgeons of England

At a meeting of the council held on April 8 the honorary fellowship was conferred on Dr. G. Gavin Miller of Montreal. The following were elected to the fellowship without examination as medical practitioners of at least 20 years' standing: Mr. J. W. H. Grice (Tunbridge Wells), Mr. D. M. E. Thomas (Sully, Glam.), Prof. G. Hadfield (London), Prof. J. Trueta (Oxford), and Mrs. D. R. Campbell (Coventry). Mr. W. A. Jackman (Bristol) and Mr. R. R. Simpson (Hull) were admitted to the fellowship ad eundem. Dr. W. D. M. Paton (University College Hospital Medical School) was admitted as the first professor of pharmacology.

The Jacksonian prize for 1953 was awarded to Mr. J. H. Peacock. The first Mitchiner medal was awarded to Brevet Colonel H. D. Chalke, and the first Lady Cade medal to Squadron-Leader R. R. L. Pryer. Prof. Martin A. Rushton (Guy's) was awarded the John Tomes prize. A Hunterian lectureship was awarded to Prof. Milroy A. Paul (Ceylon). The council selected Diaphragmatic Hernia as the subject for the Jacksonian prize for 1955.

Diplomas were granted jointly with the Royal College of Physicians to the following:

D.C.H.—Deirdre M. Airey, Enid Atkins, Herman Aufrechtig, Doris M. Beaton, Elaine M. Belton, Elizabeth F. Bennett, Jagri Ram Bhatty, Flora M. Bisset-Smith, Audrey M. Bolton, E. M. Broadfoot, J. A. Browne, D. W. Bull, June M. Burger, A. P. Camilleri, Kai Hang Chau, J. A. Cheese, Omaha Amma Cherian, Emmanuel Chigier, J. H. Clyde, G. J. Cousins, Mary Crawford, Joan M. St. V. Dawkins, Sooba Rama Deenadayalu, J. M. Doyle, Catherine M. Durkin, J. G. Edgar, C. P. E. Elliott-Binus, J. W. Fisk, D. M. Fraser, Shiba Prasad Ghosal, Sheila M. Gough, Margaret L. Gladstone, Isobel H. Grant, Sripal Tilak Gunewardene, Ann M. Haines, Margaret E. Hall, Mary Hollowell, M. J. T. Hewettson, Sai Kong Ho, Kathleen A. Hookey, K. S. Holt, Megan D. M. Johnson, Joelyn Johnston, Premal Kapur, Pathmaranee Kathiravelu, R. E. Kottler, Sylvia Lath, J. B. Lewis, Melvyn Lewis, Siew Whye Loh, G. C. Love, Margaret Luing, M. F. McDowell, Thomas McKendrick, Sheila L. McKinlay, Sohan Singh Manchanda, Cicely J. Millbank, Rhona E. Morgan, Marion E. Morris, Marion B. Morton, Chitra Mukherjee, B. K. A. Muller, N. V. O'Donoghue, R. M. Oliver, Ida S. Paranjoti, Hawa Patel, G. N. St. J. Penney, Jean Poole, Frances E. Powell, Edith I. Proctor, S. D. Roche, Sonia Rollin, Carol J. Rubidge, H. H. Shawdon, Isabel G. Smith, M. H. Southall, Joyce K. Starkie, Joan V. Stavert, Kenneth Stewart, Mary Sugden, Majuree Sundararaj, C. G. W. Sykes, I. G. Thomson, J. N. Ure, Denorah Vardy, Claudine M. R. Vesey, I. S. Wallman, Ruth M. Walters, Mogamat Arashat Warley, S. M. D. G. R. Wijegunaratne, P. S. W. Wilkins.

D.Phys. Med.—D. J. E. Cheshire, P. R. Travers.

D.O.—J. A. Akingbehin, M. R. Ashbridge, Mohamed Hassan Ashruff, D. J. Bowerman, George Davidson, Mohammad Siddiq Faridi, K. C. Garg, Harry Hardy, B. A. E. Harley, Sukhalal Udhoji Joshi, Akl bin Abdul Kadir, R. C. K. Loh, Marguerite C. Macdonald, Laurel J. MacIntosh, Mazharul Haque Malik, D. L. E. Paine, R. A. Quesada-Guardia, J. N. Rohatgi, Satyashna Roy, G. S. Sandhu, Gurbakhsh Singh, K. S. Subramaniam, A. A. Tyce, J. H. W. Wessels.

D.T.M. & H.—J. C. Aickin, F. L. Ashworth, A. S. Beare, Chandindhara Bhamarasuta, N. K. Bharucha, Z. M. A. Cader, A. T. Cook, T. M. Desai, J. K. Gajjar, G. H. K. Gentle, J. E. J. Hurman, Samir Jatinandana, A. C. Kali, Ahmad Mohammad Khatib, Y. J. Kiladjan, A. G. Leishman, W. S. Millar, H. R. Miller, K. P. Milne, Adam Muir, I. G. Murray, Leslie No Onha, Magdelen Oberhoffer, Mohan Kumar Panikkar, Kanu Hirabhai Patel, H. N. Ray, Werner Roillinghoff, P. D. Scheffel, E. K. Tagboto, Paul Yates, Ponniah Yoganathan.

British Association

This year the annual meeting of this association will be held at Oxford, from Sept. 1 to 8, under the presidency of Dr. E. D. Adrian, O.M., P.R.S.

Hunterian Society

The gold medal of this society for 1953 has been awarded to Dr. J. Lipsey (Littlehampton), and a proxime accessit award has been made to Dr. B. C. Zoob (Battersea).

The subject for the 1954 essay is Management of the Climacteric in General Practice. Further details may be had from the hon. secretary, Mr. Alec A. Badenoch, 110, Harley Street, London, W.1.

International Union of the Medical Press

The second congress of the union is to be held in Turin on May 30. The speakers will include Dr. H. Fiessinger (*Le Monde*), Dr. J. Lederer (*Association Presse Médicale Belge*), Dr. J. J. Gillon (*Concours Médical*), Dr. H. A. Clegg and Dr. J. W. P. Thompson (*British Medical Journal*), and Dr. G. C. Angela (*Minerva Medica*). Further particulars can be had from the Secretary of the Congress, Dr. F. Gavosto, Corso Bramante 83, Turin, Italy.

CORRIGENDUM: *Abnormal Nerve Impulses*.—In this leading article (March 27, 1954, p. 660) footnote 6 should read: "Lepeschkin, E. Amer. J. Med. 1954, 16, 73."

THE RIDDLE OF THE MAST CELLS A TRIBUTE TO PAUL EHRLICH *

JAMES F. RILEY

M.D., F.R.C.S.E., D.M.R.T.

From the Department of Radiotherapy, the Royal Infirmary, Dundee, and the Medical School, University of St. Andrews

ON Jan. 17, 1879, the Physiological Society of Berlin heard a remarkable paper by a remarkable young man. The speaker was Paul Ehrlich,¹¹ a newly qualified doctor; his subject a granular cell of the connective tissues, discovered by him during his student days,¹⁰ for which he proposed the name "mast cell" (*Mast=food*) because he had found them most commonly in those connective tissues whose nutrition appeared to be enhanced. Later he discovered somewhat similar cells in the blood,¹² but he was quick to realise that whereas the comparatively rare blood mast cell (basophil, mast leucocyte) takes origin in the bone-marrow, the more common tissue mast cell is born, lives, and dies in the connective tissues. The similarity of the two types of mast cell lies in their content of cytoplasmic water-soluble granules which stain metachromatically with certain basic dyes.

In view of Ehrlich's later work it is interesting to see in this his first piece of research the beginning of that golden thread which runs through the whole of his working life—the search for "specific affinities" between living protoplasm and known chemicals such as the dyes and drugs that were then appearing. That the biological action of a drug is a direct consequence of its molecular architecture is now a pharmacological axiom so firmly established as to pass without comment. In Ehrlich's day of empirical treatment this concept of chemotherapy was new.

It is said¹³ that Ehrlich's curiosity was first aroused in the laboratory in which his cousin Karl Weigert, the histologist, was working. There, chancing to look through a microscope at a prepared slide, Ehrlich fell to speculating on the mechanism which determines the staining characteristics of cytoplasm and nucleus. It must be, he argued, that the chemical configuration of the protoplasm is the opposite of that of the dye; the two fit together like pieces of a jigsaw puzzle or (in the more classical analogy) like a key in a lock. Reasoning thus, Ehrlich conceived that it might be possible to synthesise a dye with affinities specific for the bacterial cell and thereby provide the means of directing a dye or drug selectively to its target in the body.

Fired with this idea, he obtained samples of the latest commercial dyes from the great German chemical dye manufacturers who were then turning to such profitable account Perkin's original discovery in Manchester of the first synthetic dye, mauve. On applying these new dyes to fresh fragments of tissue, Ehrlich observed that the cytoplasm of certain connective-tissue cells contains granules with specific affinities for such basic dyes as dahlia, toluidine-blue, methylene-blue, and neutral red. These granular cells were particularly common around small blood-vessels and evidently formed part of the heterogeneous collection of "embryonal cells" described by his teacher Waldeyer.¹⁴

Not the least of Ehrlich's attributes was his intuitive understanding of the limitations of the experimental methods of his day. Having discovered and named the mast cells, and having described clearly their morphology, staining properties, and distribution, he left it to others to elucidate the chemical nature of their granules, contenting himself by expressing the hope that some day an interesting function would be found for these mast

cells of his.¹¹ My purpose here is to trace the further story of the mast cell and to see to what extent his hopes have been fulfilled.

The Mast Cell in Evolution

For the sixty years which followed Ehrlich's discovery of the mast cell, research on this subject remained almost entirely histological; and it is of interest to see how far down the evolutionary scale mast cells can be demonstrated.

The volutin granules of protozoa, yeasts, and bacteria have been thought by some to be the homologues of the mast-cell granules in higher organisms.¹⁵ Recent work casts doubt on this view.¹⁶ Nevertheless, in such lowly forms of life as the sponges,⁶ starfishes, sea-urchins,²⁴ and molluscs²⁶ there are already cells in the mesenchyme with basophilic metachromatic granules in their cytoplasm—by definition mast cells. At the level of the crustaceans mast cells can readily be demonstrated, as Hardy¹⁶ showed, around the arterioles of the crayfish. Many workers have failed to appreciate the high content of mast cells in the tissues of the fish, because here (as in the rabbit) the granules are extremely soluble in water and are lost when the specimen is placed in a watery fixative or stain. In the salmon mast cells are found enmeshed in the collagenous "stratum compactum" in the wall of the gut.¹⁴ They are common in the tissues of the reptiles and amphibia.²⁷

Among the warm-blooded vertebrates mast cells occur predominantly in the loose connective tissues and especially around the smaller blood-vessels.^{2,10} They are virtually absent from the central nervous system¹⁷ though present in the sheaths of peripheral nerves.⁴⁴ In general the parenchymatous organs are poor in mast cells except in the connective tissue of the capsule and trabeculae.^{19,39,51} A noteworthy exception to this is the widespread distribution of mast cells throughout the parenchyma of the dog's liver.³⁰

Mast Cells in Pathological Conditions

In choosing the name "mast cell" Ehrlich¹¹ was influenced by his finding of a high mast-cell content in connective tissues subjected to lymph stasis—especially, as he said, in chronic inflammation and in the environs of tumours.^{10,12} In the selective lymphatic blockage of elephantiasis the hypertrophied connective tissue is packed with mast cells,² and a similar histological picture on a smaller scale is seen in young well-vascularised keloid.⁴⁷

Tumours composed of mast cells are rare, occurring most commonly in dogs^{8,29} and occasionally in cattle.¹⁶ One example has been reported in man.¹⁸ The common mast-cell lesion in man is the skin disease of childhood, urticaria pigmentosa,⁵⁰ in which focal collections of mast cells are seen in the dermis. Occasionally urticaria pigmentosa presents as a solitary tumour-like nodule^{9,46}; very rarely indeed as a generalised mastocytosis.¹³ Finally we may note that an increase of the blood mast cells occurs in chronic myeloid leukaemia, the condition in which Ehrlich¹² first found mast cells in the blood. True basophilic leukaemia is extremely rare.⁷

The Mast Cell and Heparin

In 1937 Michels²⁷ compiled his monumental review on the mast cells, summarising the literature and citing 25 unresolved hypotheses concerning the function of these cells. Ironically enough in that same year reports came from Scandinavia that the "riddle of the metachromatic granules in the mast cells of Ehrlich" had been solved.^{19,22,23}

Swedish workers have been traditionally interested in anticoagulants, and Jorpes²⁸ and his colleagues in Stockholm had long been working on a powerful anticoagulant first isolated from dog liver and hence called

* Based on a postgraduate lecture delivered in the Medical School, Dundee, on Nov. 19, 1953.

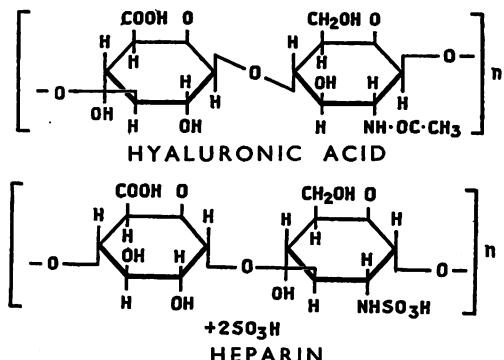


Fig. 1.—Suggested formulae for heparin and hyaluronic acid. (Redrawn from Burk 1952.⁴)

"heparin." Heparin proved to be a mucopolysaccharide rich in sulphate groups, and on finding that heparin stained metachromatically with toluidine-blue Jorpes requested his histological colleagues to search the tissues for metachromatism as a possible clue to the site of formation of heparin.¹⁹ (Cartilage, of course, stains metachromatically, but cartilage has no anticoagulant activity.) It was then that the histologists rediscovered the metachromatic granules in the mast cells and Jorpes was able to show that there is a good correlation between the mast-cell content of a particular tissue and the amount of heparin that can be extracted from it. Point has been given to this work by the recent demonstration of exceptionally high anticoagulant activity in a mast-cell tumour²⁰—a small mastocytoma from a dog yielding fifty times as much heparin as the animal's whole liver, the organ from which heparin received its name.

This newly discovered function seemed to provide an obvious and teleologically satisfactory explanation of the perivascular location of the mast cells. Mast cells are perivascular because they produce heparin which they pour into the blood-stream. It was a study of this very relation of mast cells to blood-vessels which led to the discovery of another and completely different function of the tissue mast cell.

The Mast Cell and Histamine

According to Quensel,²¹ mast cells occur almost exclusively around capillaries. However, examination of tissues from the rat²²⁻²⁴ revealed that tissue mast cells commonly arise from undifferentiated precursor cells in the adventitia of somewhat larger vessels with obvious muscle coats. As the cells mature and fill with metachromatic granules they tend to move away from the vessels into the nearby connective tissues and there slowly lose their granule substance. Whatever is released from these granules would appear to be destined for action within the tissues rather than within the blood-stream.

In the search for some function of mast cells other than the production of heparin, it was recalled that a simultaneous release of heparin and histamine could occur from the liver of the dog,²⁵ and it thus seemed of interest to see if histamine as well as heparin might perhaps come from the tissue mast cells.

The effects of chemical histamine-liberators were first studied,²⁶⁻²⁹ and it was found that when a rat is killed quickly by an intravenous dose of fluorescent histamine-liberator the fluorescence is at first sharply localised to the mast cells, especially within the loose tissues of the peritoneum. Thereafter the mast cells break up, and when this has happened the histamine content of the tissue is found to have fallen.²⁹

As with heparin,²³ there is also a good correlation between the histamine content of a particular tissue and the number of mast cells which it contains,²⁷ and this is especially evident when pathological tissues rich in mast

cells are examined.^{28,29} The lesions of urticaria pigmentosa contain two and a half times as much histamine as the adjacent skin, and with this we may correlate the well-known dermatological observation that light stroking of one of these lesions rapidly produced a reactive weal limited to the lesion itself. The mast-cell content of mouse skin increases on painting with a carcinogenic hydrocarbon, and as this takes place the histamine value also rises. Mast-cell tumours contain exceptionally high quantities of histamine, a pleomorphic mast-cell lesion from a child yielding the unprecedented value of nearly 1000 µg. (1 mg.) histamine per grammme of tissue.

Thus mast cells appear to be as rich in histamine as they are rich in heparin.⁴² But when we remember that mast cells are plentiful in lower organisms which lack a blood-vascular system, and that even in higher animals the cells appear regularly to be associated with the tissues rather than with the blood-vessels, we have grounds for doubting whether either heparin or histamine completely answers Ehrlich's riddle. Indeed it seems possible that the production of both heparin and histamine are but part of the mast cell's function, and that there remains unproved a third function which is probably a fundamental interaction between the mast cell and the connective tissues. Such views are admittedly speculative, but at least they may point the way to a further chapter in the story of the mast cells.

Heparin and Hyaluronic Acid

Heparin is a polymer, compounded of disaccharide units consisting of glucuronic acid and an amino-sugar, glucosamine.²³ In this respect heparin closely resembles another naturally occurring polymer of great physiological interest, hyaluronic acid.⁴ But whereas the amino-sugar of hyaluronic acid is acetylated, that of heparin is sulphated (fig. 1). It is the sulphate moiety especially which confers on the heparin molecule its anticoagulant

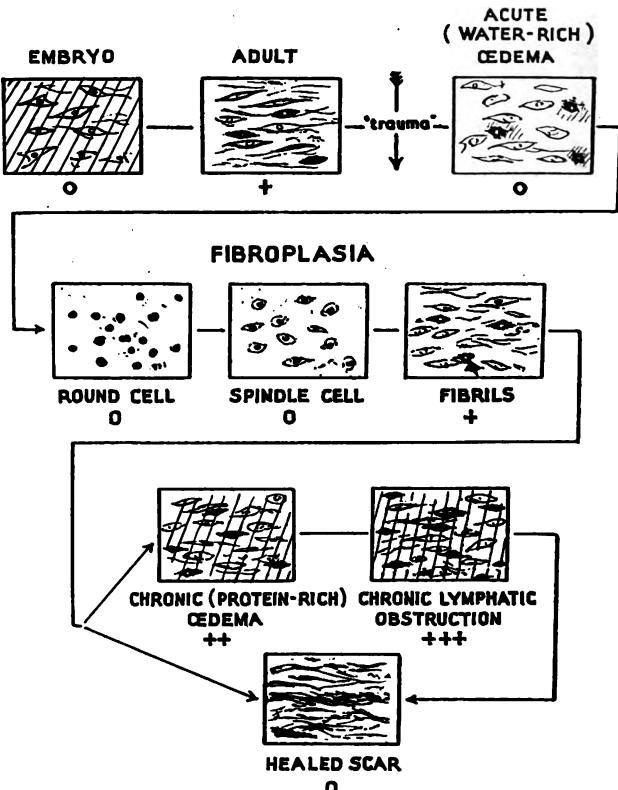


Fig. 2.—Diagram to show the participation of the mast cells in the dynamics of the connective tissues. Mast-cell content is indicated by the signs 0 to ++; the cross-hatching indicates metachromatic ground substance.

property.²³ On the basis of the similarity of composition of heparin and hyaluronic acid, Asboe-Hansen¹ in Denmark now suggests that the heparin or a heparin-like precursor secreted by the mast cells into the tissues is there gradually desulphated and becomes hyaluronic acid. If the recent formulae for heparin and hyaluronic acid are correct, so simple a conversion is unlikely; the essential building blocks are there but the internal molecular linkages are different.⁴ Nevertheless, the high mast-cell content of loose fibrillary connective tissue generally,⁴⁶ and particularly of those specialised clefts in the embryonic mesenchyme which become joints,¹ and the curiously rich mast-cell population of serous membranes and organ capsules^{19 39 51} (sites normally coated with a surface film of viscous lubricating fluid), all seem to confirm the view of Staemmler⁴⁶ that the mast cells are "unicellular glands of the connective tissue which through their activity produce the mucinous interfibrillary cement."

The participation of the mast cell in the dynamics of the connective tissues is illustrated in the sequence of events shown diagrammatically in fig. 2. Mast cells are

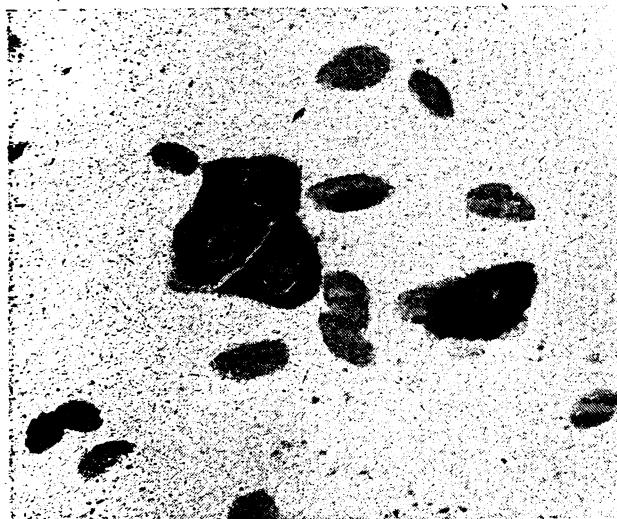


Fig. 3—Mast cells in a fresh spread of ox peritoneum; fixed alcohol, stained toluidine-blue. The cytoplasm is packed with dark metachromatic granules ($\times 535$).

not present in the early embryo, and appear in their characteristic locations only towards the end of embryonic life when they rapidly fill with granules.²⁶ If, however, the connective tissue is later subjected to trauma—mechanical, chemical, thermal, bacterial—whereby an "acute watery oedema"⁸ is produced, the mast cells promptly release their metachromatic substance into the tissues⁴⁸ (figs. 3 and 4). The appearance of tissues thus mobilised for regeneration and repair closely resembles the histological condition of embryonic connective tissue.²⁰ Fibroplasia of shorter or longer duration follows, and, as recognisable collagen begins to take its shape, mast cells once more appear in the reactive zone.^{31 46} Should fibroplasia be unduly protracted, as in chronic inflammation, the mast-cell population further increases^{11 21}; and in conditions of chronic lymphatic obstruction, in which the tissue spaces remain loaded with protein-rich oedema fluid, both mast-cell hyperplasia and connective tissue hyperplasia become extreme.² The end-point of the sequence is reached with the formation of avascular scar tissue in which neither fibroblasts nor mast cells are now present.^{21 31}

Such is the observed sequence; the difficulty lies in the interpretation. The cyclic changes in the mast-cell population of loose connective tissue certainly suggest that the mast cells are concerned in some way with



Fig. 4—A part of the same tissue spread as in fig. 3. This area was dipped in water before being fixed with alcohol. There is now disruption of the mast cells; their nuclei stain darkly; and much of the metachromatic material has diffused out of the cells and become attached to adjacent connective-tissue fibrils ($\times 535$).

the function of that tissue, and the clue may lie in the distribution of the metachromatic material, despite the reputed chemical differences between heparin and hyaluronic acid. The two types of metachromatism—the diffuse metachromatism of ground substance and the compact granular metachromatism of mast cells—are present alternately in the sequence of changes outlined above, suggesting that whatever their chemical relationship may be they bear an inverse functional relation to one another. The metachromatic ground substance present in the embryo would seem to be produced by the connective-tissue cells themselves; but, as cellular differentiation advances and the ground substance shrinks, the metachromatic mucopolysaccharides are seen to concentrate as granules in the tissue mast cells. Indeed, recent work suggests that the granules of mast cells are giant mitochondria^{5 54} some of whose enzymes actively participate in the concentration or synthesis of the metachromatic material whereby mast cells are generally recognised.³⁵

* * *

Speculating thus, a hundred years after the birth of Ehrlich, we come back to his original view of the mast cell as a "well fed cell" of the connective tissue. But the riddle is not yet solved and controversy will still surround this problem, as it surrounded so much of Ehrlich's own work. Recalling this latter fact, Sir Robert Muir²⁸ in writing Ehrlich's obituary notice, remarked "After all, truth needs little defence and nothing can affect the final issue."

My thanks are due to Prof. A. C. Lendrum for his help in the preparation of this paper.

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INTESTINAL OBSTRUCTION IN THE NEWBORN

REVIEW OF THIRTY-TWO CONSECUTIVE CASES

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UNTIL comparatively recently, operation for the relief of intestinal obstruction in the newborn held slender hope. But the outlook has been improved by wider recognition of the early symptoms, fuller knowledge of the causes, and earlier resort to surgery.

32 consecutive cases of intestinal obstruction giving rise to symptoms in the first four weeks of life are reviewed here (table I). These babies came under the surgical care of one of us (V. A. J. S.) between January, 1948, and October, 1953, and include only small-bowel and large-bowel obstruction, pyloric and anorectal obstruction having been excluded. Although the series is too small to be of any statistical significance it illustrates the pathology, diagnosis, and management of such cases.

Varieties of Obstruction

DUODENAL OBSTRUCTION : 7 CASES (TABLE II)

Intrinsic Obstruction (4 cases)

In complete occlusion of the duodenum due to atresia obstructive symptoms appeared early and persisted. Vomiting, which began as soon as feeding started, was usually copious; abdominal distension was confined to the gastric area and subsided after emptying of the stomach. In most cases straight radiographs showed gas shadows in the duodenum and stomach only (fig. 1)—an appearance which is pathognomonic. The site of obstruction was usually distal to the ampulla of Vater; in one case an atretic portion of the duodenum caused distension of the biliary passages and gall-bladder; at necropsy in another case stenosis was found to be due to a partial

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septum. At operation, when the duodenum was completely obstructed, gross distension of its proximal portion could be seen; the pylorus was dilated and appeared as a thickened rim, and the transverse colon lay in its normal situation with its mesocolon stretched over the distended duodenum (fig. 2). Enlargement of the duodenum was less when the obstruction was incomplete.

In intrinsic duodenal occlusion duodenoejejunostomy was carried out in 3 cases and gastrojejunostomy in 1.

Extrinsic Obstruction (3 cases)

The symptoms and signs of this type of obstruction were similar to those of the intrinsic type, and the two types could not be distinguished before operation; radiography was done after a barium meal in case 7 and showed partial obstruction to the flow of barium.

The condition found corresponded to that described by Ladd (1932) in that the duodenum was obstructed by a fibrous band running across the duodenoejejun junction (fig. 3); in addition the colon was malrotated, and the primitive enterocolic loop was free to rotate around the axis of the superior mesenteric vessels. In 2 cases volvulus had taken place, and its correction revealed the mal-developed arrangement of the gut with the jejunum to

TABLE I—DISTRIBUTION OF LESIONS IN 32 CASES OF NEONATAL INTESTINAL OBSTRUCTION

Lesion	No. of cases	Died	Recovered
<i>Duodenal :</i>			
Intrinsic :			
Atresia .. .	1	1	0
Stenosis .. .	3	1	2
Extrinsic .. .	3	0	3
<i>Jejunum and ileum :</i>			
Atresia .. .	4	2	2
Stenosis .. .	1	0	1
Meconium peritonitis .. .	2	2	0
Peritoneal adhesions .. .	2	0	2
Meconium ileus .. .	3	2	1
Intussusception .. .	1	0	1
Strangulated hernia .. .	3	0	3
Hirschsprung's disease .. .	9	3	6
Total .. .	32	11	21

the right and the colon to the left of the midline; in one of these cases gangrene of part of the intestine necessitated resection. The importance of dividing the obstructing fibrous bands across the distal duodenum, after untwisting the volvulus, as emphasised by Ladd, was borne out in these cases, all of which recovered.

ATRESIA AND STENOSIS OF JEJUNUM AND ILEUM : 5 CASES (TABLE III)

Stenosis of the ileum due to a partial septum was present in 1 case and atresia in 4; in the latter the obstructive symptoms and signs presented early and persisted. Radiography of the abdomen showed loops of dilated intestine contrasting with the absence of gas shadows in other parts of the film; the lower the obstruction the more numerous were the distended loops and corresponding fluid levels; these findings were useful in assessing the level of obstruction. In 2 cases of complete obstruction pale waxy trypsin-free stools were passed.

At operation the partial obstruction in case 8 (fig. 4) was relieved by a side-to-side anastomosis above and below the lesion. A year later obstruction recurred at the same site, but after excision of the obstructed segment of bowel and end-to-end anastomosis the infant finally recovered. In all 4 cases of atresia the lesions were multiple: in 1 of these exomphalos was also present, and recovery followed resection of the blind segments of the ileum and repair of the hernia; 2 infants (cases 10 and 11) were re-explored because the primary operation did not relieve the obstruction. In one of these a further site of atresia was found which had been missed by

TABLE II—DUODENAL OBSTRUCTION

Case no.	Sex	Age at onset	Age at operation	Clinical diagnosis	Anatomical findings	Type of operation	Outcome
1	F.	1 day	2 days	Duodenal obstruction	Atresia of duodenum	Gastrojejunostomy	Died
2	F.	1 day	9 wk.	Duodenal stenosis	Duodenal stenosis	Duodenojejunostomy	Recovered
3	M.	36 hr.	8 wk.	Pyloric stenosis	Duodenal stenosis	Duodenojejunostomy	Recovered
4	M.	2 days	7 days	Duodenal obstruction	Duodenal stenosis	Duodenojejunostomy	Died
5	F.	18 hr.	24 hr.	Duodenal obstruction	Extrinsic duodenal obstruction + volvulus + gangrene of jejunum	Correction of volvulus, Ladd's procedure and resection of gangrenous intestine	Recovered
6	M.	3 days	7 days	High intestinal obstruction	Extrinsic duodenal obstruction, volvulus, malrotation	Untwisting of volvulus and Ladd's procedure	Recovered
7	F.	3 days	4 days	Duodenal stenosis	Extrinsic duodenal obstruction, malrotation	Ladd's procedure	Recovered

omitting to test the patency of the *whole* length of the intestine by distension with saline solution; in the other (case 11) resection of 10 cm. of terminal ileum which had failed to function after the first operation was followed by clinical recovery, but two months later the baby died from gastro-enteritis. Case 9, with gross jejunal obstruction was a poor operative risk and the child died soon after a limited exploration.

MECONIUM PERITONITIS : 2 CASES (TABLE IV)

This is produced by leakage of meconium into the peritoneal cavity through a hole in the bowel—though the perforation may be closed by the ensuing reaction. In many cases it is associated with a primary obstruction somewhere in the intestinal tract, causing distension of the bowel above (fig. 5) and subsequent perforation (Boikan 1930).

Sterile meconium within the peritoneal cavity seems to act as a chemical irritant, and initiates inflammation which often leads to extensive fibrosis and diffuse calcification.

In case 14 (fig. 5), at operation at the age of 4 weeks, the intestines on the right side of the abdomen were found to be matted and twisted; after separation of the adhesions, which contained gritty particles, the terminal ileum was short-circuited because it seemed to be obstructed; the baby died seven hours after operation. At necropsy the abdominal cavity contained much blood, evidently from the surface of the freed bowel; in the distal ileum an incomplete septum reducing the lumen to 1-2 mm. in diameter was found; it was surrounded by adhesions, but no hole could be found; the pancreas was normal.



Fig. 1—Duodenal atresia, showing air in stomach and duodenum in contrast to absence of gas shadows from rest of abdomen.

The other case of meconium peritonitis (case 13) has been reported previously (Rashbass 1950). At operation the nature of the obstruction was obscured by dense adhesions in the right side of the abdomen; it was relieved by ileocolostomy. The infant survived for fifteen months, when necropsy showed duplication of the ileum, cystic fibrosis of the pancreas, and suppurative bronchopneumonia.

PERITONEAL BANDS AND ADHESIONS : 2 CASES (TABLE IV)

In these cases the obstruction giving rise to early symptoms was relieved by operation at the age of 5 and 10 weeks; in one case adhesions were found in the region of the transverse colon and the liver, while in the other they were more widespread; both babies recovered after the adventitious bands had been separated. The origin of these bands was obscure, but omphalitis had been present previously in both babies, and one of them had had septicæmia; possibly the adhesions arose from spread of infection from the umbilicus.

MECONIUM ILEUS : 3 CASES (TABLE IV)

Meconium ileus is produced in the newborn by blockade of the bowel, usually the small intestine, by inspissated meconium which becomes dry, tenacious, and sometimes calcified. It is associated with cystic fibrosis of the pancreas. In the present cases the signs and symptoms were those of low intestinal obstruction. In 2 of them abdominal distension was evident at birth: in 1 of these, bead-like masses of hard meconium could be felt on the right side of the abdomen; in the other a barium enema showed incomplete filling of the descending colon.

At operation in 2 cases much of the distal ileum and colon was found to contain firm pale plugs of inspissated

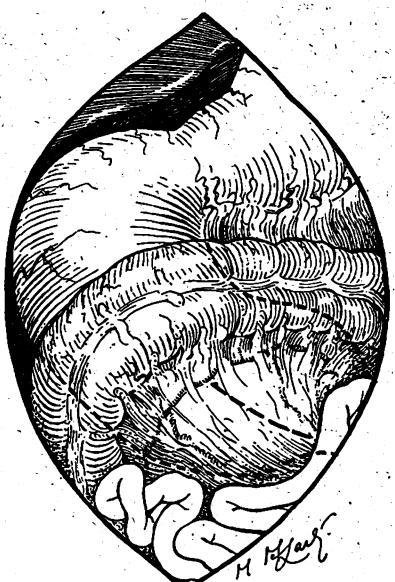


Fig. 2—Duodenal atresia, showing distension of obstructed duodenum, whose retrocolic portion is outlined by interrupted line; interrupted line in mesocolon indicates site of duodenal opening for duodeno-jejunal anastomosis; collapsed loops of jejunum are visible in lower part of wound.

material, above which the small intestine was grossly distended (fig. 6) with viscid dark-green meconium. The first of these 2 cases was treated by ileocolostomy, and in the second the meconium was removed through an opening in the bowel with the aid of saline lavage, as advised by Hiatt and Wilson (1948). Both infants died, the second baby developing hyperpyrexia and pulmonary haemorrhages five days after operation. At necropsy cystic fibrosis of the pancreas was confirmed in both cases.

The third infant was treated medically with pancreatin, because trypsin was absent from the meconium and the duodenal juice; the symptoms of intestinal obstruction which occurred on the eighth day of life subsided two or three days later without operation.

INTUSSUSCEPTION : 1 CASE (TABLE V)

Obstruction occurred on the eleventh day of life and was accompanied by rectal bleeding. Abdominal colic was not conspicuous, and the intussuscepted bowel could be palpated.

IRREDUCIBLE HERNIA : 3 CASES (TABLE V)

One case presented as a feeding problem, while another had been diagnosed as epididymo-orchitis with gastro-enteritis. All 3 babies recovered.

HIRSCHSPRUNG'S DISEASE : 9 CASES (TABLE VI)

Obstruction is the result of contraction of a variable length of the sigmoid colon. In many cases it is associated with the absence of the ganglionic cells of the intramural plexuses (Bodian et al. 1949). The symptoms came on usually within forty-eight hours of birth; vomiting,

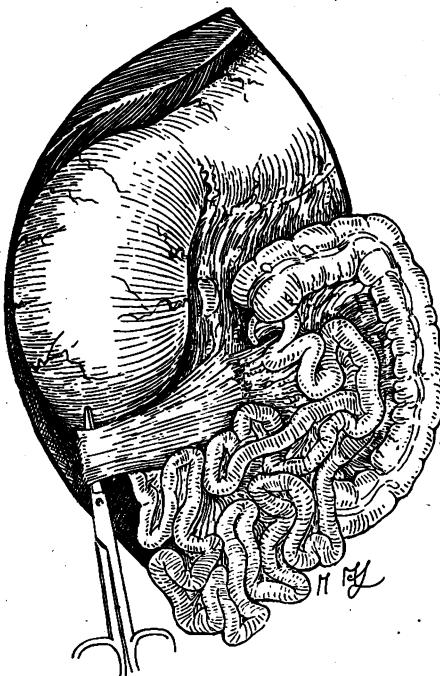


Fig. 3—Extrinsic duodenal obstruction due to fibrous band across duodenojejunal junction; showing mal-developed arrangement of intestines.

often of bile-stained fluid, occurred first and persisted, and was accompanied by increasing generalised abdominal distension and waves of visible peristalsis; there was delay in the passage of meconium, which was usually scanty. On rectal examination narrowing of the pelvic colon was detected in some cases, and sometimes faecal accumulation could be felt apparently held up by a constriction; the rectum was empty of faeces. Often the passage of a finger or a rectal tube per anum induced a bowel action, with temporary relief of obstructive symptoms. Plain radiography of the abdomen showed distension of both small and large bowel, with fluid levels in most cases. Although the diagnosis of Hirschsprung's disease was suggested radiologically in 2 cases, it was not until later in infancy that the typical segmental narrowing (fig. 7) was clearly demonstrated; with the growth of the child the narrowing portion became relatively longer, and proximal dilatation greater. In later months the distension was intermittent, and from time to time faecal accumulations could be felt in the large bowel.

Treatment aimed at relieving the intestinal obstruction until such time as the infant was fit enough to stand removal of the narrow segment by rectosigmoidectomy.

Simple measures such as laxatives, suppositories, and washouts, which were used in all the cases, were temporarily successful, but in most cases an operation to overcome the obstruction was necessary: in 2 babies, at laparotomy, disimpaction of the faeces through the narrowed segment down into the rectum, followed by the passage of a tube per anum, gave

relief; in 3 cases a colostomy was performed because the procedure just described was impossible or had failed to overcome the obstruction. Of the 3 infants who died, a premature baby had, in addition to other congenital anomalies, marked rectal stenosis; another baby died from peritonitis arising apparently from umbilical sepsis; and the third baby, who had string constriction of the pelvic colon, died after a plastic operation at that site.

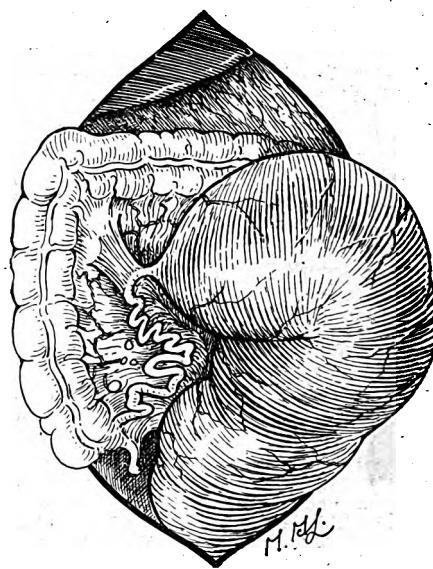


Fig. 4—Intestinal obstruction due to ileal stenosis (case 8).

TABLE III—OBSTRUCTION OF SMALL INTESTINE

Case no.	Sex	Age at onset	Age at operation	Clinical diagnosis	Anatomical findings	Type of operation	Outcome
8	M	At birth	5 days	Intestinal obstruction	Ileal stenosis	Ileo-ileostomy (resection of obstructed ileum a year later)	Recovered
9	F	8 hr.	2 days	High intestinal obstruction	Jejunal atresia	Laparotomy	Died
10	F	At birth	26 hr.	Meconium peritonitis	Multiple ileal atresia and stenoses	Resection (3 operations)	Died
11	F	24 hr.	48 hr.	Low intestinal obstruction	Atresia of ileum	Excision of atretic ileum (2 operations)	Recovered
12	F	At birth	10 hr.	Exomphalos	Multiple atresias + exomphalos	Resection and repair of exomphalos	Recovered

TABLE IV—MECONIUM PERITONITIS, PERITONEAL ADHESIONS, AND MECONIUM ILEUS

Case no.	Sex	Age at onset	Age at operation	Clinical diagnosis	Anatomical findings	Type of operation	Outcome
13	M	At birth	20 hr.	Intestinal obstruction	Meconium peritonitis; ileal stenosis and duplication of ileum (cystic fibrosis of pancreas)	Ileocolostomy	Died at 16 mos.
14	F	At birth	4 wk.	Meconium peritonitis	Meconium peritonitis; ileal stenosis	Ileo-ileostomy after separation of adhesions	Died
15	M	10 days	15 wk.	Intestinal obstruction	Plastic peritonitis	Separation of adhesions	Recovered
16	F	At birth	5 wk.	? Pyloric stenosis	Peritoneal adhesions	Separation of adhesions	Recovered
17	F	At birth	3 days	Colonic stenosis	Meconium ileus (cystic fibrosis of pancreas)	Ileotransverse colostomy	Died
18	F	At birth	20 hr.	Meconium peritonitis	Meconium ileus	Hiatt procedure	Died
19	M	8 days	..	Meconium ileus (cystic fibrosis of pancreas)	..	No operation	Recovered

Discussion

Intestinal obstruction is characterised by vomiting, abdominal distension, and constipation, which vary with the nature, site, and degree of the obstruction.

Vomiting or regurgitation of feeds occurs in the neonatal period in a variety of disorders, such as mismanagement of feeding, stenosis or spasm of the pylorus, hiatus hernia, neonatal infections, and uræmia. Only in a small proportion of cases is vomiting due to intestinal obstruction, and it is important that in these an early diagnosis be made.

Symptoms are usually more troublesome and persistent in complete obstruction, with incomplete obstruction they often vary from day to day.

Fullness of the abdomen at birth suggests intestinal obstruction arising in utero. It may, however, be found in such conditions as fetal ascites associated with abnormalities of the urogenital tract, dilatation of the bladder due to urethral obstruction, polycystic disease affecting the kidneys or the liver, and abdominal tumours. In meconium peritonitis the abdomen is sometimes distended at birth and in addition the usual signs of obstruction are present: the adhesions may cause intestinal obstruction directly or may exaggerate the symptoms of a pre-existing obstruction. In neglected cases of imperforate anus the abdomen is soft at birth but becomes increasingly distended later. Delay or the infrequent passage of scanty motions, if accompanied by increasing abdominal distension, suggests obstruction. If the meconium is pale and putty-like, there may be a deficiency of pancreatic enzyme in the lower intestine, caused either by complete obstruction or by cystic

fibrosis of the pancreas with meconium ileus; in the latter condition the ileo-caecal region is filled by a firm pale plug of inspissated material of a waxy consistence closely applied to, but not stuck to, the mucosa; the colon beyond the plug may contain some masses of this material, below which the large intestine is usually empty or contracted; the absence of trypsin from the duodenal juice, when intubation is feasible, and from the meconium will confirm the diagnosis. The obstructive symptoms and signs of meconium ileus are difficult to distinguish from ileal atresia, in which the meconium below the obstruction is of a similar nature and the presence of trypsin in the duodenum is therefore significant. The findings of amniotic squames in the meconium will exclude the presence of complete atresia (Farber 1933).

RADIOLOGICAL EXAMINATION

Plain radiography of the abdomen is invaluable. No special preparation should precede this examination, for previous stomach or bowel wash-outs may give a false impression of fluid and gas shadows. The pattern of a distended duodenum alone suggests duodenal occlusion (fig. 1), while dilatation of the small or the large bowel indicates the level of obstruction. If the cæcum is seen in its normal position, malrotation of the colon can be excluded; free gas in the peritoneal cavity may result from a perforation of the bowel; intra-abdominal calcification is commonly present in meconium peritonitis, or displacement of the intestine by an encysted mass may be seen (fig. 5). A radio-opaque meal or enema is unnecessary in most cases and should be restricted to doubtful cases when the decision to operate is uncertain. The barium should be emptied through a gastric or a rectal tube after such an examination. In Hirschsprung's disease a barium enema in the first few weeks of life is of doubtful value in the diagnosis.

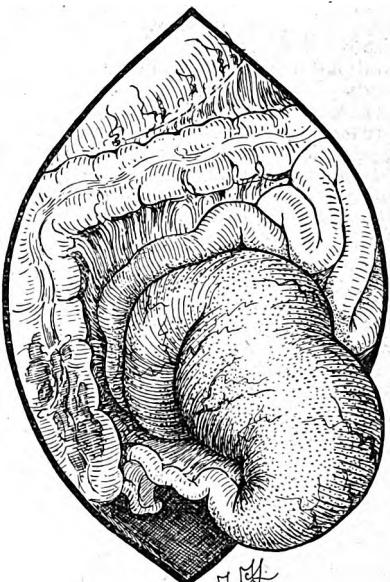


Fig. 6.—Obstruction of terminal ileum due to inspissated meconium (case 17).

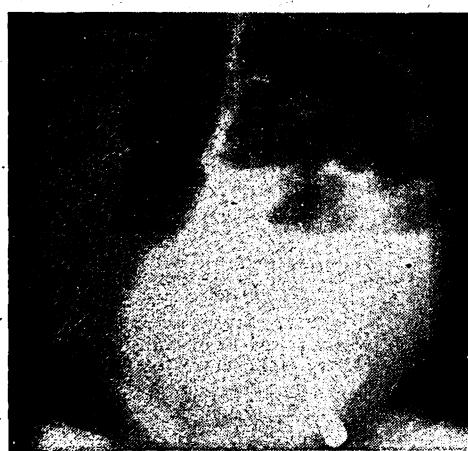


Fig. 5.—Radiograph of case 14 showing (1) abdominal distension with obstructed loops of small intestine with fluid levels and (2) areas of calcification on right side.

TABLE V—INTUSSUSCEPTION AND STRANGULATED HERNIA

Case no.	Sex	Age at onset (days)	Age at operation (days)	Clinical diagnosis	Anatomical findings	Type of operation	Outcome
20	M	11	12	Intussusception	Intussusception (ileocolic)	Reduction and ileocolostomy	Recovered
21	M	12	21	Strangulated inguinal hernia	Strangulated inguinal hernia	Reduction and repair	Recovered
22	M	19	31	? Epididymo-orchitis ? hernia	Strangulated inguinal hernia	Reduction after ileo-ileostomy and orchidectomy	Recovered
23	M	21	23	Strangulated hernia	Strangulated hernia	Reduction and repair	Recovered

OPERATIVE CONSIDERATIONS

Treatment is best carried out in a neonatal centre, where suitable nursing and medical facilities are available.

Operation as soon as possible after birth offers the best results. Unfortunately neonatal obstruction often occurs in premature infants, for whom the risk of operation is serious; but it should be borne in mind that unrelieved complete obstruction will inevitably result in death. In cases of incomplete obstruction conservative treatment should not be prolonged if the response is poor or the baby's condition begins to deteriorate.

In most cases correction and maintenance of the fluid and electrolyte loss is necessary, and should be undertaken with mathematical precision (Medical Research Council 1952).

The operative treatment for most conditions causing neonatal obstruction is on well-recognised surgical lines; but there are a few in which the treatment is not so uniform:

In *duodenal obstruction* due to atresia, duodenjejunostomy is the procedure of choice. Extrinsic duodenal occlusion is relieved by division of the peritoneal bands across the duodenum after correcting the associated volvulus.

In *occlusion of the jejunum or ileum* resection followed by anastomosis in continuity is the ideal operation, but the disparity in the size of the bowel above and below the obstruction may present difficulty. Results are better in incomplete obstruction than in complete obstruction. As complete obstruction is often multiple, the patency of the intestine should always be tested.

In *meconium ileus* the results are poor, largely because of the viscid nature of the meconium and the inability of the lower bowel to regain its function after operation. Andersen (1949), in a review of cases of cystic fibrosis of the pancreas, reports that, after she adopted the method devised by Hiatt and Wilson (1948), 5 of her 8 cases of intestinal obstruction due to meconium blockage were successfully treated. Hiatt advocated opening the bowel

and removing the sticky meconium by saline irrigation followed by closure of the enterotomy. Gross (1953) recommended Paul-Mikulicz resection of the terminal ileum which contains the firm meconium; Nixon (1953) reported a successful case after a simple enterostomy. To avoid an external ileostomy wound, one-stage resection is preferable; but it may not be feasible, owing to the length of bowel involved or to the degree of obstruction. With all the above procedures pancreatic either locally or by mouth is necessary. Volvulus or meconium peritonitis may complicate meconium ileus; the obstructed loop, being filled with dark-green or brown meconium or faeces, may twist or perforate.

If diagnosed early some cases of meconium ileus respond to conservative measures only (case 19).

After recovery from operation, babies with cystic fibrosis of the pancreas are treated with a high-protein high-vitamin and high-calorie diet, in addition to pancreatic by mouth. Should respiratory infection supervene, chemotherapy will be necessary.

Meconium peritonitis is usually fatal, but operation holds a hope for recovery. The severity of the peritoneal reaction will depend on the extent of the extravasation of meconium; if this is large it may fill the peritoneal cavity or form an encysted collection limited by the abdominal parietes and adjacent viscera, with the intestine matted round it. If, however, the leak is small, a conglomerate mass of adherent bowel is formed round the perforation; in such cases the coils of intestine will be soiled by meconium-like material and roughened by gritty particles of calcification.

When a large collection is present, preliminary paracentesis will decompress the abdomen, and the fluid can be tested for the presence of trypsin; the abdomen is then explored, and any perforation in the bowel closed by fine suturing; in most cases the primary obstruction is difficult to find, but the anatomy may be clarified by gentle separation of the adherent intestines; the obstruction is preferably treated by resection of the affected area.

Until recently the prognosis was poor, but Low et al. (1949), Forshall et al. (1952), and Franklin and Hosford (1952) have reported successfully treated cases.

In *Hirschsprung's disease* treatment consists in relieving the obstruction and establishing regular motions by the aid of enemas and laxatives until such time as the child is old enough to stand removal of the narrowed segment by rectosigmoidectomy. We consider that it is safer to wait until 2 years of age.

In cases in which the obstruction cannot be overcome by simple measures immediate operation is necessary. In such infants, the small bowel and the large bowel are distended, with narrowing usually in the descending or pelvic colon, where an accumulation of firm meconium may be held up; by squeezing this down into the rectum

TABLE VI—HIRSCHSPRUNG'S DISEASE

Case no.	Sex	Age at onset	Age at operation	Clinical diagnosis	Type of operation	Outcome
24	M	2 days	..	? Hirschsprung's disease	No operation	Recovered
25	M	1 day	6 wk.	Low intestinal obstruction	Laparotomy	Recovered
26	M	1 day	5 days	? Congenital rectal stenosis	Colostomy	Died
27	M	1 day	15 days	Stenosis of colon	Laparotomy	Died
28	F	At birth	13 days	Intestinal obstruction	Laparotomy	Recovered
29	F	At birth	5 days	Intestinal obstruction	Colostomy	Died
30	M	3 days	6 mos.	? Hirschsprung's disease	Colostomy	Recovered
31	M	1 day	2 days	? Ileal obstruction	Laparotomy (colostomy at 5 wk.)	Recovered
32	M	2 days	6 mos.	? Hirschsprung's disease	Colostomy	Recovered



Fig. 7.—Barium enema in case 24, showing characteristic appearance of Hirschsprung's disease at age of 10 months.

and passing a rectal tube the obstruction can be relieved. Where the lower segment is too narrow for this to succeed a colostomy is made.

Even if the newborn child with this condition survives the early obstructive stages, constant supervision is required to guard against a recurrence, laxatives and regular saline washouts being given as necessary. In some cases the inconvenience and risks of frequent bowel washouts and of chronic abdominal distension justify an early colostomy; in others the disadvantages of an abdominal opening are outweighed by the establishment of regular bowel actions and diminished calibre of the colon.

Whether the late results of rectosigmoidectomy are better after the early or the delayed colostomy is uncertain. In each case the progress of the child, the certainty of the diagnosis, and the adequacy of maternal or nursing care should be considered before performing a colostomy.

After operation for these various conditions constant attention is necessary to assist the recovery of these infants. They are usually nursed in an oxygen cradle, and gastric suction is maintained. Oral feeding is withheld till flatus or motions are passed, usually within forty-eight hours; then feeding is gradually introduced, and parenteral fluids are reduced and finally stopped. The discriminate use of antibiotics will lessen the chances of postoperative infection.

PROGNOSIS

Evans (1951), Rickham (1952), Jolleys (1952), and others have drawn attention to the high mortality of intestinal obstruction in infants, which is about 75%; they all emphasised the importance of early diagnosis and the application of modern developments in the management.

Prematurity, other congenital abnormalities, and associated birth injury or infection will increase the mortality.

The symptoms vary with the degree of obstruction: complete obstruction leads to persistent symptoms and rapid deterioration in the baby's condition, and therefore operation should be rarely delayed; whereas incomplete obstruction, with its intermittent symptoms, may cause conservative measures to be unduly prolonged.

Recognition of the coexistence of volvulus and extrinsic duodenal adhesions, as emphasised by Ladd (1932), has led to an increased number of survivors. The identification by Andersen (1938) of cystic fibrosis of the pancreas as a clinical entity has led to a measure of success in the treatment of the associated meconium ileus. In cases of meconium peritonitis, which was until recently always fatal, the occasional success justifies early operation. Gastro-enteritis was a feared complication in the newborn, but should now be rare. In Hirschsprung's disease operation may be required in the neonatal period to save life, and an early diagnosis must therefore be made.

In this series of 32 infants, 11 died after operation and 21 recovered, 19 of whom had undergone operation (table I).

It is encouraging that in recent years successfully treated cases are being more frequently reported than in the past. We may hope that advances in paediatrics and their surgical application will further improve the outlook.

Summary

32 consecutive cases of neonatal obstruction illustrate the pathology, clinical features, and treatment of duodenal obstruction, jejunal and ileal atresia and stenosis, meconium ileus, meconium peritonitis, intussusception, peritoneal bands, and Hirschsprung's disease. 21 of the infants in this series recovered.

The value of early diagnosis, radiological examination, and detailed attention to supportive measures of resuscitation is emphasised.

The elucidation of such clinical entities as fibrocystic disease of the pancreas, meconium ileus, meconium peritonitis, and Hirschsprung's disease has led to rational treatment. The present mortality of obstruction in the first weeks is more than 75%; but this high figure should be reducible.

We are much indebted to our colleagues, especially Dr. H. M. M. Mackay, Dr. R. H. Dobbs, and Dr. W. F. Young, for their kind co-operation; to Dr. C. J. Hodson and Dr. B. C. H. Ward for the radiological work; and to the nurses, the resident medical officers, and the anaesthetists for their valuable help.

Addendum

Since this article was completed, case 12 has died at the age of five months from congenital abnormality of the heart. There have been 3 further cases. 1 was a premature baby who was operated on unsuccessfully for high jejunal atresia when a week old. In the other 2 intermittent obstruction developed at the ages of 2 and 3 weeks, in each case after a generalised infection; 1 recovered after a week with conservative treatment, while the other is responding slowly to similar management after three months. In both cases the cause of the obstruction is uncertain.

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SUBDURAL COLLECTION OF FLUID IN TUBERCULOUS MENINGITIS

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SUBDURAL collections of fluid have been known since the time of Hippocrates, or such was the opinion of Robert Whytt (1768):

"Hippocrates has enumerated in his second book 'De Morbis' the signs of 'water in the brain,' as his words have been rendered by all the translators. But ἐπὶ τῷ ξύκεφαλῳ more properly signifies upon than in or within the brain, and that Hippocrates only speaks here of water lodged between the dura mater and brain can scarcely be doubted, since he proposes to evacuate it by making a perforation in the upper part of the cranium, which operation could have been of no use had the water been contained within the brain itself."

However, it is well known that the cortex may be so thin in gross hydrocephalus that it could have been mistaken for a membrane.

Nowadays subdural collections of fluid are well known, and they fall naturally into two groups: those due to intracranial bleeding, and those which occur in the presence of infection. Penfield (1923) described in a young boy a purulent subdural effusion due to a spread of infection from otitis media; Schiller et al. (1948) described a loculated subdural abscess complicating pneumococcal leptomeningitis due to frontal sinusitis; and since then other subdural empyemata spreading directly from infections of the paranasal sinuses and the middle ear have been described.

More recently attention has been drawn to subdural effusion in children with primary meningitis without any evidence of middle-ear or sinus infection. The two patients reported by Spitz et al. (1945) died of purulent meningitis, which in one case was due to a pneumococcus and in the other to *Haemophilus influenzae*; subdural collections of fluid were found post mortem. However, this condition, as well as subdural empyema, was known long before this: Monro (1827) gives an excellent account of both, but of especial interest is his account of a boy who had an encephalomeningocele and undoubtedly died of purulent meningitis. At necropsy turbid fluid was found in the ventricles, and there were bilateral subdural effusions containing, on the right, 6 oz. of clear highly proteinous fluid, and on the left a small quantity of similar fluid. Further cases complicating purulent meningitis have been reported by McKay et al. (1950), Smith et al. (1951), Arnold (1951), Everley Jones (1952), and Guthkeloh (1953). Everley Jones noted that in the previously reported cases the organism responsible for the meningitis had been *H. influenzae* in twenty cases, a pneumococcus in twelve, a paracolon bacillus in one, and *Pseudomonas aeruginosa* in one. The organism in three of his cases was a meningococcus, and he makes the point that subdural effusion had never previously been reported in meningococcal meningitis. Duperie and Dubourg (1913) reported a case in an infant of tuberculous meningitis complicated by a subdural haematoma; and McKay et al. (1953) have included a case of subdural effusion due to tuberculous meningitis in a table of figures, but do not refer to it in the text. I have not been able to find any other published report of a subdural collection of fluid complicating tuberculous meningitis; therefore the following case is interesting.

Case-report

A woman, aged 43, was admitted to another hospital on Sept. 15, 1952, in a stuporous condition. She could not describe her symptoms, but her husband said that she had been quite well until four months previously, when she developed, in her back, pain which extended from the cervical region to the sacrum. She had no headache and continued to work about the house and pursue her usual activities until the end of August, when she was sufficiently unwell to take to her bed. A week later she developed in her left shoulder a moderately severe aching pain which radiated down the left arm to the fingers. A few days after the onset of this pain, which persisted, occipital headache came on in such severe paroxysms that she held her hands to her head, cried out, and was completely incapacitated until the pain subsided. Three days before admission she became drowsy and confused, vomited occasionally, and developed acute retention of urine.

On examination she was confused and uncooperative. Her temperature was normal, her blood-pressure was 170/110 mm. Hg, and she showed signs of dehydration. Her bladder was distended to 6 in. above the symphysis pubis. Examination of the central nervous system showed severe neck stiffness and a positive Kernig's sign but no localising signs. Lumbar puncture produced yellow turbid cerebrospinal fluid (c.s.f.) containing 40 leucocytes per c.mm., and 65 mg. of protein, 500 mg. of chloride, and 22 mg. of sugar per 100 ml. There was a partial block on Queckenstedt compression. Examination of the blood showed haemoglobin 87% and 13,900 leucocytes per c.mm. (polymorphs 91%). Radiographs of the skull were normal, but a film of the chest showed diffuse miliary tuberculosis. At the hospital to which the patient was admitted she was treated with streptomycin 0.5 g. intramuscularly twice daily and 100 mg. intrathecally, and *p*-aminosalicylic acid 20 g. daily. Two days after admission it was found that the spinal subarachnoid pathway was blocked. The patient's state of consciousness had deteriorated, and she responded only to painful stimuli such as firm supra-orbital pressure and pinching of the facial skin, and it was suspected that the deterioration was due to an increase of intracranial pressure. It was therefore decided to cut burr-holes and make ventricular studies. Streptomycin could also be introduced into the ventricles if indicated. She was accordingly sent to this Unit on Sept. 18, 1952.

Operation.—On arrival at the theatre she was barely rousable, her pupils were equal but reacted poorly to light, and she had bilateral rigidity and extensor plantar responses. Under local anaesthesia bilateral frontal burr-holes were made over the coronal suture 2 cm. from the midline. The dura on the right side was tense, and on opening it there was a gush of clear fluid under pressure. About 50 ml. of this fluid was collected for examination. The cortex was separated from the dura by 1 cm., but no definite membrane was recognised. A cannula was passed into the lateral ventricle, and on the introduction of streptomycin 50 mg. more clear yellowish fluid welled up from the subdural space. The dura under the burr-hole on the left side was opened, and a second collection of fluid was released, rather less than on the right. The cortex here was also depressed.

Postoperative Course.—The patient's condition at the end of the operation was very much improved: she was more alert, could answer questions, and said that she had no headache. She maintained this improvement for four days, but her condition then deteriorated: she developed increasing abdominal tympanites and vomiting, and died on Sept. 24, six days after the effusions had been drained.

Necropsy Findings.—Diffuse miliary tuberculosis of the lungs was confirmed, and scattered tubercles were found in the kidneys. The stomach and intestines were atonic and distended. The brain showed flattening of the cortex over the front of the hemispheres, and some reddening of the dura at the site of operation, but no further collection of fluid was found. There were gelatinous adhesions over the base of the brain, but the striking finding was a thick jelly-like exudate covering the spinal cord from the upper cervical segments to the region of the conus medullaris; this was more organised and clearly of longest standing in the cervical region.

The subdural fluid collected at operation had clotted on arrival at the laboratory, and it must therefore have contained much protein. Attempts to culture tubercle bacilli from the clot failed.

The ventricular fluid was slightly turbid, there was no coagulum; it contained 3 lymphocytes and 183 red blood-cells per c.mm., and 28 mg. of protein and 68 mg. of sugar per 100 ml. The chloride content was not estimated. There was no excess globulin, and attempts to culture tubercle bacilli failed.

Discussion

INTERPRETATION

This patient evidently had miliary tuberculosis, and her central nervous system became involved, beginning with spread to the cervical cord—a rare mode of onset, but important to recognise if such cases are to be diagnosed early enough for treatment to be successful. The history of her illness indicated that some weeks elapsed before the onset of severe headache heralded intracranial extension of the spinal infection. This was followed by rapid deterioration in her level of consciousness which was, no doubt, due to the development of the subdural effusions. As often happens, this patient had widespread foci of active infection in places other than the central nervous system, and death might easily have resulted ultimately from one or other of these.

MANAGEMENT OF TUBERCULOUS MENINGITIS

Since the introduction of streptomycin the management of tuberculous meningitis has undergone very critical examination from time to time, and in recent years it has become evident that surgery has an important but limited part to play, not in a desperate attempt to rescue patients with advanced meningeal infection which, because of inflammatory exudate, is already beyond the reach of streptomycin, but in the treatment of the few cases which, after cure or control of the initial infection, develop a tuberculoma, a tuberculous abscess, or a block somewhere in the cerebrospinal subarachnoid pathways, with resulting hydrocephalus.

In the active stage of tuberculosis attempts to prevent or short-circuit the obstructing granulations in the basal and ambient cisterns have proved disappointing, for in most cases the deterioration has been due not to obstruc-

tion but to neuronal damage following thrombosis of vessels surrounded by granulations.

There are, however, very good reasons for making exploratory burr-holes in any case of tuberculous meningitis when the level of consciousness deteriorates fairly suddenly and evidence of an acute rise of pressure is found.

Cairns (1951) described two cases in which the intracranial pressure rose suddenly. One of these patients died and was found at necropsy to have a tuberculous abscess in the left parietal lobe. The other, a boy aged 3 years, developed signs of an acute rise of intracranial pressure and was found to have localised hydrocephalus of the temporal horn of the right lateral ventricle; this was relieved by operation and he recovered.

A third case which illustrates the importance of burr-holes and ventriculography was recently transferred to this Unit from another hospital. This patient, a married woman aged 26, had been treated for about three months for tuberculous meningitis and had made a good recovery, when she began to have severe intermittent headache suggesting attacks of hydrocephalus. Ventriculography revealed a space-occupying lesion in the right cerebellar hemisphere, and at operation a tuberculous abscess was successfully removed.

In the present case the subdural collection of fluid rapidly produced a severe impairment of consciousness. This was immediately relieved by drainage; so possibly more cases of subdural effusion await discovery in patients with tuberculous meningitis whose symptoms suggest raised intracranial pressure of acute onset, and drainage may be beneficial and even life-saving.

AETIOLOGY OF SUBDURAL COLLECTIONS OF FLUID

The aetiology of subdural haematoma and hydroma resulting from trauma is well understood; so it is sufficient here to point out that in both conditions the arachnoid may be torn (Quincke 1906, Hardman 1939). The cause of subdural collections of fluid associated with meningitis is not so clear, but they are probably in most cases also due to rupture of the arachnoid membrane. Although Spitz et al. (1945) have been widely cited as believing that these effusions are due to escape of blood from a thrombosed subdural vein, they suggested five different possible mechanisms.

(1) *Direct Extension through a Necrotic Arachnoid Membrane, either at the Arachnoid Villi or over the Hemispheres.*—This is an obvious mechanism of spread of infection to the subdural space in cases where the causal organism has strong cytolytic power, but this has been a necropsy finding in cases of virulent infection (especially by *H. influenzae*) and is unlikely to explain the effusions found in mild cases.

(2) *Simple Transudate through Damaged Arachnoid.*—This theory has received support from Smith et al. (1951), Everley Jones (1952), Gitlin (1952), Guthkelch (1953) (for effusions containing little protein), and McKay et al. (1953). It is natural to believe that a membrane such as the arachnoid could permit transudation when it is inflamed, just as do the pleura and peritoneum. It is, however, very unlikely that simple transudation can be the sole cause, because all cases of meningitis are accompanied by meningeal inflammation, yet few of them develop subdural effusions of sufficient size to cause symptoms.

(3) *Escape of Blood from Thrombosed Vein.*—Aseptic thrombosis of cerebral veins and sinuses is known to be associated with intracerebral, subarachnoid, and subdural haemorrhage (Russell 1949, Barnett and Hyland 1953); but in such cases the bleeding has clearly taken place not from thrombosed subdural veins but from engorged capillaries in areas of infarction. Guthkelch (1953) suggested that this might be the mechanism in effusions containing much protein; but the protein content of effusions, like that of C.S.F., varies with the infecting organism and the chronicity of the disease.

(4) *Involvement of Subdural Space secondary to Thrombosis of Venous Sinus.*—It is most unlikely that this is the cause of subdural collections, since the incidence of such effusions has not lessened with the advent and use of antibiotics, which are very effective in preventing sinus thrombosis; and the fact that sinus thrombosis and effusions may be present together is not proof that the one is the cause of the other.

(5) *Simultaneous Involvement of both Arachnoid and Dura by Blood-borne Infection.*—Although Spitz et al. (1945) had no evidence from their material that this ever happened, they mention this theory, which may be very important. Consideration of the portals of entry of meningitis leaves little doubt that focal embolic sepsis in the bone, the emissary veins, or the cortex may be the start of meningitis, brain abscess, and subdural infection (Johnson 1953).

Rupture of Arachnoid Membrane.—I suggest an alternative mechanism—simple rupture of the arachnoid membrane due to raised subarachnoid pressure.

In meningitis, probably because of arachnoidal inflammation and impaired absorption of C.S.F., the subarachnoid pressure is raised. An inflammatory exudate from the vascular pia-arachnoid passes into the subarachnoid space and, together with oedema in the underlying cortex, produces obstructions at various places in the cerebrospinal subarachnoid pathways.

The arachnoid mater is normally thinner over the hemispheres than at the base and, unlike the pia mater, bridges over the sulci, except where it dips into them a little on the walls of emerging veins. The subarachnoid space is shallow over the summits of the gyri but deeper over the sulci, and the pia and arachnoid are connected by fine connective-tissue trabeculae. These trabeculae are not normally under tension.

With exudate adding to the volume of fluid in the ventricles and subarachnoid space, and at the same time seriously diminishing absorption at the villi, the intracranial tension rises, the brain becomes oedematous, and the gyri become wider, partially obliterating the sulci and squeezing the fluid out of them. This fluid, which may be loculated by adhesive arachnoiditis, distends the subarachnoid space and tears the delicate arachnoid, allowing a spurt of C.S.F. and exudate to reach the subdural space. Tight trabeculae may determine the point of rupture.

Once in the subdural space, such a collection would tend to spread, and the protein in it might form a membrane which would become vascularised by new capillaries from the dura. Moreover, once the effusion had formed, the obstruction to the absorptive area would be increased and a pressure gradient would exist from the subarachnoid space, deep to the thin inner membrane of the effusion, to the arachnoid villi adjacent to the sinus. This would probably increase the effusion, aided perhaps by osmosis and a leakage of red cells from the membrane as its young vessels were stretched.

Effusions are a result of a tear in the arachnoid is supported by Cairns et al. (1946), who described a trial of intrathecal penicillin in a case of suppurative meningitis. Penicillin was administered by lumbar puncture, and twelve hours later it had disappeared from the C.S.F.; so these workers introduced penicillin directly into the ventricles. On making frontal burr-holes they found a large subdural collection of yellow fluid containing 0.5 units of penicillin per ml., while the ventricular fluid contained 1 unit per ml. Some of this penicillin must clearly have passed through a hole in the arachnoid membrane. It did not simply diffuse, for after the injection of 8000 units of penicillin into the subdural space at the site of the effusion none appeared in the C.S.F., indicating that either the hole had closed or it was a valve-like one-way opening.

Everley Jones (1952), by injecting indigo carmine into an effusion, showed that effusions do not remain in contact with the subarachnoid space. Further evidence that rupture of the arachnoid may follow increased subarachnoid pressure is to be found in descriptions by Dandy (1944), Bassett and Lemmen (1952), and Logue (1951) of subdural haematoma complicating subarachnoid haemorrhage.

The rarity of subdural collections in tuberculous meningitis may possibly be explained by the fact that

sudden rises in subarachnoid pressure with distension of the subarachnoid space are rare in this disease.

Summary

A fatal case of subdural collection of fluid complicating tuberculous meningitis is described.

It is important to make burr-holes in cases where the level of consciousness suddenly deteriorates.

A tear in the arachnoid is probably the important factor in the aetiology of subdural collections of fluid.

I wish to thank Dr. G. H. H. Benham, who referred the case, for the use of his records and the necropsy report; Sir Geoffrey Jefferson, F.R.S., for drawing my attention to Monro's book; and Mr. R. T. Johnson, O.B.E., F.R.C.S., for permission to publish and for kindly advice and criticism.

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POST-TRANSFUSION SURVIVAL OF RED CELLS STORED AT -20°C

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RED blood-cells mixed with glycerol can be frozen to -79°C and thawed without haemolysis (Smith 1950). If the cells are freed from glycerol and transfused they survive normally in the recipient's circulation (Sloviter 1951, Mollison and Sloviter 1951). Red cells suspended in citrate-plasma and mixed with an equal volume of 30% (w/v) glycerol in 0.9% saline solution (i.e., final glycerol concentration 15% w/v) undergo progressive lysis if stored at -79°C, with the result that after six months only 60% of them may be recovered. However, these red cells have an almost unimpaired survival in vivo (Mollison et al. 1952). Red cells stored in the same mixture at -20°C undergo even more rapid lysis; but the cells recovered after three months' storage may survive well in vivo (Mollison et al. 1952). This last finding suggested that at -20°C chemical changes in red cells might be virtually arrested and that, if physical damage could be prevented, prolonged storage at -20°C could be achieved. -20°C is a temperature that can be maintained very easily—for example, in an ordinary ice-cream cabinet. It would therefore be a great advantage

if prolonged preservation of red cells were possible at this temperature rather than at some lower temperature.

Chaplin and Mollison (1953) reported that, if red cells were mixed with citrate-glycerol rather than with saline-glycerol, and if the final concentration of glycerol were raised from 15% (w/v) to 30% (w/v), the rate of haemolysis during storage at -20°C was enormously reduced. After three months' storage 98% of the red cells were intact. In view of the previous demonstration that red cells stored at -20°C for three months survived normally, it seemed likely that red cells stored in the new solution would survive well; but these workers pointed out that measurements of survival in vivo would have to be made before the usefulness of the method of storage for transfusion was established.

We report here mainly the post-transfusion survival of red cells stored in different glycerol mixtures at -20°C. Red cells stored in the citrate-glycerol mixture originally described do not survive well, but in slightly modified mixtures survival remains very good until the period of storage exceeds three months. Thereafter viability is lost progressively with time. Red cells stored at -20°C slowly consume dextrose, and their loss of viability is probably due to the fact that chemical changes are not completely arrested at -20°C.

Methods

STORAGE TEMPERATURES

A temperature of about -20°C was maintained in a 'Prestcold' refrigerator cabinet, model CC 82. Bottles of blood for transfusion were kept in the lower compartment, in which the temperature ranged from -21°C to -24°C. Smaller samples of blood were kept in the upper compartment of the refrigerator, in which the temperature ranged from -18°C to -20°C. For convenience storage in the range from -18°C to -24°C is referred to here as " -20°C."

A few experiments made at other temperatures are included here. These temperatures were maintained as follows:

For storage at -79°C a special insulated box was used containing a large tank in which solid carbon dioxide was placed as often as necessary, and a smaller tank containing alcohol in which the bottles or tubes of blood were kept. Solid carbon dioxide was added to the alcohol bath two or three times a week; this kept the temperature in the bath between -75°C and -79°C. Occasionally the temperature in the bath rose to -70°C. A temperature of -10°C was maintained in a cold-room, and +4°C in an ordinary domestic refrigerator.

BLOOD-GLYCEROL MIXTURES

Red cells of group O type M or of group A type N were obtained from blood collected at routine bleeding sessions of the North London Transfusion Centre. This blood was taken into A.C.D. solution (disodium citrate 2 g., dextrose 3 g., water 120 ml., mixed with 420 ml. of blood) and stored for either twenty-four or forty-eight hours at +4°C. The red cells were next packed by centrifugation, and almost all the supernatant plasma-citrate solution was removed. The bottles usually contained about 230 ml. of packed red-cell suspension; it was estimated that about 20 ml. of this volume consisted of plasma citrate either trapped among the red cells or lying on the surface of the suspension. To this packed-cell suspension was added an equal volume (about 230 ml.) of one of the following mixtures:

Solution I (trisodium citrate/glycerol).—This mixture was the one described by Chaplin and Mollison (1953). 40 volumes of glycerol was added to 60 volumes of 5% trisodium citrate (the pH of this solution is 7.7). On the assumption that glycerol diffuses freely into 60% of the red-cell volume, the final concentration of glycerol after mixture with the packed cells is 30% (w/v), or 3.3 M; citrate is assumed not to penetrate the red cells, and its final concentration in this

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mixture is therefore 0.1 M. In two additional experiments described below this solution was modified to give a final glycerol concentration of 20% and 40%.

Solution II (tripotassium citrate/glycerol).—40 volumes of glycerol was added to 60 volumes of 5.5% tripotassium citrate (final concentration of citrate about 0.1 M).

Solution III (buffered tripotassium citrate/glycerol).—40 volumes of glycerol was added to 60 volumes of a solution containing tripotassium citrate 3.25%, dipotassium hydrogen phosphate 0.6%, and potassium dihydrogen phosphate 0.47% to give the following final concentrations: citrate 0.06 M, each phosphate 0.02 M. The pH of this solution is 6.9.

Solution IV (plasma citrate/glycerol).—150 ml. of supernatant plasma-citrate was saved after centrifuging the blood and mixed with 90 ml. of glycerol and 9 ml. of 30% trisodium citrate (solution IVA) or with 20 ml. of 30% citrate (solution IVB). The concentration of citrate is about 0.05 M (IVA or 0.09 M (IVB), and the pH of the solution is 7.4. The final concentration of glycerol after mixture with red cells is 3.3 M.

A few investigations were made with two other solutions: (1) in one solution "dextran-citrate-glycerol," dextran (Bengers) was substituted for plasma-citrate in mixture IVA (the final concentration in this mixture was 0.03 M); and (2) in the other solution "lactate-glycerol (with added calcium)," 1 volume of the following solution was added to 1 volume of packed red cells from heparinised blood: glycerol 40 volumes mixed with 60 volumes of sodium-lactate solution to give a final concentration of 0.16 M; calcium chloride was added to give a final concentration of 0.005 M.

In each case the glycerol solution was added slowly to the packed red cells with constant agitation of the mixture. After about thirty minutes the bottles were placed in the -20°C refrigerator.

In some further experiments blood was kept solely for tests in vitro; in these cases heparinised blood was used. Packed red cells were obtained by centrifugation and mixed with one of the four solutions already described or with various modifications described below in the results.

REMOVAL OF GLYCEROL FROM RED CELLS AFTER STORAGE

The blood was thawed by placing the container in water at 40°C and agitating it until no ice was visible. The mixture was then centrifuged and the supernatant fluid replaced by a solution containing 16% glycerol in 3% trisodium citrate. The solution and red cells were well mixed and then immediately centrifuged again. The supernatant fluid was now replaced with 8% glycerol in 3% citrate and then successively with 4% glycerol in 3% citrate, 2% glycerol in 3% citrate, and saline solution. Either two or three washes in saline solution were used. The red cells were finally suspended in an approximately equal volume of saline solution.

In a few cases the glycerol content of the final supernatant solution was estimated by oxidation with periodic acid and determination of the formaldehyde formed (Karnovsky and Brumm 1954, MacFadyen 1945).

ESTIMATION OF HÆMOLYSIS IN VITRO

The percentage hæmolysis in a sample was calculated as follows:

The haemoglobin concentration sample of the supernatant fluid (Hb_s) and of the whole (Hb_w) were determined in a photo-electric colorimeter with an Ilford 625 filter. Percentage hæmolysis was expressed as

$$Hb_s \times \frac{100 - P.C.V.}{100} \times 100,$$

P.C.V. being the packed-cell volume of the whole sample.

In most cases appreciable additional hæmolysis occurred during the washing of the red cells to remove glycerol. The over-all recovery of red cells was estimated as the total haemoglobin content of the sample after washing, divided by the total haemoglobin content of the sample immediately after thawing.

MEASUREMENT OF SURVIVAL IN VIVO

All the recipients were of group A type M, and most of them were women whose anaemia was related to pregnancy or to parturition. To ensure an adequate rise in haemoglobin concentration, fresh blood of group AM was often transfused in addition to the stored red cells (of group OM and AN).

Transfused red cells in the recipient's blood were counted after differential agglutination by Dacie and Mollison's (1943) modification of Ashby's method. Counts were made twenty-four and forty-eight hours after transfusion and after a week; in most cases further counts were made at intervals until most of the transfused cells had been eliminated.

The sera used were either anti-M powdered globulin obtained from Lederle Laboratories or anti-A produced in rabbits by the method of Morgan (1943); with the anti-M serum pre-transfusion ("blank") counts were 5000 or less per c.mm. in each of 19 cases, and with the anti-A serum 10,000 or less per c.mm. in 15 out of 19 cases; in the remaining 4 cases the blanks were between 12,000 and 25,000 per c.mm.

The concentration of transfused cells expected on the day after transfusion, if 100% had survived, was calculated from the formula:

$$\frac{\text{number of red cells transfused}}{\text{total red-cell volume}} \times P.C.V.$$

(No allowance was made for the small fraction of red cells—about 0.85%—which would be expected to disappear in a day.)

The number of red cells transfused was estimated from the volume and red-cell count of the transfused red-cell suspension; the volume was calculated by weighing the bottle with its contents before and after transfusion and determining the specific gravity of the cell suspension; the red-cell count of a well-mixed sample was determined by counting not less than 4000 red cells.

Red-cell volume was determined, on the day after transfusion, by a modification (Chaplin 1954) of the ^{32}P method of Reeve and Veall (1949).

Packed-cell volume was determined in Wintrobe haematoocrit tubes spun for fifty-five minutes at 3000 r.p.m. in a centrifuge of radius 15 cm.; correction for trapped plasma was made by the method of Chaplin and Mollison (1952).

The packed-cell volume of a sample taken forty-eight hours after transfusion was often a little higher than that of a sample taken at twenty-four hours. Accordingly, in estimating the percentage survival at forty-eight hours and subsequently, the predicted 100% survival, calculated as described above, was corrected by the factor:

$$\frac{P.C.V. \text{ two days after transfusion}}{P.C.V. \text{ one day after transfusion}}$$

No corrections were made for changes in P.C.V. after forty-eight hours since many of the recipients were anaemic women in whom the rise in P.C.V. during the period of the observations was due partly to an increase in red-cell volume.

CHANGES IN CELL VOLUME

Mean cell volume (M.C.V.) was determined in the usual way from packed-cell volume and red-cell count (4000 cells counted); it was arbitrarily assumed that initially M.C.V. was 90 c. μ in all cases, and observed values were expressed as percentages of this figure. A second estimate of cell swelling or shrinking was obtained by measuring mean corpuscular haemoglobin concentration (M.C.H.C.) from the haemoglobin concentration and packed-cell volume of the sample; it was assumed that the M.C.H.C. was initially 34%, and departure of observed values from this figure was taken to indicate alteration in cell volume. In 50 cases in which changes in cell volume were estimated

TABLE I—POST-TRANSFUSION SURVIVAL OF RED CELLS STORED ABOUT TWELVE WEEKS IN VARIOUS SOLUTIONS AT -20°C

Solution	No. of cases	Average period of storage (weeks)	Percentage survival after transfusion (days)		
			1	2	7
I. Trisodium citrate/glycerol ..	7	12.6	56	48	44
II. Tripotassium citrate/glycerol ..	5	12.6	64	64	59
III. Buffered tripotassium citrate/glycerol	3	13.3	84	80	73
IV. A.C.D. plasma-citrate-glycerol ..	6	12.2	92	89	84

by these two methods the standard error of the difference between the two estimates, expressed as a coefficient of variation, was 8%.

In table II the figure given for cell volume (expressed as percentage of normal) is the mean of estimates obtained by the two methods.

INTRACELLULAR SODIUM AND POTASSIUM CONCENTRATIONS

Sodium and potassium concentrations were determined with the flame photometer (Domingo and Klyne 1949) by the method of Selwyn and Dacie (1954). The results were corrected by the factor

$$\frac{\text{M.C.V. after storage}}{\text{M.C.V. before storage}}$$

to allow for changes in cell volume; M.C.V. before storage was assumed to be 90 c.u..

OSMOTIC FRAGILITY

The method of Parpart et al. (1947), as modified by Crawford et al. (1953), was used.

ESTIMATION OF DEXTROSE

Experiments were made to compare the rate of dextrose consumption by red cells at different temperatures. Dextrose was estimated by the method described by King (1951), except that the blood was pipetted into distilled water instead of isotonic sodium-sulphate solution; and thus the estimate of dextrose concentration includes some of the reducing substances in red cells. In preliminary tests it was shown that the presence of glycerol did not interfere with the estimations.

TABLE II—INTRACELLULAR CATION CONCENTRATION, CELL VOLUME, AND OSMOTIC FRAGILITY IN RED CELLS STORED FOR ABOUT THREE MONTHS AT -20°C IN FIVE CITRATE-GLYCEROL MIXTURES

Solution	No. of samples	Period of storage (weeks)	Mean survival in vivo at 24 hours (%)	Intracellular cation concentration (m.eq. per litre)			Cell volume (% of normal)	Median osmotic fragility (% NaCl)
				Na	K	Total		
I. Trisodium citrate/glycerol ..	3	11-13	63	49	16	65	76	0.264
II. Tripotassium citrate/glycerol ..	3	10-15	64	14	45	59	74	0.276
III. Buffered tripotassium citrate/glycerol	2	14-15	84	19	68	87	88	0.350
IVa. A.C.D. plasma-citrate-glycerol ..	2	11-12	92	65	31	96	86	..
IVb. A.C.D. plasma-citrate-glycerol ..	1	14	78	65	20	85	88	0.350
Normal values	15	100	115	100	0.424

The intracellular cation concentrations have been corrected for changes in cell volume. The median osmotic fragility is in some cases derived from single samples only.

Red cells from heparinised blood were mixed with trisodium-citrate-glycerol (solution I), and then sufficient dextrose was added to bring the final concentration to 90-140 mg. per 100 ml. Aliquots of the blood were then stored at each of the following temperatures: -79°C, -20°C, -10°C, and +4°C. At intervals a sample stored at each of these temperatures was thawed and its dextrose concentration estimated.

RED-CELL ANTIGENS

Blood from 7 donors was stored at -20°C in citrate-glycerol mixtures for a year. In most cases the blood mixtures were stored in 2-3 ml. amounts in small tubes. The ability of the red-cell antigens to react with standard antisera was tested at intervals during the year. After three months' storage samples were tested with only a few antisera (anti-A, anti-M, anti-N, anti-S, anti-P, and anti-D); after five months' and twelve months' storage at least two samples were tested with anti-A, anti-M, anti-N, anti-S, anti-D, anti-C, anti-e, anti-P, anti-Le^a, anti-Le^b, anti-Lu, and anti-Fy^b; only one sample was tested with anti-B, anti-E, and anti-K.

On the day of the test a fresh sample of blood was taken from the same donor, and 1% cell suspensions of both

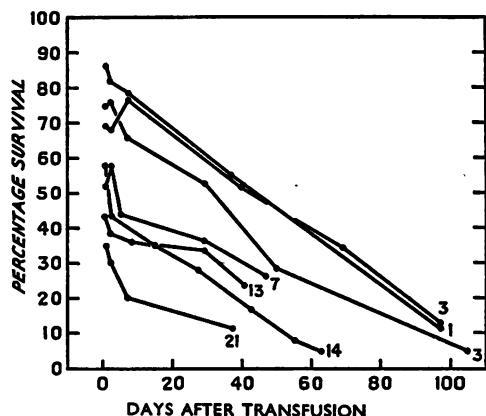


Fig. 1—Post-transfusion survival of red cells stored at -20°C in trisodium citrate/glycerol (solution I). In this figure and in figs. 2 and 3 the numbers at the end of each curve indicate the period of storage in weeks.

stored and fresh cells were prepared. Serial dilutions of each antiserum were made in bulk, and then a small volume of each was mixed with an equal volume of the cell suspension to be tested. The reactions of the frozen cells were compared with those of the fresh cells on the same slide, both macroscopically and microscopically.

Results

RATE OF SPONTANEOUS HÆMOLYSIS IN VITRO

In experiments in which packed red cells from heparinised blood were mixed with citrate-glycerol solution and stored at -20°C the effect of varying the glycerol concentration and the citrate concentration was assessed.

When the final concentration of glycerol was 30% (w/v), the average percentage lysis after a year's storage was about 15%. Increasing the concentration of glycerol to 40% (w/v) produced no appreciable decrease in lysis. When the concentration of glycerol was lowered to 20% (w/v), there was an increase in lysis—namely, 6% lysis after three months' and 50% lysis after six months' storage.

After a year's storage no consistent differences were observed between mixtures containing concentrations of trisodium citrate varying from 2.6 to 3.2%. However, when part of the sodium citrate was replaced by citric acid, the rate of lysis was slightly diminished—e.g., in one experiment the average haemolysis after a year in

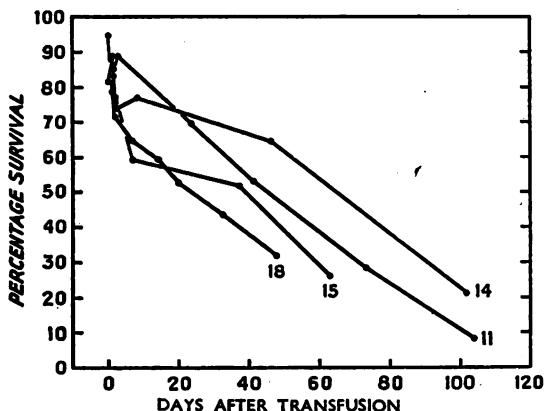


Fig. 2.—Post-transfusion survival of red cells stored at -20°C in buffered tripotassium citrate/glycerol (solution III).

8 mixtures containing 2.9-2.3% trisodium citrate and 0.1-0.5% citric acid was 5.3% (range 3.7-6.3%) compared with 8.3% (range 7.9-8.6%) in 3 mixtures containing trisodium citrate alone. The substitution of 3% potassium citrate for 3% sodium citrate did not affect the rate of haemolysis.

When the red cells were washed three times in saline solution before being mixed with trisodium-citrate-glycerol and stored they did not haemolyse more rapidly than unwashed cells in the same solution.

These results were all obtained with red cells from heparinised blood stored in small test-tubes. Additional information about the rate of spontaneous haemolysis was obtained from estimations made on the bottles used for transfusion. Red cells stored in solution III for eleven to fifteen weeks showed less than 2.5% haemolysis. Red cells stored in solution IV for up to nineteen weeks showed less than 3% haemolysis; after from twenty-four to thirty-one weeks there was between 3% and 7% haemolysis.

Red cells stored in dextran-citrate-plasma for sixteen weeks showed 7% haemolysis; heparinised red cells stored for twelve weeks in the lactate-glycerol solution showed 44% haemolysis. However, experiments in vitro undertaken subsequently showed that in a solution of sodium lactate and glycerol buffered with phosphates haemolysis took place only slowly.

The figures for haemolysis given so far refer to the mixtures immediately after thawing. During the "recovery" of the cells—i.e., the washing, first in decreasing concentrations of glycerol and subsequently in saline solution—further haemolysis took place, but

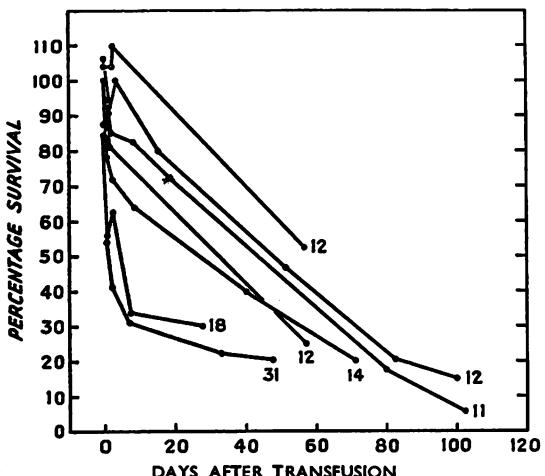


Fig. 3.—Post-transfusion survival of red cells stored at -20°C in plasma-citrate-glycerol (solution IV).

usually only about 5% in red cells stored in solutions I-IV. As mentioned above, the percentage recovery expresses the proportion of red cells actually available for transfusion compared with the number originally frozen. In solutions I-IV recoveries were usually about 90%; in solution IV recovery was estimated on 9 bottles, stored for eleven to thirty-one weeks, and the average was 91.5%.

In the unbuffered lactate-glycerol solution there was gross haemolysis on thawing, followed by considerable further lysis on washing; thus, in the bottle stored for twelve weeks in which there was 44% haemolysis on thawing, the final recovery was only 31%.

SURVIVAL OF RED CELLS IN VIVO

Solution I (trisodium citrate/glycerol).—14 transfusions of blood stored for two days to twenty-one weeks were given; in 10 the red cells had been stored with 30% glycerol, and the survival of 7 of these is plotted in fig. 1. Note that viability diminishes rapidly during storage, with the result that after only three weeks at -20°C the percentage survival twenty-four hours after transfusion has fallen to 70%.

The twenty-four-hour survival of all 14 cases is shown in fig. 4. Note that the post-transfusion survival of red cells stored in 20% glycerol and 40% glycerol appears to be the same as that of the cells stored in 30% glycerol.

For comparison with results obtained with other solutions the average survival in 7 cases in which the period of storage was eleven to fourteen weeks is given in table I.

Solution II (tripotassium citrate/glycerol).—5 transfusions were given; the period of storage ranged from ten to fifteen weeks.

The average post-transfusion survival is shown in table I for comparison with the survival of red cells stored for a similar period in the other solutions.

Red cells stored in solution II had a slightly higher average survival than red cells stored in solution I, but the difference was not significant.

Solution III (buffered tripotassium citrate/glycerol).—4 transfusions were given; the period of storage ranged from eleven to eighteen weeks. The survival of the red cells is illustrated in fig. 2, and the twenty-four-hour survival is also shown in fig. 5. The average survival of 3 cases in which the period of storage ranged from eleven to fifteen weeks is given in table I. It is evident that viability is far better maintained in this solution than in solutions I and II.

Solution IV (plasma-citrate-glycerol).—11 transfusions were given: 9 of red cells stored in solution IVa and 2 in solution IVb. The period of storage ranged from eleven to thirty-one weeks. There was little difference between the survival of the red cells stored in solution IVb and those stored in solution IVa, and the results are therefore

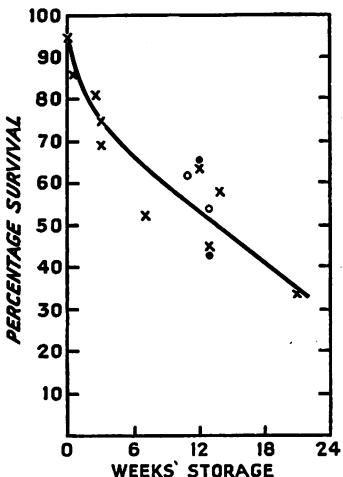


Fig. 4.—Percentage survival twenty-four hours after transfusion of red cells stored at -20°C for various periods in trisodium citrate/glycerol (solution I). Crosses represent cases stored in standard solution, final glycerol concentration 30%; two circles are cases in which the glycerol concentration was 20%; and two solid dots cases in which glycerol concentration was 40%.

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considered together. In 7 cases the survival of the red cells was followed for more than a week after transfusion, and the results in these 7 cases are illustrated in fig. 3. The percentage survival of all 11 cases at twenty-four hours after transfusion is shown in fig. 5.

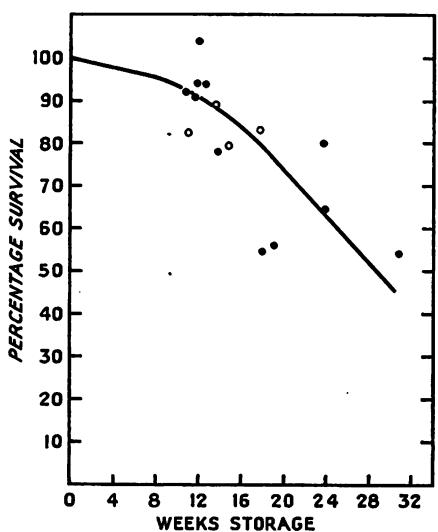


Fig. 5—Percentage survival twenty-four hours after transfusion of red cells stored at -20°C for various periods in plasma-citrate-glycerol (solution IV), marked by solid dots, and in buffered potassium citrate/glycerol (solution III), marked by circles.

twelve or fourteen weeks' storage but thereafter diminished more rapidly. As fig. 3 shows, red cells stored for twelve to fourteen weeks often had a post-transfusion survival scarcely distinguishable from that of fresh red cells.

Other solutions.—A single transfusion of red cells stored in dextran-citrate-glycerol for sixteen weeks was given. The percentage survival twenty-four hours after transfusion was 70%.

3 transfusions of blood stored in lactate-glycerol solution (with added calcium) were given. In the first 2 cases, in which the periods of storage were nine and eleven weeks, the survival twenty-four hours after transfusion was about 80%. In the 3rd case, in which the red cells were stored for twelve weeks, survival was only 25%. No reason for this gross discrepancy was found. It did not seem worth while making further experiments with this solution in view of the rapid rate of spontaneous haemolysis in vitro (see above).

EFFECT OF WASHING ON SURVIVAL OF RED CELLS

Fresh Red Cells Washed in Saline Solution

2 transfusions were given of fresh red cells washed seven times in 0.85% unbuffered saline solution. In the

1st case the red cells were from blood which had been taken into A.C.D. solution and kept ten hours at $+4^{\circ}\text{C}$; in the 2nd case the blood was taken into heparin immediately before being washed. At twenty-four hours the survival figures were 100% and 101% respectively; at forty-eight hours 100% and 95%; and at twenty-eight days 79% and 69%. It was concluded that seven washes in physiological saline solution did not affect the viability of fresh red cells.

Stored Red Cells Washed in Citrate Solutions of Different pH

A second experiment was made to discover whether the survival of stored red cells was affected by the pH and dextrose content of the solution in which they were washed. Two bottles of stored red cells were mixed, and the red cells were then put in two separate bottles. The red cells in one bottle were washed in the ordinary solutions (a) of glycerol in 3% trisodium citrate (pH 7.7, dextrose nil). Those in the second bottle were washed in solutions (b) to which one part in twenty of A.C.D. solution was added to give a pH of 6.9 and a dextrose content of 0.125%. In the actual experiment two bottles of group-AN red cells stored for sixteen months at -79°C were pooled and then divided into two lots and washed differently as described; two bottles of group-OM red cells stored for six months at -20°C were treated in the same way.

The red cells were then transfused as follows: one patient received group-AN cells washed in solutions (a) and group-OM cells washed in solutions (b); the second patient received group-AN cells washed in solutions (b) and group-OM cells washed in solutions (a). This plan was adopted to eliminate systematic errors due to differences between recipients. The mean percentage survival of the cells washed in solutions (a) was the same as that of the cells washed in solutions (b). It was concluded that there was no advantage in adjusting the pH of the wash solutions from 7.7 to 6.9 or in adding dextrose to them in a final concentration of 0.125%.

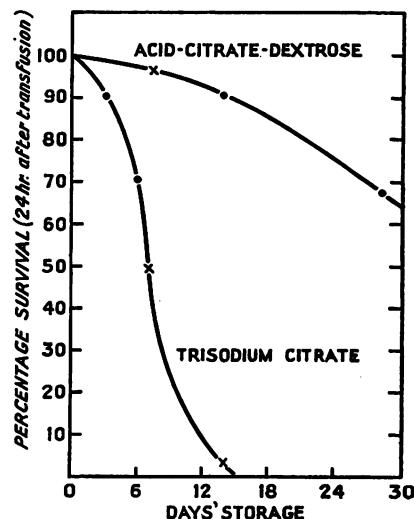


Fig. 7—Percentage survival twenty-four hours after transfusion of red cells stored at $+4^{\circ}\text{C}$ for various periods in trisodium citrate and in A.C.D. solution. Crosses are from data published by Ross et al. (1947) and solid dots from data assembled by Mollison (1951).

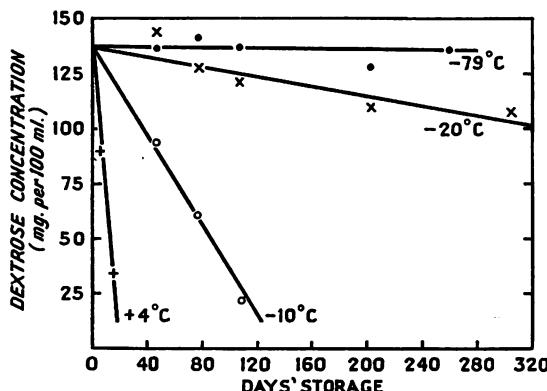


Fig. 6—Estimates of dextrose concentration in red cells mixed with citrate/glycerol (solution I) after various periods of storage at $+4^{\circ}\text{C}$, -10°C , -20°C , and -79°C .

GLYCEROL CONCENTRATION IN WASHED RED-CELL SUSPENSION

In 10 cases a sample of the red-cell suspension used for transfusion was centrifuged and the glycerol concentration of the supernatant fluid determined. Preliminary observations had shown that the glycerol concentration of the whole red-cell suspension was very close to that of its supernatant fluid. The glycerol concentration in the supernatant fluid was found to vary between 0.01 and 0.1%, the higher figures being found in cases in which the red cells had received only two washes in saline solution (following the washes in decreasing concentrations of glycerol, as described above), and the

lower figures in cases in which three washes in saline solution had been given. No correlation was observed between glycerol concentration and red-cell survival.

CELL VOLUME, INTRACELLULAR CATION CONCENTRATION, AND OSMOTIC FRAGILITY

Red cells mixed with glycerol-citrate solutions show some initial swelling, amounting to about 20% in solution I. This swelling is maximal within an hour; thereafter the cells begin to shrink, but at the end of twenty-four hours they are still about 10% above their original volume. During storage at -20°C there is progressive shrinkage, which is associated with a loss of total base and a decrease in osmotic fragility. By the end of about a month red cells mixed with solution I have shrunk to about 80% of their original volume and have lost about 50 m.eq. of base per litre of cells. Little further change takes place during a further five months' storage. Some examples of the changes observed in red cells stored for three months in solutions I-IV are given in table II.

Measurements of sodium transport on red cells stored three months in solution I were kindly made by Prof. M. Maizels and Dr. E. J. Harris. It was found that the sodium transport was substantially normal but that cell permeability was increased. In a second estimation cells stored five months in solution I were examined; these cells showed little change in active sodium transport but, again, were much more permeable than normal.

DEXTROSE CONSUMPTION

Fig. 6 shows the results of estimates of dextrose concentration after various periods of storage at different temperatures. The rates of disappearance of dextrose in this experiment, expressed as mg. per g. of haemoglobin a day, were calculated to be as follows:

At +4°C 0.62; at -10°C 0.084; at -20°C 0.008; at -79°C probably nil.

In a second experiment (not shown in fig. 6) the figures were as follows:

At -10°C 0.067; at -20°C 0.006; at -79°C probably nil.

Since it is of considerable interest to know whether dextrose concentration does diminish in red cells stored at -20°C the correlation coefficient for the observations shown in fig. 6 was calculated: -0.784, S.E. 0.378; hence $0.02 < P < 0.05$.

In a further experiment the rate of dextrose consumption in mixtures containing respectively 25% and 50% glycerol (final concentrations) was compared. During storage at -20°C the mixtures containing 25% glycerol were solid, and those containing 50% glycerol were liquid. During a period of four months the consumption of dextrose did not differ significantly in the two mixtures.

PRESERVATION OF RED-CELL ANTIGENS

Tests were made to detect the following red-cell antigens in blood stored for a year at -20°C: A, B, M, N, S, D, C, c, E, P, Lu, Le^a, Le^b, K, and Fy^a. In all cases these antigens were still detectable, although the reactions were weaker than those given by fresh cells. There was considerable variation between blood samples: for instance, in some a particular antigen seemed to have deteriorated after three months' storage, whereas in others this antigen seemed almost unimpaired after a year's storage. It seems likely that the A antigen and the antigens of the Rh system deteriorate less rapidly than antigens of the other blood-group systems.

Discussion

The present results show that in an appropriate medium—e.g., solutions III and IV—red cells stored at -20°C not only undergo very little haemolysis during

three months but retain, almost unimpaired, the ability to survive after transfusion. With longer periods of storage post-transfusion survival diminishes progressively. In other media—e.g., solutions I and II—red cells stored at -20°C show a progressive diminution in post-transfusion survival from the very beginning of the storage period. This pattern of survival of red cells stored in different solutions at -20°C strongly recalls the pattern observed in different solutions at +4°C; this is illustrated by comparing figs. 4 and 5 with fig. 7.

Note that in A.C.D. solution at +4°C and in solutions III and IV at -20°C there is only a slight loss of viability for an initial period (fourteen days at +4°C, and fourteen weeks at -20°C). Thereafter viability diminishes at an increased rate. By contrast, in trisodium-citrate solution at +4°C and in solution I at -20°C viability is lost rapidly from the beginning of the storage period. It does not seem likely that this big difference in behaviour in the different solutions can be explained by a slowing of chemical processes in the "favourable" solutions. It seems more probable that the rapid loss of viability in trisodium-citrate solution, both at +4°C and at -20°C, is due to physical damage. Lovelock (1954) estimated the lipid content of red cells stored for fourteen weeks in solutions I and IV and found that in solution IV there was no loss of cell lipids, whereas in solution I about 30% of the cell lipids was lost.

It seems likely that the damage observed in red cells stored in solutions I and II is due to the alkalinity of these mixtures. In the two solutions (III and IV) in which viability is well maintained at -20°C buffer systems are present: potassium dihydrogen phosphate and dipotassium hydrogen phosphate in solution III, and trisodium citrate and disodium hydrogen citrate together with a relatively large volume of plasma in solution IV.

Possibly further improvement in the maintenance of viability at -20°C could be obtained by modifying one of the solutions described here—e.g., the optimal pH may be different from that of the present mixtures. However, the fact that chemical change takes place at -20°C, shown by the consumption of dextrose, suggests that preservation for an indefinite period cannot be expected at this temperature.

In this connection some results published previously by Ross et al. (1947) are of the greatest interest. The survivals *in vivo* of red cells stored in Alsever's solution at 25°C and at 4°C were compared. The period of storage after which post-transfusion survival decreased to 50% was just under three days at 25°C and about seventeen days at +4°C—i.e., a fall in temperature of 21°C was associated with about a sixfold lengthening of the period during which the red cells maintained 50% viability. If the process responsible for the loss of viability were chemical, it would be expected that storage at -20°C—i.e., 24°C lower than +4°C—would lengthen the storage period rather more than sixfold. Fig. 5 shows that the viability of red cells stored in solution IVa at -20°C decreases to 50% after about thirty weeks. The viability of red cells stored at +4°C in A.C.D. solution decreases to 50% after about thirty-five days (fig. 7). Thus it seems that viability is maintained about six times as long at -20°C as at +4°C. This is shown in another way by figs. 5 and 7, from which it will be seen that the loss of viability is very slow for fourteen days in A.C.D. at +4°C, and for about fourteen weeks in solution IV at -20°C; thereafter in both solutions the rate of loss of viability rises.

The results of only 4 transfusions of red cells stored at -20°C have previously been reported. Mollison et al. (1952) transfused red cells stored for twenty-nine, seventy-seven, and eighty-four days; in addition to the period of storage at -20°C the red cells had been kept ten days at +4°C. Survival at twenty-four hours was 75-95% (average 82%), and the remaining cells dis-

appeared at about 1% a day. These red cells were stored in a mixture of their own plasma containing a proportion of A.C.D. solution and glycerol-saline solution. Although viability was well maintained in this solution, relatively rapid haemolysis took place during storage, and it was for this reason that citrate was substituted for saline solution in the present solutions. Brown and Hardin (1953), who gave a transfusion of red cells stored fifty days in glycerol-lactate at -15°C, found a post-transfusion survival of about 50% and thought that the post-transfusion loss of red cells was due to failure to remove all the glycerol from the cells. However, the present results make it seem more likely that the loss was due to physical damage to the red cells during storage.

The results in table II show that red cells stored in sodium citrate (solutions I and IV) contain more sodium than potassium, whereas those stored in potassium citrate contain more potassium than sodium. It appears that the ratio of sodium to potassium does not affect survival in vivo, although there appears to be an association between total base content and viability. A reduction in cell volume, a loss of base, and a decrease in osmotic fragility appear to be associated with one another.

Cell shrinkage and loss of base do not seem to be due solely to the concentration of citrate in the medium. For example, cells stored for fourteen weeks in solution IVB, which has almost the same citrate content as solution I, show less shrinkage and a smaller loss of base than do cells stored in solution I. This difference may be due to the fact that cells stored in solution I suffer more physical damage than do cells stored in solution IV, or to the fact that solution IV contains some penetrating anions (Cl').

As mentioned above, there is some evidence that red cells stored in solution I become abnormally permeable to cations. Experiments have not yet been made to determine whether this permeability is reduced in solutions III and IV. Meanwhile it seems likely that the increased permeability is further evidence of physical damage occurring in solution I.

Although it may not be possible to maintain the viability of red cells for more than a few months at -20°C, even in buffered glycerol mixtures, it is of practical importance to know that the red-cell antigens are still detectable after at least a year's storage at this temperature. Grove-Rasmussen et al. (1953) have reported that red cells stored for twenty weeks in trisodium citrate at -20°C react as well as fresh cells. Our results suggest that there is considerable variation and that some antigens (such as P) undoubtedly deteriorate during this period and may not be detectable with weak antisera. However, many of the antigens are relatively well preserved and, in a laboratory where potent sera are used for genotyping, it has been found very convenient to keep a panel of cells of known groups readily available in a -20°C refrigerator.

In the present work on storing red cells for blood-grouping tests, only trisodium citrate/glycerol solution (solution I) was used. It is likely that better results would be obtained by using a solution—such as one with buffered phosphate (solution III)—in which red-cell viability is better maintained.

Summary

Red cells stored at -20°C in a solution of trisodium citrate (3%) and glycerol (30%) undergo only slow haemolysis, but they rapidly lose their ability to survive after transfusion.

In modified citrate-glycerol solutions, the essential feature of which is probably the presence of buffers, survival is maintained, almost unimpaired, for about three months. Thereafter viability diminishes with time;

after thirty weeks' storage only about 50% of the red cells survive after transfusion. This slow loss of viability may be due to the fact that chemical change is not arrested at -20°C, and it is demonstrated that dextrose is in fact slowly utilised under these conditions.

Red cells stored for a year at -20°C in unbuffered citrate-glycerol mixtures react specifically with blood-grouping sera, although their reactions may be weaker than those of fresh cells.

We wish to thank Dr. J. D. James, Dr. P. D. Booth, and Dr. G. Plaut, of the North London Blood Transfusion Centre, for making blood available. Lederle Laboratories, New York, supplied the anti-M serum.

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ORAL PENICILLIN

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THE necessity for parenteral injection has been one of the major disadvantages of penicillin, and repeated attempts have been made to devise effective oral preparations. Trials with earlier products proved unsatisfactory because of poor and irregular absorption in spite of large dosage; so, supplies of penicillin being strictly limited, the oral route was not considered a practical proposition. Since then there has been a tremendous increase in the production of penicillin, with a great reduction in cost, and oral administration has been subjected to frequent investigation.

Benzathine penicillin, a new insoluble compound (N : N'-dibenzylethylenediamine dipenicillin G, known also as D.B.E.D. penicillin and benzethacil) has recently been produced, and preliminary tests by the oral route suggest that it gives reliable, effective, and prolonged blood-penicillin levels, particularly in children. As a result of these claims considerable interest has again been aroused in oral penicillin, and many different preparations are now available.

Controlled trials have so far been limited, but nevertheless the results have tended to be inconsistent:

Finberg et al. (1953) obtained excellent clinical results by treating pneumococcal and haemolytic streptococcal infections in children with benzathine penicillin.

Coriell et al. (1953) reported good results, as well as satisfactory blood-penicillin levels, in the treatment of scarlet fever in children with the same compound.

Cathie and MacFarlane (1953) found some absorption of penicillin after a single dose of 300,000 units of benzathine penicillin in all of 118 people, of whom 101 were children.

Bayne et al. (1953) gave a single dose of 300,000 units of benzathine penicillin to 6 adults and found detectable blood-penicillin levels for four hours but not after six hours; and after a dose of 600,000 units, only 1 of 6 adults lacked a blood-penicillin level of 0.03 unit per ml.

Foltz and Schimmel (1953) showed that, after the administration of single doses of 300,000 units to the same 12 adults, higher blood-penicillin levels were obtained with potassium penicillin G and procaine penicillin than with benzathine penicillin, and that, with each preparation, penicillin was absent from some serum samples at the end of six hours.

Wright et al. (1953) gave tablets of different oral preparations to the same 12 persons in a dosage of 200,000 units and found that absorption was more consistent with buffered potassium penicillin G than with benzathine penicillin.

Welch et al. (1953) estimated the blood-penicillin levels of ambulant adults at intervals after oral administration of benzathine penicillin in tablet form. Penicillin was usually detected for two or three hours after a dose of 200,000 units; with larger doses, up to 750,000 units, absorption was more consistent, and the blood-penicillin levels tended to be higher and more prolonged; there was, however, considerable individual variation in the amount of absorption, levels of only 0.012 unit per ml. being recorded in some cases.

In view of these irregular results it seems important that further information should be obtained about oral penicillin, so that its scope and limitations can be more clearly defined. Consequently we made tests, mainly in adults, to determine particularly the degree of absorption after a single dose of various oral preparations; at the same time we undertook a few clinical trials.

Methods

The various preparations were usually given before breakfast, and in many instances the dose was accurately measured. At times teaspoons were used, but these vary considerably in capacity, moderate to large types usually holding 3-5 ml., and accurate dosage is impossible; but in this trial there was usually a close approximation to the desired amount.

Samples of blood were collected at definite intervals, and the blood-penicillin levels were estimated by a standard serial-dilution technique using *Staphylococcus aureus* (Oxford) as the test organism. When any delay in making the tests was likely, the serum was kept in the refrigerator until required.

Results

Previous findings indicate that there is considerable individual variation in the amount of absorption after the oral administration of penicillin. It was consequently considered that more valuable information would be obtained by making single estimations in a large number of people rather than by making many estimations in a few. This was the main object of the investigation, and 330 tests have been made on patients and volunteers.

TABLE I—BLOOD-PENICILLIN LEVELS AFTER A SINGLE DOSE OF BENZATHINE PENICILLIN

Group	Dosage (units)	Time after dose (hr.)	Blood-penicillin (unit per ml.)							No. of persons
			None detected	0.03	0.06	0.125	0.25	0.5	0.5 or more	
Adults	300,000	2-3	4	5	2	8	1	0	0	20
		5-6	3	3	1	3	0	0	0	10
Children	600,000	1-3	1	10	14	18	19	5	1	68
		5-6	11	11	23	13	1	0	0	59
	300,000	2-3	0	0	0	0	8	2	0	10
		4-6	0	2	3	1	1	1	2	10
	600,000	3	0	2	5	2	2	0	0	11
									Total	188

TABLE II—BLOOD-PENICILLIN LEVELS IN ADULTS AFTER A SINGLE DOSE OF SOLUBLE PENICILLIN G

Dosage (units)	Preparation	Time after dose (hr.)	Blood-penicillin (unit per ml.)							No. of persons
			None detected	0.03	0.06	0.125	0.25	0.5	1 or more	
300,000	Eskacillin	1-3	1	3	5	6	5	2	2	27
		4-6	2	3	2	3	0	0	0	12
600,000	Pradupen	1-3	0	0	0	0	0	1	0	1
		4-6	0	1	3	3	2	0	0	9
	Eskacillin	1-3	0	1	5	4	17	11	8	46
		4-6	0	5	8	10	4	1	2	30
	Pradupen	1-3	0	0	0	0	2	5	5	12
		4-6	1	3	1	0	0	0	0	5
									Total	142

Two distinct types of oral penicillin have been used: (1) the insoluble benzathine penicillin ('Penidural,' Wyeth); and (2) soluble compounds: (a) potassium penicillin G ('Eskacillin,' Menley & James), and (b) potassium salt of benzylpenicillin B.P. ('Pradupen,' Evans Medical Supplies).

BENZATHINE PENICILLIN

Penidural is a stable and palatable suspension, which is well tolerated. A single dose of 300,000 or 600,000 units was given to 181 people (150 adults and 31 children). Usually, only one sample of blood was taken from each person; it was collected either two or three hours after oral administration which is considered to be the peak period of absorption, or after five or six hours (table I).

There was no uniform pattern of absorption, and the blood-penicillin levels showed considerable individual variation irrespective of the dosage.

In adults a dose of 300,000 units gave disappointing results and was discontinued because occasionally there appeared to be little or no absorption. Better results were obtained with a dosage of 600,000 units. A detectable blood-penicillin level was found within three hours of administration in 67 of 68 assays, and in 6 instances a level of 0.5 unit per ml. or more was obtained. After five or six hours 37 of 59 persons still had levels of 0.06 unit per ml. or more.

Only a limited investigation was made in children, but the results were more striking: evidence of absorption was found in all the cases, and 2 young infants had 1 or 2 units per ml. from four to six hours after a dose of 300,000 units. A dose of 600,000 units did not produce any increase in the blood-penicillin levels.

These irregular results are not surprising, because penidural is an insoluble compound and probably has to be broken down in the alimentary tract to liberate a soluble form of penicillin G. The precise mechanism of the reaction has not been determined, but Lozinski and Gleason (1953) consider that the complex penicillin compound undergoes rapid hydrolysis in normal gastric juice and some hydrolysis in an alkaline medium. Considerable individual variation might therefore be found in not only the release of soluble penicillin from the compound but also its subsequent absorption.

In some cases blood-penicillin levels were estimated five or six hours after a second or third dose of 600,000 units, and evidence of a cumulative response was usually, but not invariably, found.

11 men with acute gonorrhoea were treated with penidural. 2 of them each received one dose of 600,000 units; there was an immediate improvement, but both cases relapsed. 9 of them were given a second dose of

600,000 units after an interval of six hours; 7 of these were cured, and 2 relapsed.

SOLUBLE COMPOUNDS

The two compounds eskacillin and pradupen are similar preparations which vary slightly in composition and method of preparation. Eskacillin is crystalline potassium penicillin G which, when required for use, is dissolved in a special flavoured and buffered solution. It is palatable and, at room-temperature, retains its potency for at least seven days. Pradupen is a powder containing potassium benzylpenicillin as well as buffering and flavouring agents; solution is effected by the addition of tap-water.

These preparations were given to 142 adults, and the resulting blood-penicillin levels are given in table II.

Irregular readings were again obtained in a similar group of adults; but usually absorption was quicker and blood-penicillin levels tended to be higher than with penidural.

With a dose of 300,000 units high blood-penicillin levels (1 unit per ml. or more) were obtained at the peak period in a few cases, but in 1 instance absorption was not detected, and on several occasions levels of 0.03 unit per ml. were found. Better results were produced by increasing the dose to 600,000 units, when all the 58 persons gave evidence of absorption at the peak period, the range varying from 0.03 to 1 unit per ml. With eskacillin some penicillin was still present in all of 30 cases at the end of from four to six hours.

15 male cases of acute gonorrhoea were each treated with two doses of 600,000 units, the second dose being given after an interval of six hours; all showed rapid improvement, but with eskacillin 2 of 7 cases relapsed. Another case was treated with pradupen in two doses of 400,000 units, with an interval of six hours, but relapsed after an initial improvement.

Discussion

It is generally accepted that a variable, and sometimes small, proportion of penicillin is absorbed after oral administration, and consequently this route is not recommended in the initial stages of acute severe infections. These views are supported by the results of the present investigation. Absorption after oral dosage was irregular, irrespective of the nature of the penicillin compound or the age of the recipient.

The present work was mainly concerned with adults, in whom a dose of 300,000 units gave disappointing results. In a few instances there was no evidence of absorption, and in some cases the absorbed penicillin was eliminated within six hours. Better results were given with a dose of 600,000 units, but there was again found considerable inconsistency not only in the peak blood-penicillin levels but also in the persistence of penicillin in the blood. In the great majority of tests made up to three hours after administration—i.e., the peak period—blood-penicillin levels of at least 0.03 unit per ml. were obtained, and in many of them considerably higher levels were found.

It is often stated that 0.03 unit per ml. represents the minimal effective level of penicillin, but this figure has little, if any, therapeutic significance. It can be readily demonstrated by in-vitro tests that, with moderate numbers—e.g., 2,000,000 per ml.—of a sensitive strain of *Staph. aureus*, a level of 0.03 unit per ml. of penicillin has merely a transient bacteriostatic effect, whereas a level of 0.3 unit per ml. has considerable bactericidal activity. With a pneumococcus, which is a highly sensitive organism, a level of 0.03 unit per ml. may, however, have some bactericidal effect.

The blood-penicillin level is not a direct index of therapeutic activity, because many other factors, including the sensitivity and accessibility of the infecting organisms,

must also be considered. There is, however, little doubt that, in most acute infections, levels of 0.03 unit per ml. are likely to have limited therapeutic activity.

In the present investigation blood-penicillin levels of 0.03 unit per ml. or less have been obtained in each group of subjects with all the preparations used; moreover it is impossible to predict when absorption is likely to be so small. It must therefore be emphasised that in the treatment of acute infections, even with sensitive organisms, the initial doses of penicillin should be given parenterally to ensure rapid bactericidal activity. When the clinical response to parenteral penicillin is satisfactory, continuation treatment with oral preparations should prove adequate in most cases; this form of therapy should be particularly advantageous in children, in whom parenteral injection may be a very disturbing experience. Oral administration may also prove useful when the prophylactic use of penicillin is considered advisable.

It has been shown that, by combination with probenecid, which delays the renal excretion of penicillin, oral products give consistently higher and more prolonged levels. Severe reactions to penicillin are becoming a serious problem; and, though oral administration reduces, but does not eliminate, this risk, the combination of penicillin with another potential sensitising agent may not be entirely beneficial.

The main advantage of oral penicillin is convenience of administration; but, even with the new products, there still remains the serious objection of irregular, and sometimes poor, absorption, particularly in adults. It must also be realised that oral administration constitutes a relatively expensive form of penicillin therapy. A dosage of 300,000 or 600,000 units six-hourly costs considerably more than a daily injection of 400,000 units of procaine penicillin, which gives similar, but more uniform, blood-penicillin levels (Fairbrother and Daber 1950).

The increasing number of potent antibiotics, the great variety of proprietary preparations, and the potential dangers of these agents necessitate a careful assessment of each case before advising any form of antibiotic therapy. It is therefore important that convenience of administration should not lead to widespread and indiscriminate use of oral penicillin, especially in the treatment of minor infections.

Summary

Blood-penicillin levels have been estimated on 330 occasions after the oral administration of various preparations of penicillin.

A single dose of 300,000 units gave disappointing results in adults.

Absorption was more consistent after a dosage of 600,000 units, but considerable variation was found in the amount absorbed by different people.

It is a pleasure to thank our medical colleagues and the nurses for their ready co-operation throughout this investigation. Messrs. J. Wyeth & Brother Ltd., Menley & James Ltd., and Evans Medical Supplies Ltd. supplied the oral preparations of penicillin.

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BENZATHINE PENICILLIN BY MOUTH IN CHILDREN

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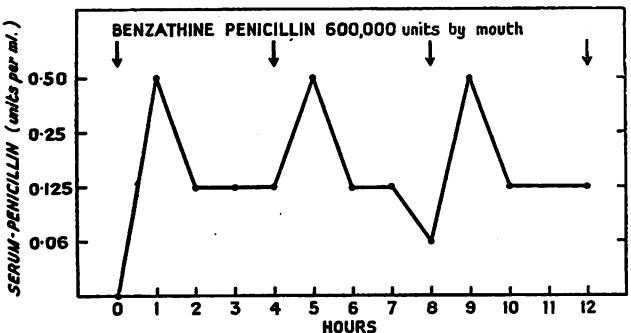
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An effective, reliable, and inexpensive oral penicillin preparation is much to be desired. N,N'-dibenzylethyl-enediamine penicillin (benzathine penicillin or 'Penidural'), which has been suggested as such a preparation, is a sparingly soluble compound of penicillin first described by Szabo et al. (1951) and Seifter et al. (1951). Lepper et al. (1952) estimated the blood-penicillin levels obtained after the oral administration of benzathine penicillin to children aged less than 5 years and found blood-penicillin levels of not less than 0.03 unit per ml. of serum in five of seven children six hours after the administration of 250,000 units. Coriell et al. (1953), who administered benzathine penicillin to nine children aged 4-11 years in a dosage of 7000 units per kg. body-weight, reported that none of them had a serum-penicillin level as high as 0.03 unit per ml. at six hours. Cathie and MacFarlane (1953) showed that benzathine penicillin 300,000 units, given orally to 95 children weighing 10-70 lb., produced a serum-penicillin level of not less than 0.03 unit per ml. three hours after administration. The serum-penicillin levels at four and six hours after administration were not recorded.

The trial of benzathine penicillin reported here was planned to establish for children a scheme of dosage,



Serum-penicillin levels with repeated doses of benzathine penicillin 600,000 units four-hourly in a child weighing 40 lb.

based on body-weight, which would maintain a constant serum-penicillin level of at least 0.03 unit per ml.

Materials and Method

Penicillin-serum levels were estimated by a capillary technique using a strain of *Streptococcus pyogenes* as the assay organism.

Assays were made in each child before the start of treatment to ensure that there was no penicillin present in the serum.

Benzathine penicillin was given, irrespective of meal-times, in single doses of 5, 10, 15, and 20 ml. (5 ml. = 300,000 units of penicillin) to children in different weight-groups, and serum-penicillin levels were estimated at regular intervals up to six, eight, or twelve hours after its administration. The possible cumulative effect of repeated six-hourly doses on the serum-penicillin level was also studied.

Results

The minimal satisfactory serum-penicillin level was taken as 0.03 unit per ml.

Benzathine penicillin was rapidly absorbed, and satisfactory serum-penicillin levels were found an hour after administration. Thus the dose which at six hours produced satisfactory serum-penicillin levels produced at an hour in 28 of the 30 patients serum-penicillin levels of 0.125-1.000 units per ml. From three to six hours the serum-penicillin levels fell steadily.

The results summarised in table I show that 300,000 units of benzathine penicillin maintained a satisfactory serum-penicillin level for four hours in children weighing up to 40 lb., and for six hours in children weighing up to 25 lb.; and 600,000 units of benzathine penicillin was needed to maintain a satisfactory serum-penicillin level

TABLE I—PENICILLIN-SERUM LEVELS AFTER ADMINISTRATION OF ORAL BENZATHINE PENICILLIN

Dose (units)	Interval after administration (hr.)	Weight range (lb.)	Patients showing satisfactory serum-penicillin levels
300,000	4	0-40	19 of 19 (100%)
	6	<40	0 of 7 (0%)
	6	0-25	8 of 8 (100%)
600,000	4	25-40	0 of 13 (0%)
	6	40-70	16 of 17 (94%)
	6	<70	6 of 16 (37%)
900,000	4	25-40	7 of 9 (78%)
	6	<40	6 of 29 (24%)
	6	40-70	8 of 9 (89%)
1,200,000	4	40-70	5 of 9 (55%)
	6	<70	2 of 8 (25%)
	8	70	11 of 11 (100%)
		>70	8 of 11 (82%)
		>70	4 of 6 (67%)

for four hours in children weighing 40-70 lb., and for six hours in children weighing 25-40 lb. In heavier children even higher doses were needed to maintain satisfactory serum-penicillin levels throughout the six hours between doses. Serum-penicillin levels estimated in 6 patients during a course of treatment were not significantly higher than those obtained after a single dose of benzathine penicillin. A typical example is shown in the accompanying figure.

From the results in table I a scheme of dosage is suggested (table II). Six-hourly doses of benzathine penicillin should be about 12,000 units per lb. body-weight, and four-hourly doses about 8000 units per lb. body-weight.

With a few exceptions children liked the flavour of benzathine penicillin. It was not, however, free from side-effects. There were no rashes, but of 131 children treated with benzathine penicillin 26 had loose stools and 3 had some nausea and vomiting. In no case, however, were these symptoms really troublesome.

Summary

Benzathine penicillin was given by mouth to children of different ages, and serum-penicillin levels were estimated.

Benzathine penicillin 300,000 units ('Penidural' 5 ml.) maintained satisfactory serum-penicillin levels for four hours in children weighing up to 40 lb. and for six hours in children weighing up to 25 lb., and 600,000 units for four hours in children weighing 40-70 lb. and for six

TABLE II—SCHEME OF DOSAGE BASED ON BODY-WEIGHT FOR BENZATHINE PENICILLIN

Weight (lb.)	Interval between doses (hr.)	Units of benzathine penicillin (300,000 units = 5 ml.)
0-25	6	300,000
25-40	4	300,000
25-40	6	600,000
40-70	6	900,000-1,200,000
>70	6-8	1,200,000

hours in children weighing 25-40 lb. Heavier children required correspondingly higher doses.

A scheme of dosage based on body-weight is suggested for children.

It is a pleasure to acknowledge the help and encouragement given to us by Prof. R. S. Illingworth and Dr. J. L. Emery. Messrs. John Wyeth Ltd. supplied the penidural.

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TREATMENT OF MOLLUSCUM SEBACEUM

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THE condition known alternatively as molluscum sebaceum, kerato-acanthoma, or molluscum pseudo-carcinomatosum is now an established entity becoming increasingly well recognised (MacCormac and Scarff 1936, Musso and Gordon 1950, Rook and Whimster 1950, Beare 1953). The treatment of these cases is still, however, not generally agreed on (Beare 1954, Halnan 1953, 1954, Gold 1954). Indeed molluscum sebaceum is a self-limiting self-healing condition, and it might be argued that any treatment is therefore unnecessary. Against this its natural course may last up to six months, during which time the patient is left with an unsightly ulcerating tumour; hence treatment would appear to be justifiable to limit the life-cycle of the tumour and procure early healing.

Diagnosis

The danger of mistakenly diagnosing and treating a squamous epithelioma as molluscum sebaceum has been emphasised (Halnan 1953, 1954). Such difficulties may arise during the first two months of the tumour's life—i.e., before the formation of the central keratin plug. An adequate and representative biopsy specimen, however, examined by a pathologist familiar with the histological structure of molluscum sebaceum, taken in conjunction with the clinical history and findings, should make the diagnosis certain, in all cases. There is no doubt, however, that in the past many of these cases have been treated as squamous epitheliomata; hence statistics of treatment of epitheliomata should be reviewed in the light of recent knowledge. Once the keratin plug has been formed, the diagnosis is usually obvious clinically. If any doubt persists, the histological findings will once again be confirmatory. In short, the difficulties of diagnosis in these cases should be dealt with as for basal-cell carcinoma, squamous papillomata, or other conditions which may be confused with squamous epitheliomata—i.e., if in doubt biopsy and if necessary re-biopsy, rather than if in doubt treat all as epitheliomata.

Treatment

There appears to be two main methods of treating this condition: surgical removal, and radiotherapy.

SURGICAL REMOVAL

Surgical procedures have included diathermy or electrolysis, local excision and suture, and excision or curettage of the superficial parts of the tumour followed by cautery or application of caustics to the base.

MacCormac and Scarff (1936), describing their original 10 cases, recommended electrolysis followed by the application of carbon-dioxide snow. There were no recurrences among these cases.

Beare (1953) reports on treatment by combined curettage and diathermy in 76 cases with excellent cosmetic results. In 27 of these cases curettage was followed by a single exposure of superficial X rays in a dosage of 800-1200r. This post-operative irradiation has now been abandoned because "there is little if any advantage in giving X rays in addition to curettage." One case was noted in this series which had recurred after previous diathermy.

I. W. Whimster (personal communication) reports on 40 cases treated at St. Thomas's Hospital by surgical excision under local anaesthesia. Many of these lesions were unduly large, compared with the maximum of 1·0-1·5 cm. in diameter cited by Beare (1953).

RADIOTHERAPY

The treatment of molluscum sebaceum by radiotherapy has been likened to "using a sledgehammer to drive in a nail" (Beare 1954), and has been criticised on the grounds that large doses of either radium or X rays have to be used. The earliest cases of molluscum sebaceum were referred to the radiotherapy department at St. Thomas's Hospital in 1949, when the condition was not so well recognised and little was known about the preferential form of treatment. It was felt that treatment by radiotherapy alone could play a part in the treatment of the condition just as in other benign skin lesions—e.g., haemangioma, keloid scars, and plantar warts—and without resorting to a "sledgehammer" dosage. It was therefore in an attempt to determine the optimum dosage to cause regression of the tumour that the following 25 cases were treated by radiotherapy alone.

Technique

Identical methods were used in treating all the cases. A Chaoul tube was used delivering X rays at a voltage of 60 kV, 4 mA, and a half-value layer of 3·3 mm. of aluminium. The volume of tissue irradiated was confined to an amount just wide of the lesion. The treatment was given as a single exposure but in varying dosage. After treatment the area treated was inspected weekly or fortnightly so that the degree of reaction and the rate of regression of the tumour could be assessed. In 6 of these cases treated by varying dosage a biopsy specimen

RESULTS OF RADIOTHERAPY

Case no.	Dose (r)	Degree of reaction †	Tumour-regression time (weeks)	Reaction-regression time (weeks)
<i>Group A :</i>				
1	2500	3	4	8
2	2500	3	3	8
3	2500	3	4	7
4	2250*	3	3	6
<i>Group B :</i>				
5	2000	3	4	7
6	2000	2	4	5
7	1800	2	4	5
8	1750*	2	3	6
9	1750	2	4	5
10	1750*	2	3	4
<i>Group C :</i>				
11	1500	2	5	6
12	1500	2	5	6
13	1500	2	4	4
14	1500	2	4	4
15	1500	2	3	4
16	1500	2	3	4
17	1500	2	4	4
18	1500	2	4	4
19	1500*	2	4	4
20	1500	2	3	3
21	1500	2	3	3
<i>Group D :</i>				
22	1250*	1	8	4
23	1250*	1	8	3
24	1250	1	6	4
25	1200	1	6	4

Average tumour-regression time in groups B and C = 4 weeks.
 Average reaction-regression time in groups B and C = 4½ weeks.

* Cases subjected to post-irradiation biopsy.

† 1, erythema only.

2, erythema + dry scaling.

3, erythema + vesicle formation + ulceration.

was taken of a representative portion of the tumour a week after irradiation and submitted to histological examination.

Results

Of the 25 cases of molluscum sebaceum treated by radiotherapy alone 5 had been treated by other methods previously. 1 case had been treated on three separate occasions: twice by local excision, and once by application of carbon-dioxide snow. 2 other cases had recurred after local excision on one occasion each, and of 2 other recurrences 1 had followed local applications of caustics and the other removal by diathermy.

The accompanying table shows the dosage given, the degree of reaction, and the length of time taken until the tumour had regressed completely and the reaction healed. In all the cases the cosmetic result has been good, leaving a typical flat slightly depressed scar. No recurrence has yet been noted after radiotherapy alone. An attempt has been made to assess these results from two aspects: (1) the rate of tumour regression correlated with the quantity of irradiation and hence also with the reaction produced; and (2) in cases subjected to post-irradiation biopsy, the quantitative cytological changes resulting, correlated with the quantity of radiation given.

From the table it will be seen that there are four separate dosage levels:

Group A.—A dosage equivalent to that used in treating squamous epitheliomata—2250–2500r. In all the cases the reaction was severe, labelled as 3rd degree, and because of this the rate of regression of the tumour was difficult to assess accurately. The reaction subsided in 6–8 weeks and tumour regression was complete by 4 weeks.

Group B.—A "subradical" dose was given—1750–2000r. The resulting reaction was less, being 3rd degree in only 1 case, and 2nd degree in the remainder. Tumour regression was complete in 4 weeks, and reaction healing lasted correspondingly shorter than in group A and was complete in 4–6 weeks.

Group C.—The dosage given was 1500r. The reaction was 2nd degree only and had settled within 3–6 weeks. Tumour regression took place within 3–5 weeks.

Group D.—The dosage used was roughly half that given for the radical treatment of squamous carcinomata—1200–1250r. The reaction was 1st degree in all the cases, being healed in 3–4 weeks. The rate of tumour regression was, however, appreciably slower than in the preceding groups, taking 6–8 weeks to be completed.

The average tumour-regression time for all the groups was about 4½ weeks, and for groups B and C about 4 weeks. The average reaction-regression time for all the groups was about 5 weeks, and for groups B and C about 4½ weeks.

This analysis shows that at the extremes of dosage levels the resultant tumour regression/reaction ratio is disproportionate. In group A the reaction produced was excessive, the dose level being too high. In group D the tumour-regression rate was appreciably slower, suggesting that the dosage was too low. The optimal range of dosage producing a satisfactory tumour-regression rate without an excessive degree of reaction therefore seems to be that used in groups B and C—i.e., 1500–1750r. The 1500r dose produced slightly less reaction than the higher dosages, and this therefore seems to be a satisfactory dosage. In bulkier lesions probably the larger dose of 1750r should be used.

Attempts to correlate cytological response with dosage have been more difficult because of the small numbers dealt with. In 6 cases biopsy specimens taken after irradiation at different dosage levels were submitted to histological examination, which showed that cytological changes due to irradiation were present in all specimens studied, but quantitatively there appeared to be little difference in the number of cells damaged irrespective of the dosage at 1250 or 2250r. It must, however, be emphasised that the numbers dealt with were small, and a

larger series would have to be studied before a definite conclusion could be drawn.

Conclusions

Molluscum sebaceum may be effectively treated by radiotherapy. Histological examination after irradiation of these tumours suggests that there is little quantitative difference in cytological damage over a wide range of dosage. A satisfactory tumour-regression rate follows a dosage level of 1500–1750r. A dosage above this produces an unnecessarily more severe and prolonged reaction.

Summary

The diagnosis and results of various surgical treatments of molluscum sebaceum are reviewed.

The treatment of 25 cases by radiotherapy alone is reported, and the results are analysed.

Four groups of dosage levels were used and correlated with reaction and tumour-regression rate.

Correlation with cytological response in 6 cases showed little quantitative difference at various dosage levels.

I wish to thank Dr. J. A. C. Fleming, director of the department of radiotherapy, St. Thomas's Hospital, for his help and encouragement in publication, and Dr. I. W. Whimster for the histological reports on the biopsy specimens, and for permission to review his cases which were treated surgically.

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SPONTANEOUS RUPTURE OF THE BLADDER

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THIS case is recorded because of the rarity of spontaneous rupture of the bladder. The events took place in private practice in a small isolated community, with no ready source of reference, so I shall refrain from comment, other than to reiterate the admonitions of one of my late chiefs, "Watch the bladder," and to point out the relative harmlessness of non-infected urine spilt intraperitoneally, so long as it is removed at once.

A man, aged 65, slipped in the snow on Jan. 1, 1952, and injured his left hip. He crawled some distance to a road, where he was picked up by a passing lorry and brought into town.

Examination showed a fractured left femoral neck; this was confirmed by radiography on admission to hospital. He was put to bed, and traction was applied to the leg with adhesive plaster. During the period of delay before open reduction could be carried out (occurred by seasonal lack of staff) the patient complained of difficulty in micturition, on one occasion only. On the afternoon of Jan. 2 he could not urinate; so the orderly was instructed to catheterise him, which he did with ease.

Operation.—On the morning of Jan. 6 open reduction of the fracture was done under spinal anaesthesia, and a Smith-Petersen nail was inserted in the usual manner.

Progress.—Next day exercises of the hip were started. Each day the patient appeared rather depressed and irritable, being worried about his heart, having been told on some previous occasion that it was weak. He had some difficulty in urinating and frequently asked for the bottle; but although he passed adequate quantities of urine, he must have had some retention. On the morning of Jan. 10 he developed severe epigastric pain after using the bedpan. When I saw him he was

shocked and in great discomfort. His abdomen was very tender and as hard as a board. Perforated peptic ulcer was diagnosed, and a long history of indigestion elicited to suit the diagnosis!

Laparotomy was done two hours later through an upper right paramedian incision. Much clear fluid was found, but no perforation, after diligent exploration of the stomach, although a sessile papilloma was found high up on the anterior surface. The possibility that the fluid might be urine was confirmed by feeling a small contracted bladder with a hole at its apex exactly like an old-fashioned ink-well. Through a lower midline incision a perforation was found on the posterior surface of the bladder about midway between its base and its apex. The bladder was opened through the retroperitoneal space. The prostate was not enlarged, and the internal meatus appeared normal. The rent was sutured intravesically with interrupted catgut and reinforced intraperitoneally. The bladder was closed about a large rubber tube, a drain inserted to the retroperitoneal space, and the incision closed in the usual manner. The gastric papilloma (which proved to be a leiomyoma) was excised with an inch margin of healthy stomach wall and the deficiency closed with two layers of continuous catgut.

Postoperatively I discovered that in 1944 the patient had undergone a transurethral resection for impaction

of a stone in his urethra. Since then he had had no urinary symptoms. He was now treated by continuous gastric suction, intravenous fluid containing oxytetracycline, and 'flocillin D.S.' (a repository penicillin-streptomycin mixture). On Jan. 14 the gastric suction and the intravenous fluid were discontinued, and the patient began to take fluids by mouth. The flocillin was continued prophylactically until Jan. 20 in view of the assortment of surgical wounds. The suprapubic drain was removed on Jan. 18 and a self-retaining catheter inserted after sounding the urethra. On Feb. 2 the suprapubic wound appeared dry and the catheter was removed. The patient, however, had some difficulty in micturition, and urine soon began to leak suprapubically. The catheter was reinserted, and drainage was continued until Feb. 14, when the catheter was removed and the patient could urinate freely. On this date he was transferred to a urologist in Sudbury, Dr. M. L. Mader, who reported scarring at the vesical neck and did a transurethral resection.

Follow-up.—The patient made an uneventful recovery and is now in excellent health and able to walk ten miles daily without difficulty.

I wish to thank my partner, Dr. K. C. Soper, whose skill in anaesthesia made possible the successful outcome.

Reviews of Books

The Health of the Community

C. FRASER BROCKINGTON, M.A., M.D. Camb., D.P.H., barrister-at-Law, professor of social and preventive medicine, University of Manchester. London: J. & A. Churchill. 1954. Pp. 400. 32s.

THE factual content of this book is not so very different from that of other books of like title and subject, yet it is bright with new approach. The pieces of paper one puts into a kaleidoscope are only pieces of paper, but they become changed to patterns. Professor Brockington composes his pattern finely and has the power of capturing in few words a meaning, a doubt, an explanation, or a reassurance. Admittedly there are a few slips here and there—one in the author's words on child minding, and another in the section dealing with housing and standards of overcrowding. But this is not a work of reference, nor another primer of public health. Read as a whole or in part, it provides plenty of material for serious discussion and readers will argue, for example, over Professor Brockington's forthright claim that the future medical officer of health should coöordinate all community health and welfare services. (Some of them may also argue over his horrifying statement that "Mary, Queen of Scots, does not seem very beautiful now by her pictures; she may have been thought a beauty . . . because of the fact that she had never been disfigured by smallpox.") The book is comprehensive, dealing historically and critically with the functions of the medical officer of health and nearly every aspect of his work.

Synopsis of Children's Diseases

JOHN RENDLE-SHORT, M.A., M.B. Camb., M.R.C.P., D.C.H., senior registrar, department of child health, Welsh National School of Medicine. Bristol: John Wright. 1954. Pp. 620. 32s. 6d.

THE "Synopsis" series have a reputation for authority combined with brevity. This youngest member of the series, appropriately enough, deals with children's diseases, and it lives up to the standard of its predecessors. The staccato style, reminiscent of Mr. Jingle, does not make for easy reading; but then the book is not intended to be read in the normal manner but to be used for rapid revision and easy reference. As nothing of importance has been omitted, it will be helpful to undergraduates to have most of the diseases described as common, rare, or very rare. (Two major triumphs of preventive medicine are well demonstrated by the classification of rickets and diphtheria as very uncommon diseases.) The text is much more up to date than are most textbooks by the time that they reach publication. Such comparative newcomers as idiopathic pulmonary

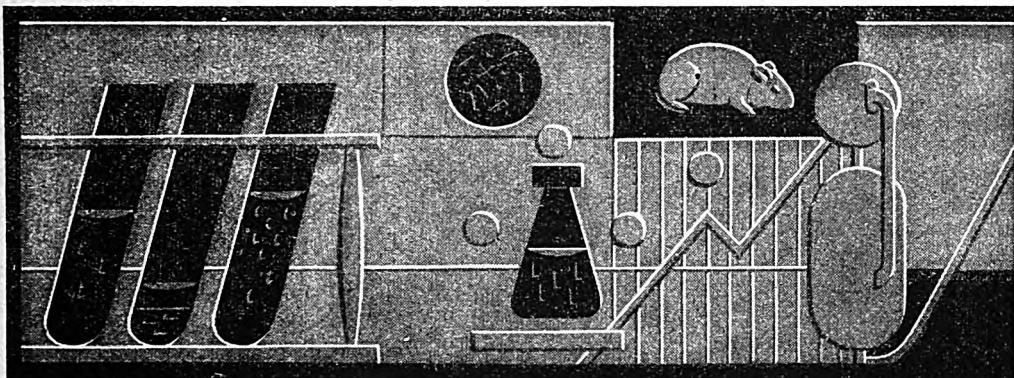
haemosiderosis, hyaline membrane disease, and idiopathic hypercalcæmia are given brief but suitable descriptions.

The first section, dealing with normal growth and development and with infant feeding, lays particular stress on breast-feeding, and there is an excellent section on the newborn infant, with a sensible note on the psychological aspects of prematurity (which may affect the relation between the mother and child). Each main section has an introductory note on normal variations of infancy and childhood, and on special methods of investigation and examination. The tables of differential diagnosis of such symptoms and signs as jaundice, muscle wasting, stridor, and haematemesis are useful, and the section on the treatment of dehydration is particularly good. At the end of the book there is a list of the dosage of some common drugs for various age-periods from the newborn infant up to the age of 9 years. A surprising omission is the absence of any reference to the use of isoniazid in the treatment of tuberculosis—no doubt an oversight.

This is a work that should be deservedly popular, not only with examination candidates but also with doctors in practice.

Handatlas der Cystoskopie und Urethrocytostoskopie (3rd ed. Leipzig: Thieme. 1953. Pp. 110. DM. 50).—This book consists mainly of paintings; and the late Prof. O. Kneise and Dr. M. Stolze, the authors, both experienced urologists, were themselves the artists. The first edition was published as long ago as 1907. There are 124 paintings, all in colour, arranged in seven sections depicting various types of bladder lesion, each section preceded by a brief discussion of the disease to be illustrated and the part played by cystoscopy in its diagnosis and treatment. There are some rather more general articles on the cystoscope and its use at the beginning of the book. The quality of the pictures is on the whole very good, though it does vary: thus the only nine pictures of urethrocytoscopic findings are poor. A still picture in one plane of one cystoscopic field is necessarily a fragmentary and artificial representation of the living bladder disorder, no matter how excellent the painting. This atlas cannot escape this limitation, but it provides interest, pleasure, and some instruction.

The Silent Shore (London: Hodder & Stoughton. 1954. Pp. 384. 12s. 6d.).—In this book by Mr. Denis B. Wylie, a strong-minded woman doctor, having delivered a school-friend of twins, a boy and a girl, takes an interest in the future history of the babies and the rest of the family, and extracts from her diary fill in the gaps in the narrative. Mr. Wylie's ebullience leads him to offer his readers a plot with too many incidents, lively conversations with too many jokes, and discussions on too many social problems. But his humanity ensures that none of these are trivial, and his hero's interest in the problems of the aged is an important part of the book. The book is pleasant reading, though perhaps not for strong-minded women doctors.



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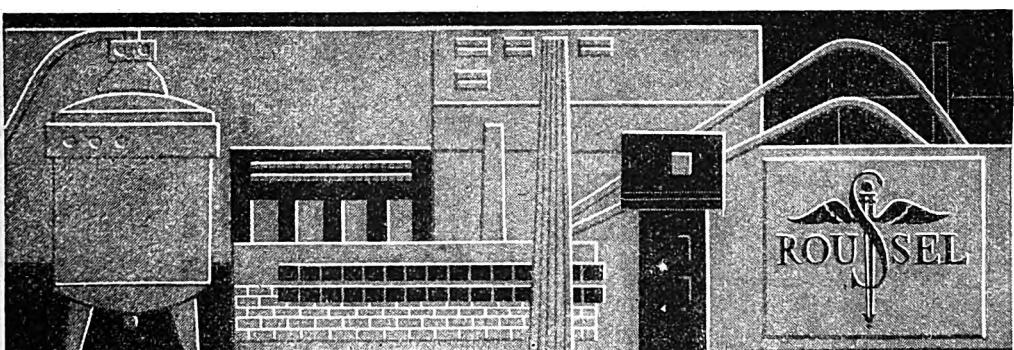
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LONDON : SATURDAY, APRIL 24, 1954

Pernicious Anæmia—a General Disease

PERNICIOUS anæmia is a misleading title. The disease is no longer "pernicious," since it can be successfully treated and controlled; and anæmia is only the most prominent of its manifestations. The curious megaloblastic change in the erythroblasts is not the only abnormality in the bone-marrow cells. The granulocytes also are affected; the leucopenia and the presence of multilobed polymorphs were known to the earliest investigators, and bone-marrow studies have shown significant gigantism among the metamyelocytes—the nucleus is unusually large and occupies more of the cell than normally. Another recognised complication of pernicious anæmia is a low platelet-count, sometimes with serious hemorrhage. This again is now known to be paralleled by abnormalities in the platelet-producing cells of the bone-marrow—the megakaryocytes. EPSTEIN¹ has studied the megakaryocytes in bone-marrow biopsies of patients with pernicious anæmia in relapse, and in some found giant megakaryocytes with excessive nuclear segmentation. KISSMEYER-NIELSEN² thought that the megakaryocytes might not be producing platelets, and such platelets as could be found were large and coarse; but the number of megakaryocytes was normal. All these changes in the granulocytes and in the megakaryocytes are reversed when vitamin B₁₂, or any active treatment, is given.

The pathological changes in the nervous system that accompany pernicious anæmia have been known for over half a century. At one time it was suggested that these were due to a different deficiency from that responsible for the blood changes. Thus Sir ARTHUR HURST postulated the presence of a factor, "neuropoietin" (to contrast with haemopoietin, the gastric intrinsic factor), that was necessary for the proper nutrition of cells in the spinal cord: the clinical syndrome of subacute combined degeneration of the spinal-cord tracts was the clinical expression of deficiency of this factor—a deficiency that might develop independently of haemopoietin deficiency, thus accounting for the non-anæmic cases of the syndrome. But today it is recognised that vitamin B₁₂, a single substance which effectively corrects the anæmia, will also bring about certain arrest and some remission of the neurological changes; and it seems clear that the changes in the nerve-cells are part of the pernicious-anæmia syndrome. SAMSON and his co-workers³ have investigated the changes in cerebral function associated with clinical pernicious anæmia and noted a significant diminution in awareness, accompanied by electro-encephalographic abnormalities. These changes, too, are completely relieved by treatment with vitamin B₁₂ (such improvement precedes changes in the blood-count), and this they attribute to the effect of vitamin B₁₂ on cerebral metabolism.

The well-known glossitis of pernicious anæmia is also apparently a symptom of metabolic disturbance, this time in the epithelial tissues. It too can be controlled by vitamin B₁₂; but the action may not always be direct, since BROWN,⁴ in Glasgow, showed that other single members of the B-vitamin complex, such as pantothenic acid or nicotinic acid, were effective by themselves.

GRAHAM and RHEAULT⁵ now report changes in epithelial cells in patients with pernicious anæmia. In their laboratory cytological examination of gastric contents has revealed two types of cell. The majority are squamous epithelial cells from the upper respiratory tract and the oesophagus, most of which have been swallowed; they come from the superficial layer of the squamous epithelium. The other cells, which are fewer, are columnar epithelial cells from the gastric epithelium itself. In patients with untreated pernicious anæmia both these types show characteristic abnormalities. The squamous cells are considerably larger than usual; they sometimes have multiple nuclei as a result of abnormal mitosis; and the nuclear pattern, instead of being regular, is irregular with odd clumping of the chromatin. The gastric columnar cells are also larger than normal; and their nuclei show distinct increase of chromatin, which is irregularly distributed. When the patient is treated with vitamin B₁₂ these abnormal cell changes become less pronounced, and in full clinical remission they cannot be detected at all. No such abnormalities were found in patients with comparable haemoglobin levels due to iron-deficiency anæmia or acute blood-loss; so anæmia alone is not the cause. Nor do GRAHAM and RHEAULT think that the absence of free hydrochloric acid in the stomach is responsible. Once again lack of vitamin B₁₂ seems to be the reason. It is noteworthy that in pernicious anæmia the cellular abnormalities—excessive size and distorted arrangement of chromatin in the nucleus—are similar in the epithelial and the haemopoietic cells. What other cells, it may be asked, are likewise affected, and do the neurological changes follow cellular changes in the central nervous system? The mode of action of vitamin B₁₂ is not yet clear, but VILTER and co-workers⁶ and others have suggested that it is one of the essential components of the enzyme system concerned with the formation of nucleic acids. The blood-forming tissues are most severely affected because throughout life there is in them such a rapid turnover of cells. Both THORELL⁷ and J. N. DAVIDSON and co-workers⁸ have found that in pernicious anæmia erythroblasts tend to accumulate desoxyribonucleic acid in the nucleus, and ribonucleic acid in the cytoplasm, beyond the normal levels. The effect of vitamin B₁₂ on the growth of animals⁹ supports the view that it plays an important part in general cellular maintenance and multiplication. These nucleic-acid changes are engaging the attention of many investigators. Meanwhile it becomes clearer that megaloblastic anæmias are, as MALLARMÉ¹⁰ puts it, cytological dystrophies;

4. Brown, A. *Brit. med. J.* 1949, i, 704.

5. Graham, R. M., Rheault, M. H. *J. Lab. clin. Med.* 1954, 43, 235.

6. Vilter, R. W., Horrigan, D., Mueller, J. F., Jarrold, T., Vilter, C. F., Hawkins, V., Seaman, A. *Blood*, 1950, 5, 695.

7. Thorell, B. *Akt. med. scand.* 1947, suppl. 200, p. 52.

8. Davidson, J. N., Leslie, I., White, J. C. *Lancet*, 1951, i, 1287.

9. Zucker, T. F., Zucker, L. M. *Vitam. & Horm.* 1950, 8, 1.

10. Mallarmé, J. *Blood*, 1948, 3, 103.

1. Epstein, R. D. *Amer. J. Path.* 1949, 25, 239.

2. Kissmeyer-Nielsen, F. *Acta med. scand.* 1951, 141, 125.

3. Samson, D. C., Swisher, S. N., Christian, R. M., Engel, G. L. *Arch. intern. Med.* 1952, 90, 4.

in pernicious anaemia absence of vitamin B_{12} seems to be the cause, while in the megaloblastic anaemias of steatorrhœa and pregnancy folic-acid deficiency seems to be responsible.

All this new evidence makes it difficult to maintain the original idea that pernicious anaemia was due to a reversion of erythropoiesis to an embryonic form that produced red cells which could not stand up to the wear and tear of the adult circulation. It seems more likely that pernicious anaemia is a generalised disease of cell formation, and that the effect of lack of vitamin B_{12} on cell size and nuclear pattern becomes manifest in erythroblasts after the proerythroblast stage, and in granulocytes after the myelocyte stage. It is fortunate that so simple a treatment as the exhibition of vitamin B_{12} rectifies the multiple changes in this generalised disease.

Ureterocolic Anastomosis

DISSATISFACTION with the results of ureterocolic anastomosis has led to the development of new techniques. The pioneer methods of COFFEY¹ and STILES,² by which the ureter is led through the wall of the colon without direct anastomosis between the mucosæ of colon and ureter, have become less popular owing to their tendency to cause a stricture; this, though it may prevent reflux of gas or faeces up the ureter, interferes with drainage of the kidney, and hydronephrosis is very likely to develop. The direct techniques of NESBIT³ and CORDONNIER⁴ have the opposite disadvantage of often allowing reflux, and thus increasing the risk of renal infection. LEADBETTER⁵ has sought to combine the advantages of both methods by a direct mucosa-to-mucosa anastomosis, with a valvular arrangement fashioned by burying the lower end of the ureter in a tunnel formed by the wall of the colon. PYRAH⁶ reports that with this operation his own early results have been satisfactory.

Hardly any other abdominal operation gives rise to complications more commonly or in greater variety. Among the 1673 operations analysed by JACOBS and STIRLING⁷ the immediate-morbidity rate was over 40%. Partly, no doubt, this rate is so high because the operation is usually done for severe genito-urinary disease, very often in elderly patients; but even in young patients in good general condition complications are common. JACOBS and STIRLING find that these number no fewer than fifty-nine. Of the "non-specific" complications in the large series that they review, ileus developed in 114 (6.7%) cases; and they suggest that excessive preoperative preparation of the bowel may have helped to precipitate this disorder. Burst abdomen occurred in 41 (2.5%) cases; and probable factors here were abdominal distension due to ileus, or simple gaseous distension in a weakened patient. Intestinal obstruction may result from adhesions or from strangulation of a loop of bowel between the ureter and the posterior abdominal wall. Fistulae (urinary or faecal, or combined) occurred in 9% of cases, and renal complications (including infection, uræmia, and urinary calculi) in 5%. The most important late complication is electro-

lyte imbalance.⁸ As regards the clinical picture of this disturbance, nothing has been added to the description by FERRIS and ODEL⁹; and, despite much investigation, unanimity has not been reached on its cause. Most workers, including KEKWIKE et al.,¹⁰ LAPIDES,¹¹ and CREEVY,¹² believe that impaired renal function is the most important factor, but ROSENBERG¹³ states: "the primary factor in the production of hyperchloræmic acidosis following uretero-sigmoidostomy is, in most cases, reabsorption of urinary constituents, primarily anions, from the large bowel." The experimental work of PARSONS and his colleagues^{14 15} at Leeds and of ANNIS and ALEXANDER¹⁶ has clearly shown that differential absorption of electrolytes takes place, chloride being absorbed in excess of sodium. PYRAH suggests that in cases of electrolyte imbalance with severe clinical symptoms the sequence of events is probably as follows: differential absorption of chlorides from the colon; renal infection leading to interference with the acid-base regulating mechanism of the kidney; excessive loss of base from the kidney and acidosis; progressive dehydration; nausea and vomiting leading to increased dehydration.

The treatment of electrolyte imbalance should be started in the immediate postoperative period. Continuous rectal drainage by an indwelling catheter should be maintained for seven days to prevent any rise in pressure at the site of the anastomosis, and to diminish the total amount of urine in the colon. Fluid balance must be carefully maintained, and the administration of electrolytes limited to the body's requirements. Sodium chloride must be given sparingly because of the differential absorption of chloride, and any sodium deficit must be met by giving sodium lactate as well as sodium chloride so that the final ratio of sodium to chloride is 1.4 to 1. When oral feeding is started a mixture containing 4 g. each of sodium and potassium bicarbonate is given every twenty-four hours. Fluid intake should be as great as is compatible with urinary output, to prevent renal infection; and any infection should be vigorously treated with a broad-spectrum antibiotic. PYRAH decides on the later treatment of electrolyte imbalance by the severity of the symptoms:

1. Patients who have no symptoms should be instructed to restrict the amount of sodium chloride in their diet, to take sodium bicarbonate 4 g. daily, and to micturate fairly often.
2. Patients with mild symptoms may be quickly relieved by reducing their sodium chloride intake and giving sodium bicarbonate 2-3 g. eight-hourly until the acidosis has been corrected.
3. Patients with severe symptoms, such as dehydration and nausea, should be treated in hospital under close laboratory control. The complex electrolyte disturbances require individual correction, but with rational treatment even apparently hopeless cases can be revived.

The many disadvantages of the operation have led to a search for alternative measures, and several

8. *Lancet*, 1952, i, 453.
9. Ferris, D. O., Odel, H. M. *J. Amer. med. Ass.* 1950, **142**, 634.
10. Kekwick, A., Paulley, J. W., Riches, E. W., Semple, R. *Brit. J. Urol.* 1951, **23**, 112.
11. Lapides, J. *Surg. Gynec. Obstet.* 1951, **93**, 691.
12. Creevy, C. D. *J. Urol.* 1953, **70**, 196.
13. Rosenberg, M. L. *Ibid.* p. 569.
14. Parsons, F. M., Pyrah, L. N., Powell, F. J. N., Reed, J. W., Spiers, F. W. *Brit. J. Urol.* 1952, **24**, 317.
15. Parsons, F. M., Powell, F. J. N., Pyrah, L. N. *Lancet*, 1952, ii, 599.
16. Annis, D., Alexander, M. K. *Ibid.* p. 603.

1. Coffey, R. C. *J. Amer. med. Ass.* 1911, **56**, 397.
 2. Stiles, H. J. *Surg. Gynec. Obstet.* 1911, **12**, 127.
 3. Nesbit, R. M. *Univ. Hosp. Bull. Mich.* 1948, **14**, 45.
 4. Cordonnier, J. J. *J. Urol.* 1950, **63**, 276.
 5. Leadbetter, W. F. *Ibid.* 1951, **65**, 818.
 6. Pyrah, L. N. *Ann. R. Coll. Surg. Engl.* 1954, **14**, 169.
 7. Jacobs, A., Stirling, W. B. *Brit. J. Urol.* 1952, **24**, 259.

methods of constructing an artificial bladder have been devised.¹⁷ One of the minor disadvantages of an artificial bladder is the production of considerable quantities of mucus, which may lead to blocking of a catheter. GODFREY¹⁸ has found that preliminary irradiation of the ascending colon greatly reduces the secretion of mucus, and he suggests that it also diminishes the reabsorption of electrolytes. PYRAH describes a method of avoiding a ureterocolic anastomosis which may prove useful in some cases of contracted bladder. An isolated loop of lower ileum is prepared, one end is closed, and the other end is anastomosed to the solitary ureter. A wide side-to-side anastomosis is then made between the bladder and the ileal loop. This considerably increases the bladder storage capacity and relieves frequency of micturition.

By the development of such techniques, the conditions for which there is no alternative to ureterocolic anastomosis may be reduced in number. In PYRAH's⁶ words :

"The operation of ureterocolic anastomosis is not a procedure like appendectomy for gangrenous appendicitis or cholecystectomy for gallstones, which finally removes from the patient a diseased organ which may be threatening life; it is rather a procedure which, by producing a fundamental change in the excretory arrangements of the body, often confers great benefits on the patient, but also carries risks of renal infection and derangement of the blood electrolytes that are sometimes inimical to health and occasionally dangerous to life. It is reasonable, therefore, that . . . attempts should be made to relieve the pathological process for which it is performed by some alternative procedure."

The A.R.D. Virus?

SOMEWHERE in the no-man's-land between epidemic influenza and the common cold lies a group of febrile upper respiratory infections which are not normally epidemic. In 1938 STUART-HARRIS, ANDREWES, and SMITH¹⁹ described a syndrome which was more insidious in onset, and was more usually accompanied by sore throat and cough, than infection with influenza-A virus. This syndrome was named "febrile catarrh" to indicate the catarrhal manifestations—obstructed nose, hoarse voice, signs of tonsillitis or pharyngitis, and exudation of mucous or mucopurulent secretion. Individual cases could not be separated from influenzal infections, but the two conditions were thought to be distinguishable in the mass. The U.S. Army Commission on Acute Respiratory Diseases²⁰ described a similar condition which they called "undifferentiated acute respiratory disease," or A.R.D.; and they also spoke of cases of atypical pneumonia and exudative pharyngitis, although it was not known whether these three conditions represented different clinical manifestations of the same aetiological agent. A.R.D. was particularly common among new entrants to the army—unlike influenza, which attacked new recruits and old stagers indiscriminately. The commission²¹ also investigated the aetiology of this disease in volunteers. In 12 out of 14 volunteers, a filtrate of nasopharyngeal secretions from a typical case produced a mildly febrile

17. *Ibid.* 1953, i, 1188.

18. Godfrey, G. *Aust. N.Z. J. Surg.* 1954, 23, 161.

19. Stuart-Harris, C. H., Andrewes, C. H., Smith, W. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1938, no. 228.

20. U.S. Army Commission on Acute Respiratory Diseases. *Amer. J. publ. Hlth.* 1944, 34, 347.

21. U.S. Army Commission on Acute Respiratory Diseases. *J. clin. Invest.* 1947, 26, 957.

respiratory illness five to six days after inoculation, and tests of immunity distinguished this infection from the common cold. These findings suggested that A.R.D., which is probably the same condition as "febrile catarrh," is a distinct entity with a rather longer incubation period than has been described for influenza and the common cold and is probably caused by a filtrable virus. The extent of A.R.D. in the general population is unknown, and this would be extremely difficult to assess without a laboratory test for the aetiological agent.

It is good news, therefore, that attempts to isolate an aetiological agent from an outbreak of A.R.D. at Fort Lennox Wood, Missouri, by inoculating tissue-cultures of HeLa cells (from a uterine carcinoma), have resulted in the recovery of a new virus. HILLEMAN and WERNER²² examined 29 throat washings and recovered 5 cytopathogenic agents, presumably viruses, from 3 cases diagnosed as primary atypical pneumonia and 2 diagnosed as A.R.D. Apart from its cytopathogenic action, the distinguishing features of the virus are not yet known; but serological tests by neutralisation of the virus's cytopathogenic action, and complement-fixation tests, have yielded important results. Each of 7 cases of primary atypical pneumonia and 6 of 7 cases of A.R.D. from this outbreak showed a fourfold or greater rise in antibody to the new virus. No rise in antibody to this virus was found in sera from patients with influenza A or B, psittacosis, ornithosis, or Q fever, or in 3 cases diagnosed as primary atypical pneumonia in which there were significant increases in cold or streptococcus MG agglutinins. The results suggest that the new virus may be a cause of some cases of A.R.D. or primary atypical pneumonia. HILLEMAN and WERNER mention that the agent they describe has proved to be immunologically related to a virus recovered earlier by ROWE et al.²³ from cultures of adenoid tissue. These workers noted that during long in-vitro cultivation of adenoids obtained at operation on young children many of the cells showed a characteristic rounding, progressing to complete destruction of the epithelium. Transfer of these cultures to HeLa cells resulted in identical changes in the recipient cells; and the causative agent, which was filtrable, has been called the "adenoid-degenerating" or A.D. agent. It is important to find out whether the A.R.D. and A.D. agents are the same or are simply members of the same family. Possibly the upper respiratory passages harbour a group of related viruses (cf. the pneumococci) of which some members are latent and harmless commensals while others can cause A.R.D. or primary atypical pneumonia. Alternatively this virus may be of no aetiological significance in A.R.D. but may multiply when the ground has been prepared by the A.R.D. virus. This does not seem very likely, but the recovery of Coxsackie and poliomyelitis viruses from the same patients should warn us against jumping too readily to conclusions. It will be of great interest to see what the new virus and the A.D. virus do to the long-suffering volunteer who is prepared to risk febrile catarrh and possibly degeneration of his adenoids.

22. Hilleman, M. R., Werner, J. H. *Proc. Soc. exp. Biol., N.Y.* 1954, 85, 183.

23. Rowe, W. P., Huebner, R. J., Gilmore, L. K., Parrott, R. H., Ward, T. G. *Ibid.* 1953, 84, 570.

Annotations

PROSPECTS IN THE CIVIL SERVICE

THE long deadlock over the salaries of Civil Service doctors has at last been broken, on the terms which we publish on p. 878. The commencing salary of a medical officer (at the age of 35) is to be £1500, and the maximum salary in this basic grade will be £2100, which is a substantial advance on the present scale of £1250-1725. The Treasury would like the new scale to be permanent, but the committee which represents Civil Service doctors does not accept it as adequate and will be putting its arguments before the Royal Commission on the Civil Service, of which Sir Raymond Priestley is chairman. Increases of £100 and £50 are also made in the salaries of senior medical officers and principal medical officers; but these are regarded by all parties as no more than a token, and the Royal Commission will be asked to consider what the appropriate salaries should be. In the medical Civil Service as elsewhere, outstanding merit should bring commensurate reward, and responsibility should have pecuniary recognition.

The new scales operate retrospectively from Jan. 1, 1952; and this is only proper, for their negotiation has a long and not a happy history. As far back as 1948 the Institution of Professional Civil Servants asked that the recommendations of the two medical Spens reports should be applied to Civil Service medical officers; to which the Treasury replied that Spens was not applicable. In conjunction with the Ministry of Health Medical Staff Association and the B.M.A., the institution then formed a Civil Service Medical Officers' Joint Committee, which in August, 1949, presented a salary claim based on the two reports. After rejecting this in February, 1950, the Chancellor of the Exchequer said that he would appoint a committee to consider the remuneration, structure, and organisation of the medical Civil Service; and in the autumn of 1951 the Government accepted the recommendations of the Howitt Committee which had been charged with this task. But neither the constitution nor the conclusions of the Howitt Committee were acceptable to the profession,¹ which did not feel that the problem had had the full and judicial examination it deserved. The British Medical Association declined to accept further advertisements for Civil Service medical appointments; and, in associating ourselves with a request for fuller and more objective consideration of the subject, we said that "in the (perhaps unlikely) event of advertisements being submitted, we intend to add to each of them an indication to possible applicants that conditions of remuneration and promotion for doctors in the Civil Service have not yet been satisfactorily settled."² With this rupture the difficulty of obtaining good medical officers became even greater.

In the further study of recruitment for the medical Civil Service which the Royal Commission will no doubt undertake, we hope that emphasis will be placed as much on prospects of promotion as on the level of remuneration in the basic grade. In some departments there are few senior posts and the prospects for an able man are poor—a situation recognised by the Howitt Committee when it suggested that a doctor with exceptional qualifications, bearing responsibilities heavier than those usually falling on officers of his grade, should (with Treasury sanction) be allowed personal promotion. Commenting on this, we said: "Our impression is that, unless this loophole is greatly enlarged, the service, on the proposed salary scales, is unlikely to secure first-rate specialist members in the future."¹ This remains true; yet it seems to be nobody's business to see that the loophole is made into something more useful.

1. *Lancet*, 1951, ii, 921.
2. *Ibid.*, 1952, ii, 119.

PENICILLIN BY MOUTH

SINCE penicillin first became available in quantity many attempts have been made to find a reliable method of administering it by mouth, and many vehicles have been suggested for this purpose. The relative instability of penicillin in acid solution, and the low blood levels following its oral administration, led to the belief that acid in the stomach destroyed much of each dose. Preparations in alkaline or buffered solutions, or in enteric-coated capsules designed to dissolve after passage through the stomach, were therefore investigated in an attempt to prevent such destruction; but no method has given constant and reproducible results. In all the earlier investigations high serum concentrations were attained in some patients, while in others penicillin could not be detected in the blood, whatever buffers or capsules were used as the vehicles.

The explanation now generally accepted for this unpredictability is that the power to absorb the drug from the intestine varies widely between different people, and that destruction by gastric acid is of minor importance. The capacity to absorb penicillin can be assessed only by trial and error, which is usually impracticable; so clearly progress in this field can come only from the development of compounds that are uniformly and reliably absorbed by all patients. This property has been claimed for N:N'-dibenzylethylenediamine penicillin (benzathine penicillin), though the inconsistencies in the reported trials suggest that the requirements may not be completely satisfied.¹⁻⁴ Elsewhere in this issue we include two further reports on benzathine penicillin. Dr. Fairbrother and Dr. Daber have compared its value with that of potassium penicillin, mainly in adults; while Dr. Beasley and Dr. MacPherson have investigated the absorption of benzathine penicillin in children of various weights.

The outstanding conclusion to be drawn from Fairbrother and Daber's report is that the absorption of benzathine penicillin from the intestine is no more constant or reliable than that of the potassium salt. In fact the results suggest that potassium penicillin is possibly the more satisfactory compound. In only 1 of 35 patients to whom 600,000 units of potassium penicillin was given by mouth was no penicillin detected in the blood four to six hours later. In a further 8 patients the blood level at this time was only 0.03 unit per ml.; this is often regarded as the minimum therapeutic level, though, as Fairbrother and Daber point out, it may often be clinically ineffective. Among 59 adult patients, four to six hours after administration of 600,000 units of benzathine penicillin no penicillin was detectable in 11 instances, and only 0.03 unit per ml. was found in another 11. Thus blood levels exceeding 0.03 unit per ml. four to six hours after the dose were observed in 74% of patients receiving potassium penicillin and in 62% of patients receiving benzathine penicillin. The absorption of benzathine penicillin by 31 children seemed more satisfactory in that no instances were encountered in which penicillin was undetectable in the blood. The interpretation of these findings is difficult, however, since the ages and weights of the children are not specified, and no comparable study of potassium penicillin is reported.

The importance of weight in relation to dosage is clearly seen from the report by Dr. Beasley and Dr. MacPherson, who have determined for children of various sizes the doses of benzathine penicillin required to give 0.03 unit per ml. in the blood after four, six, and eight

1. Bayne, G. M., Gylfe, J., Carfagno, S., Boger, W. P. *Amer. J. med. Sci.* 1953, 225, 180.
2. Cathie, I. A. B., MacFarlane, J. C. W. *Brit. med. J.* 1953, i, 805.
3. Welch, H., Randall, W. A., Hendricks, F. D. *Antibiot. Chemother.* 1953, 3, 1053.
4. Wright, S. S., Purcell, E. M., Kass, E. H., Finland, M. *J. Lab. clin. Med.* 1953, 42, 417.

hours. No parallel study of other types of penicillin was made; but the large size of the doses required to ensure absorption, even in quite small children, suggests that benzathine penicillin cannot be greatly superior to the potassium salt.

These reports focus attention once more on the practicability of oral administration of penicillin. Repeated injections are always inconvenient in general practice, and in children they should be avoided if possible. Possibly, too, the incidence of sensitivity reactions might be diminished by oral administration. Nevertheless, the attainment of an effective concentration at the site of the infection has priority over these considerations; and, as Fairbrother and Daber point out, a single daily injection of 400,000 units of procaine penicillin costs less and gives more uniform results than 600,000 units of penicillin by mouth every six hours. For severe infections the administration of penicillin by mouth in any form seems clearly to be unjustified unless the antibiotic is also given parenterally in the early stages. In all other cases, before resorting to administration by mouth on the ground of convenience very careful consideration should be given to such factors as the sensitivity of the infecting organism, the danger of encouraging resistant organisms by inadequate dosage, and the severity of the infection.

CORTICOTROPHIN AND ADRENAL HORMONE IN URINE

MUCH of our knowledge of metabolism is derived from the analysis of urine. Although this gives only indirect information about what is going on inside the body there are advantages in using such material, which the patient can provide without hardship and which is in some ways more pure than the body-fluids themselves.

Rubin et al.¹ have recently demonstrated corticotrophin-like activity in the urine of some normal persons by injecting the urine into hypophysectomised rats and measuring the fall in the ascorbic acid content of the rats' adrenals. The urine of one patient with Cushing's syndrome possibly had a greater effect than normal urine. On the other hand Rubin et al. did not find any increase in the activity of urine from children with rheumatic fever who were receiving corticotrophin. The significance of these findings is not yet clear.

The effect of corticotrophin on the excretion of adrenocortical hormone is a fruitful field for research. The adrenal steroids in urine have been measured chemically and by biological assay, and certain derivatives without biological activity can be demonstrated after hydrolysis with glucuronidase. Cope and Hurlock² have applied the method of paper partition chromatography to the separation of cortical steroids in human urine. They have distinguished hydrocortisone (compound F) and cortisone, and two important steroid metabolites—tetrahydro-compound F and tetrahydrocortisone. The tetrahydro-compounds do not possess hormonal activity and may represent breakdown products of hydrocortisone and cortisone. The excretion-rates of all four compounds increased with administration of corticotrophin and after a major operation. Tetrahydrocortisone was usually present in greater amounts than tetrahydro-compound F, but the excretion of hydrocortisone often exceeded that of cortisone. All the compounds were much reduced in patients with hypopituitarism. When these patients were given cortisone, the excretion of cortisone and also of hydrocortisone and of the two tetrahydro-compounds increased. This suggests that cortisone is converted to hydrocortisone in the body, and that the adrenals do not necessarily play a part in the conversion. Evidence is accumulating that hydrocortisone may be the active

"sugar hormone" of the adrenal cortex; and this would explain, for instance, why hydrocortisone is more effective than cortisone when injected into rheumatic joints.³

MICROGYRIA

MICROGYRIA is a manifestation of severe dysplasia of the cerebral or cerebellar cortex, in which the convolutions are not only reduced in depth but also seemingly increased in number. It has to be distinguished from ulegyria, which is a thinning of the gyri due to scarring acquired after birth and often as a result of it; and to make the distinction clearer it is sometimes called polymicrogyria. It may be seen in the cerebrum or cerebellum of mental defectives and even in those of more normal mentality, while its association with other congenital anomalies, both in the brain and elsewhere, is well known: Norman⁴ noted the condition in 8 out of 45 cases of cerebral palsy. The convolutions are often rather wide, and their surface is finely wrinkled—an appearance that has been likened to a chestnut kernel. The abnormality, however, may be confined to the deeper convolutions, as Obersteiner showed in 1902, and may not be visible on the surface. A brain with microgyria involving many convolutions may be unduly small,⁵ but this association with micrencephaly is by no means invariable. The cortical architectonics vary considerably, but not infrequently they conform to a pattern in which there are four instead of the usual six layers of cells, with a conspicuous fibre lamina dividing them up into two main layers. The junction between the normal and the pathological may be abrupt.

Bielschowsky⁶ explained the anomaly as a failure of the neuroblasts migrating from the matrix to reach the periphery. One would thus expect the condition to be bilateral, but it was unilateral in 2 of the 6 cases, unassociated with porencephaly, reported by Norman.⁴ Ulegyria, too, may be bilateral, usually in the neighbourhood of the sagittal sinus; on the other hand, it tends to affect small areas of the cortex, to be sharply defined, and to be especially severe in the depths of sulci.⁷ Hallervorden⁸ thought that this characteristic deep-seated position was the result of severe congestion during birth. Clearly, therefore, it may be difficult to distinguish ulegyria from polymicrogyria. Doubtless many cases of ulegyria have, in the past, been regarded as examples of true microgyria, and this confusion is likely to continue in the future. Referring to brains which show structural anomalies at an early age, Norman⁴ remarks: "In the absence of clear-cut signs of malformation pathological criteria alone are usually insufficient to allow one to determine with confidence whether the damage to the brain has occurred during the later stage of pregnancy, during birth, or in early infancy"; and Malamud⁹ has arrived at the same conclusion. It would seem, therefore, that ulegyria tends to be labelled microgyria (or polymicrogyria) more often than the converse.

Of 3 cases of microgyria reported by Crome,¹⁰ instrumental deliveries are mentioned in 2 but in the third no clear history was available. One child, who died at the age of 12, had been retarded from birth and had been epileptic from the age of 18 months; a dissimilar twin was normal. The other 2 children survived until the ages of 7½ and almost 2. In all 3 brains the microgyria was associated with micrencephaly

1. Rubin, B. L., Dorfman, R. I., Dorfman, A. *J. clin. Endocrin.* 1954, 14, 154.

2. Cope, C. L., Hurlock, B. *Clin. Sci.* 1954, 13, 69.

3. Dixon, A. St. J., Bywaters, E. G. L. *Ibid.* 1953, 12, 15. See also *Lancet*, Feb. 27, 1954, p. 448.

4. Norman, R. M. *Proc. R. Soc. Med.* 1953, 46, 627.

5. Greenfield, J. G., Wolfsohn, J. M. *Arch. Neurol. Psychiat.* 1935, 33, 1296.

6. Bielschowsky, M. *J. Psychol. Neurol.* 1915, 22, 1 *Ibid.* 1923, 30, 29.

7. Norman, R. M. *Arch. Dis. Childh.* 1944, 19, 111.

8. Hallervorden, J. *Z. ges. Neurol. Psychiat.* 1939, 167, 527.

9. Malamud, N. International Congress of Neuropathology, September, 1952; see *Lancet*, 1952, ii, 635.

10. Crome, L. *J. Path. Bact.* 1952, 64, 479.

and compensatory hydrocephalus, and in 2 of them there was paraventricular calcification, so that radiologically some confusion might arise in distinguishing this disease from tuberous sclerosis or even toxoplasmosis. Crome noted that the microgyria was usually more extensive than it first seemed, for when the sulci were examined closely cryptomicrogyria was often found. His third case was associated with arhinencephaly and porencephaly, but the microgyria was restricted in each hemisphere to an area around the Sylvian fissure. He concluded that there must have been defective development of the brain, and the symmetrical distribution supported this view; but the covering membrane over the porencephalic cyst showed histological evidence of the destruction of existing brain tissue, so the defective development might itself have been the result of a destructive lesion during early development. This deduction is in keeping with the view of Cohen and Neumann¹¹ who believe that vascular occlusion early in foetal life will cause maldevelopment or even agenesis.

When microgyria is associated with porencephaly the question arises whether the second condition is strictly a complication of the first—the result, for instance, of a secondary vascular softening—or whether the disturbance of the foetal brain which gives rise to porencephaly also causes microgyria in the adjoining cortex. Yakovlev and Wadsworth,¹² in their extensive studies, divide the porencephalies into the schizencephalies—"a manifest disorder of tectogenesis"—and the encephaloclastic porencephalies, but they do not seem to exclude the possibility of mixed forms. In one of their cases lesions of three different ages were found; one of them probably dated from birth, and the other two were earlier, thus illustrating, they suggest, a sequence of superimposed events brought about by a chain of largely obscure causes "in which the circulatory disturbances and the destructive encephalomalacic lesions represent an incidental and fortuitous factor." If the cause of porencephaly is complex, the same can be expected of microgyria, which it so often accompanies. Provided, however, that there is no question of delay in the migration of neuroblasts to the cortex, the disturbance of the foetal brain that produces true microgyria would be expected during the fourth or fifth month—the time when migration normally takes place.

Hydrocephalus, it seems, may also be looked for in association with microgyria. Crome described it in each of his 3 cases, but Norman found it in only 2 out of 6 cases, and in both of these the cortical defect was bilateral. Of particular interest in this respect is a case described by Hallervorden.¹³ A married woman in the fifth month of pregnancy made an unsuccessful attempt to commit suicide with coal gas. The baby was born at the expected time, but failed to develop normally and later suffered from athetosis. The head was retracted and there was severe lordosis of the lumbar spine. The child died at the age of 1. True microgyria was present in parts of both frontal lobes; and microscopically there was widespread loss of nerve-cells in the third layer of the cerebral cortex. Both putamina showed cavitation and scarring, and so did the lateral thalamic nuclei on the right side. The brain thus showed what was apparently a prenatal malformation dating from about the fifth month of foetal life, and in addition there was evidence of gross softening of the basal ganglia and other vascular lesions. The possible part played by anoxia in microgyria is referred to by Meyer and Cook,¹⁴ who found gliosis in the white matter of mental defectives, including those with microgyria; but they pointed out that defective tissue oxygenation

is often merely a final common pathway of etiologically distinct disease processes.

There is clearly much to learn about the cause of microgyria. A history of trauma at and after birth in defectives is hard to elicit, and it is known that serious birth injury may take place in apparently normal labour¹⁵; but reliable evidence of intra-uterine events likely to cause encephaloclastis or otherwise disturb the development of the nervous system is impossible to obtain.

THE DRAUGHT REFLEX

THOSE in charge of the management of lactation need to understand the draught reflex. The mother finds description elusive, and exact recording sometimes takes part in the conditioned reflexes which set it off. The mere act of thinking of the reflex may bring it into action before its proper time. Yet the doctor or midwife depends largely on subjective accounts since there is little objective evidence by which to detect vagaries of the reflex that may be producing feeding difficulties.

Dr. Isbister¹⁶ has sought to analyse the usual behaviour of the reflex and some of its variations by questioning many mothers as well as making observations on herself. She confirms Waller's¹⁷ finding that most primiparae feel the reflex for the first time only after about three weeks, whereas multiparae may feel it even before delivery; and she confirms, too, that nearly all successful feeders experience it. Many of the mothers questioned had noted that sometimes the draught was delayed and seemed to last less long than usual—particularly when they had been suffering embarrassment, fatigue, or worry. Anger roused just before feeding delayed the draught by two minutes. Dr. Isbister suggests that too vigorous action of the reflex may in some instances be responsible for wind, colic, vomiting, and frequent stools in the baby; and, to avoid this difficulty, she recommends evoking the reflex before the feed by expressing a little milk. Like Waller, she believes that gastrointestinal symptoms in the infant may be due to gulping large quantities of milk; but perhaps they may sometimes be the outcome of maternal fear transmitted humorally in the milk. The mother's fear of suffocating her baby may be great, and assurances that the baby can manage the situation if given his head are often as effective as any other remedy for the baby's disturbances.

HALF-WAY HOUSE

ON March 31 an important experiment was set in train at Liverpool when Sir Henry Cohen and the Bishop of Liverpool opened a hostel administered by the Liverpool Personal Service Society. The regional hospital board has contracted for the use of 18 of the beds by patients transferred from hospital who are not yet fit to return home. The remaining 20 beds are available to the local health authority for patients who are aged and frail but who do not require medical and nursing care. Experience with this hostel may answer some of the questions concerning borderline cases that are neither fully the responsibility of the hospital service nor fit enough for the type of hostel provided by the local health authority under the National Assistance Act. The progress of this experiment will be keenly watched not only by the administrators of these two branches but also by general practitioners, who are in a good position to see the ill effects of the hiatus that the new hostel is designed to fill.

ON April 12 Sir RUSSELL BRAIN was re-elected president of the Royal College of Physicians of London for the ensuing year.

11. Cohen, R., Neumann, M. A. *J. Neuropath.* 1946, 5, 257.
 12. Yakovlev, P. I., Wadsworth, R. G. *Ibid.* p. 116.
 13. Hallervorden, J. *Allg. Z. Psychiat.* 1949, 124, 289.
 14. Meyer, A., Cook, I. C. *J. ment. Sci.* 1937, 83, 258.

15. Brouwer, B. *Proc. R. Soc. Med.* 1949, 42, 603.
 16. Isbister, C. *Arch. Dis. Childh.* 1954, 29, 66.
 17. Waller, H. *Clinical Studies in Lactation.* London, 1937; p. 37.

Reconstruction

A DIAGNOSTIC CENTRE

THE Nuffield Diagnostic Centre at Corby in Northamptonshire is being opened on April 23 by Lord Nuffield. The centre has been sponsored by the Nuffield Provincial Hospitals Trust and the Oxford Regional Hospital Board, and it has been designed as part of a plan to meet the medical needs of the rapidly growing town of Corby.

The Plan for Corby

In 1934 Corby was a village with a population of about 1500. Messrs. Stewarts & Lloyds then opened the first part of the steelworks there; the industry has been expanding ever since, and Corby has grown with it. In 1950 a development corporation was established, under the terms of the New Towns Act, to help the urban district council in their work of development. The steel industry is to be further enlarged, and light industries will, it is hoped, increase too. The aim is a town of 40,000; and one of the corporation's main tasks was the provision of a town centre, and this is now well under way. Close to the town centre there is a large area of woodland, and it is here that the diagnostic centre has been built; and an adjoining site has been reserved for the hospital and clinic buildings that may be added later.

In 1949 the Nuffield Provincial Hospitals Trust examined the medical needs and opportunities of Corby, and the result was the formation of a committee which was asked to draw up a plan to meet these needs. The committee included representatives of the Trust, the Oxford Regional Hospital Board, the Northamptonshire County Council, the Northamptonshire Executive Council, the Corby Urban District Council, and Stewarts & Lloyds. It was clear that no new hospital could be built for a long time, yet something had to be done to meet the difficulties of the general practitioners, who had no convenient means of investigation or consultation for their patients. As things were, they had to refer them to Kettering (8 miles away) or Northampton (25 miles);

and this meant much inconvenience and loss of time for the people of Corby, and much extra work for the nearest hospital, at Kettering. So the Trust proposed to all concerned that there should be set up

"a diagnostic centre, which will include examination and treatment rooms to be used by the general practitioners, and also by the hospital service as a consultant outpatient department; chest clinic, and X-ray and physiotherapy departments; and a dental suite."

And this centre forms the first stage in the plan for Corby. (For the time being, at the suggestion of the Ministry of Health, the dental suite has been omitted.) Later, a maternity unit will be added by the regional board, and there may also be a unit of general-practitioner beds. The existing local-authority clinics in the area are at present sufficient, but when extra clinics are needed they will be built beside the diagnostic centre.

The hopes are that this scheme will not only enable the Corby doctors to provide a better service for their patients but also lessen the burden on Kettering General Hospital and other hospitals in the district.

The Design

The centre has been designed by Mr. R. Llewelyn Davies, A.R.I.B.A., the director and architect of the Trust's Investigation into the Functions and Design of Hospitals; and he has had the help of Messrs. Gotch, Saunders, & Surridge, architects, of Kettering. One purpose of the experiment was to show that the essentials for a diagnostic centre of this kind could be provided at a reasonable cost. The contract price for the building was rather less than £34,400, and the cost of furnishing and equipping it was about £13,000; and this is certainly modest by health-centre standards. The contract price works out at a few pence over £3 10s. per sq. ft. of floor space; the permitted expenditure on private houses is usually around £2 per sq. ft., but the architect clearly has a lot more to do in each square foot in a diagnostic centre than in an ordinary house. And Mr. Llewelyn Davies and his colleagues have done very well in building an efficient and pleasant building for such a sum.

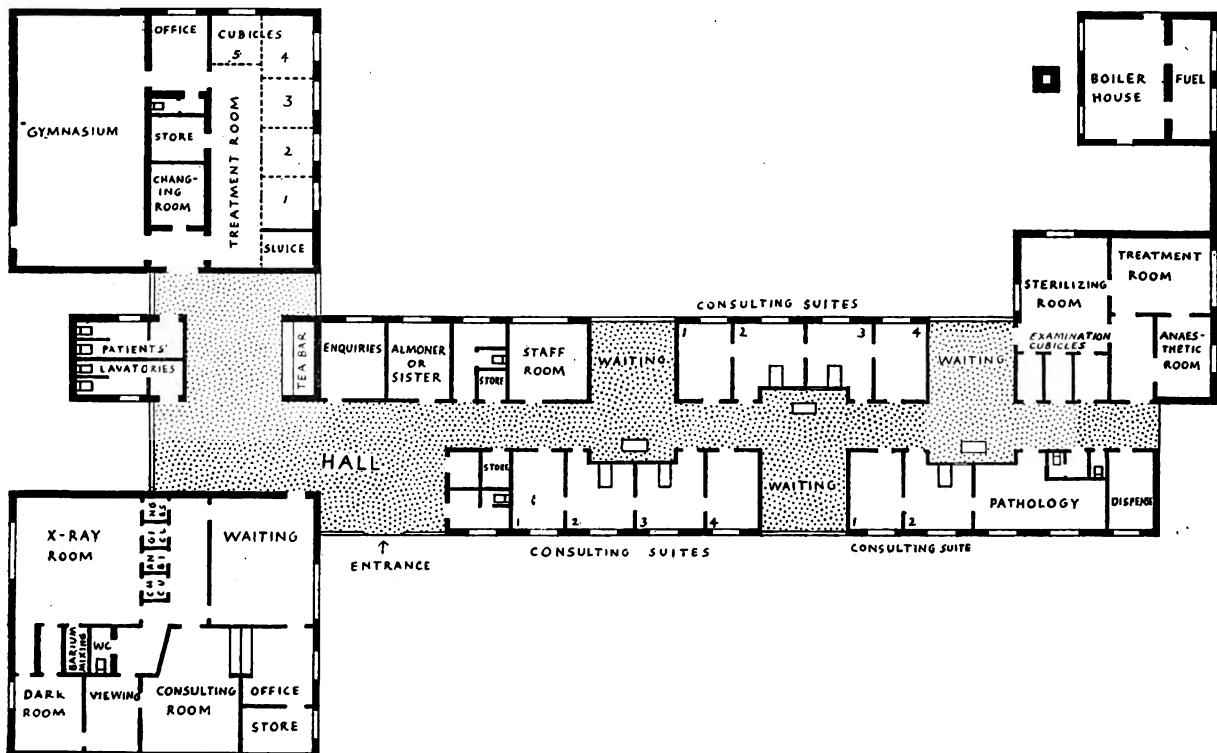


Fig. I.—Plan of the diagnostic centre.

The three parts of the building—the consulting and treatment wing, the physiotherapy department, and the combined chest clinic and X-ray department—are neatly arranged around a central entrance hall and reception desk (fig. 1). Waiting-spaces, rather than waiting-rooms, have been fitted into the design, and there are splendid wall-high windows to light them (fig. 2). The consulting-rooms, which will be used by both G.P.s and consultants, have examination rooms alongside, and one of the consulting-rooms is equipped for the ophthalmologist. They all have 'Anglepoise' lamps and viewing-boxes fitted to the walls.

The compact and well-provided pathological laboratory is down the same corridor; and further on there are the treatment rooms. Three small cubicles are equipped for dealing with patients who have dressings to be changed, and the small treatment room and anaesthetics room will enable the doctors to undertake many more minor operations than they could hope to do in their surgeries.

The physiotherapy block includes a remarkably roomy gymnasium (fig. 3) with plenty of things to keep the patients hard at it. The department can take on anything that a bigger hospital one can do; the only limitation is its size and the physiotherapist's one pair of hands. It remains to be seen how great will be the call on his services and those of the specialist in physical medicine: they could be the busiest people in the place.

The X-ray department is superbly equipped; the tilting table will be the envy of visiting radiologists. Again, it is difficult to say straight away how much work there will be for the radiographer, but there is no doubt that it will be well done. If the planners have been lavish anywhere in the centre, it is here. No serious casualties will be brought to the centre for X-ray examination, because there are at present no beds to receive them or resident medical staff to attend them. But this may come later.

To keep the bills down, the architects have had to be pretty strict in their choice of materials. They have used plenty of glass to give a cheerful exterior—always difficult to achieve in a single-storey building. And they have chosen a pale sandy-coloured brick of pleasant texture which does not, as the yellowish bricks often do, emphasise the virtues of the reds. Internal walls in corridors and waiting-spaces have been left unplastered; and on these walls bold colour-washes have been used to distinguish one part of the building from another.

The Working of the Centre

The centre does not qualify to be called a "health centre" under the definition of the N.H.S. Act of 1946, for it does not include all the facilities laid down in the Act. Moreover, it is not provided by a local health authority, and the G.P.s will not work in it as a group. The doctors will continue to use their own surgeries in Corby; but when they see a patient who needs a more thorough examination and investigation than they have the time or means to undertake immediately, they will arrange to see him later at the centre, where the G.P.s will rent some of the consulting-rooms. There they will be able to deal with the case more effectively

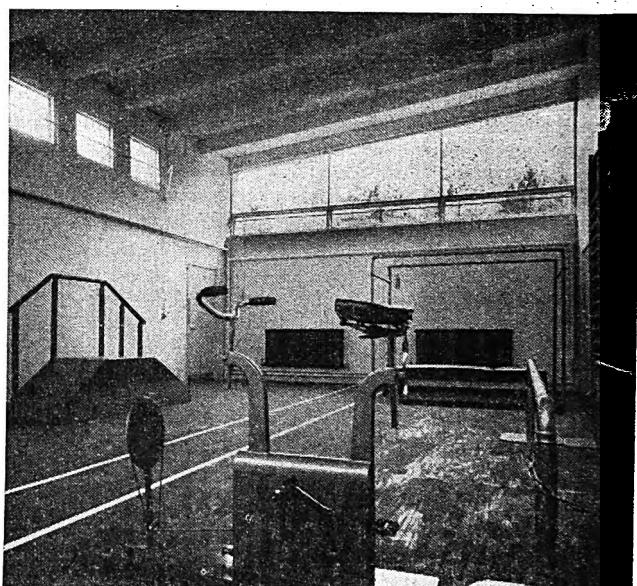


Fig. 3—The gymnasium in the physiotherapy department.

than they can usually do during busy surgery hours. The X-ray department and pathological laboratory will be to hand, and they will be able to consult colleagues who are using the centre in the same way or arrange for an opinion from one of the consultants who visit the centre for specialist clinics. If he is able to be there when the consultant sees his patient, the G.P. (and the consultant) will have the added advantage of direct contact; and, indeed, it is hoped that direct consultation between G.P. and consultant will be one of the most useful features of the new centre. To encourage this side of things, arrangements have been made for G.P.s to become clinical assistants to the consultants visiting the centre.

The Authorities Concerned

The Oxford Regional Board is providing and staffing the chest clinic and the X-ray and physiotherapy departments, and the board will pay a fee for the use of the consulting-rooms by its consultants and specialists. At the start, the clinics to be held at the centre will be: medical, surgical, obstetric, and gynaecological, paediatric, chest diseases, physical medicine, psychiatric, ear, nose, and throat, radiological, dermatological, ophthalmological, and orthopaedic. The pathological laboratory, the X-ray department, and the physiotherapy department will be under the direction of the corresponding consultant at Kettering.

At the end of the five-year experimental period, the Northamptonshire County Council will have the opportunity of buying the Trust's share in the centre. Meanwhile, the council is contributing £100 a year towards the maintenance expenses; and it will pay for any accommodation that may be needed when its existing clinics are unable to cope with the growing population.

The Corby Urban District Council has no statutory place in the affairs of the centre, but it is paying the rent of two cottages for the resident staff and is also meeting the cost of the laying-down and the upkeep of the lawns and flower-beds.

The Corby Development Corporation is providing a house for a physiotherapist.

Stewarts & Lloyds will contribute to the running costs of the centre during the early years of the experiment.

The capital for building and equipping the consulting and minor-treatment rooms and the pathological laboratory has come from the *Nuffield Provincial Hospitals Trust*, which is also helping with the initial running costs. The *Nuffield Health and Social Services Fund* has transacted much of the business for the



Fig. 2—A view of the centre showing one of the large windows.

Trust, and the ultimate control and coöordination of the centre has been vested in the Fund. The Fund has sold part of the site to the regional board, and it is keeping another 5 acres ready for the board to build the maternity and G.P. units.

Administration and Staff

The day-to-day running of the centre is in the hands of a local management committee, appointed by the Fund. The Kettering and District Hospital Management Committee is responsible to the regional board for its part of the centre, but by a happy arrangement the house committee chosen to look after this part of the centre is man-for-man the same as that appointed by the Fund for the Trust's side of things. The group secretary of the Kettering committee is administrator in charge of the centre. The staff, at any rate for the time being, is a sister, staff nurse, assistant nurse, physiotherapist, radiographer, laboratory technician, almoner, receptionist, and 2 typists. Stewarts & Lloyds have also offered the help of their social relations officer.

The Value of the Experiment

Whatever the differences between a "diagnostic centre" and a "health centre," it is certain that progress at Corby will be judged partly in relation to the health-centre experiments that are under way in various parts of the country. In the matter of cost, the Corby centre is dearer than the centres at Harlow,¹ Bristol,² and Nottingham³ (where no attempt was made to provide special methods of investigation), and inexpensive by the standards of Woodberry Down⁴ and Sighthill.⁵ But, in counting the cost, the important point is that something was urgently needed at Corby: a hospital was out of the question, and the Nuffield centre was a likely answer. The particular interest of the experiment lies in the possibility that it will turn out to be an answer applicable in other districts where populations are large and hospitals small or far away.

To enable them to keep a close watch on developments, the Trust organised, in the late summer of 1953, a survey of the domestic, social, and economic difficulties that arose from the lack of a hospital and outpatient department in Corby. A year or two from now the same details will be re-examined, and it will then be possible to make a preliminary judgment of what the centre has done for the people of Corby. It will also be interesting to know what weight of work it has taken off the back of Kettering Hospital and other hospitals. There will be less doubt of the advantages to the general practitioners, who will have a splendid surgery-from-home, as well as an opportunity to draw added help from the consultant service and, indeed, to take part in it.

Medicine and the Law

Spinal Anæsthesia

THE decision in Woolley and Roe *v.* Ministry of Health and others,⁶ which we announced briefly last week, may not only mystify the layman but also leave the lawyers in some uncertainty.

The two plaintiffs, after undergoing minor operations in the Chesterfield and North Derbyshire Royal Hospital, became permanently paralysed from the waist downwards. 'Nupercaine,' supplied in glass ampoules, had been administered as a spinal anæsthetic, and at the trial Mr. Justice McNair found that injuries were caused by phenol percolating through invisible cracks into the ampoules from the solution in which they had been immersed. The layman may be surprised that patients could be refused compensation when so grave and apparently inexcusable an injury could happen to them in hospital. The lawyers may feel puzzled because, although the trial judge decided that the facts did not

speak for themselves (thereby establishing a *prima facie* case of negligence), Lord Justice Denning now holds the contrary view. The hospital authorities in his opinion were responsible for the whole of the staff; he did not think that the hospital authorities and the anæsthetist could both avoid an explanation by each throwing the responsibility on the other. Lord Justice Somervell was prepared to regard the visiting anæsthetist as part of the permanent staff of the hospital, like the orthopaedic surgeon in *Cassidy v. Ministry of Health* in the case which he helped to decide in 1951. The visiting anæsthetist, he said, was (like the orthopaedic surgeon) a qualified skilled man, controlling as such his own methods. "The position of surgeons and others under the National Health Act will have to be decided when it arises, the position of hospitals under that Act may or may not be different from that of voluntary or municipal hospitals." We must wait, it appears, for further expensive litigation in order to find out how the law stands.

In the recent appeals the trial judge had found that phenol could find its way into an ampoule of nupercaine, stored in a phenol solution, through cracks undiscoverable by ordinary visual or tactile examination. The anæsthetist had not appreciated this risk, but, judged by the standard of medical knowledge to be imputed to competent anæsthetists in the year 1947, the anæsthetist was not negligent in failing to appreciate the risk; a fortiori the theatre staff were not negligent. The Court of Appeal accepted and adopted this view; and so, however sympathetic everyone must feel to the plaintiffs, the claim for damages failed. In Lord Justice Denning's words which we have already quoted, "we must not condemn as negligence that which is only a misadventure."

Injury during Removal of Plaster

IN Sunderland County Court,⁷ a 65-year-old man was recently awarded £60 damages for a 14-inch cut inflicted by the shears when a male staff-nurse removed a plaster cast from his leg. The man had to have 28 stitches in his leg and was kept in hospital another three weeks. In his evidence, the senior orthopaedic surgeon at the hospital described the staff-nurse, who had won a merit award since the accident, as an extremely conscientious worker, and he thought he had been unfortunate in dealing with a patient who did not say he was being cut; there must have been some diminution of sensation. Lord Uvedale, resident surgeon at Manor House Hospital, to which the patient was subsequently admitted, said he had never before seen such an injury from plaster removal.

The judge said it was not a case in which the hospital had to be punished for injuring the patient, but a matter of compensation. He had come to the conclusion that the patient had not felt the pain normally and that the sensitivity of the skin was diminished because the plaster had been on for 6 months. The staff-nurse had not carried out the removal with his customary skill.

Death from Anti-tetanus Serum

A verdict of misadventure was returned at an inquest at Southwark⁸ on a girl machinist who had died soon after a small test injection of anti-tetanus serum. She had run a needle into a finger at work and it became infected. When she attended St. Olave's Hospital, Rotherhithe, the surgeon ordered her to have anti-tetanus serum, and in preparation for this a test dose was injected by a nurse into the girl's leg. She became unconscious, had convulsions, and died despite artificial respiration and injection of "heart stimulants." Dr. F. E. Camps, the Home Office pathologist, said that a section cut through the injection site showed that the needle had entered a small vein so that the serum was injected straight into the blood-stream.

1. Taylor, S. *Lancet*, 1952, i, 253.
2. Wofindon, R. C., Parry, R. H. *Ibid.*, p. 1297.
3. *Ibid.*, 1952, ii, 931.
4. *Ibid.*, p. 772.
5. *Ibid.*, 1953, i, 1039.
6. *Times*, April 9, 1954.

7. *Yorkshire Post*, April 2, 1954.
8. *South London Press*. April 6.

Special Articles

DIFFERENTIAL DIAGNOSIS AN APPARATUS TO ASSIST THE LOGICAL FACULTIES

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THERE are at least three ways in which one learns medicine: from first-hand experience at the bedside, from spoken and written accounts by others of individual cases they have seen, and from written generalised accounts of many similar illnesses grouped into what we call diseases. The student has two tasks: he must learn the symptoms and signs of all the important diseases, and he may also try to learn all the diseases that cause each particular symptom. The former task is usually better done than the latter. To help him to learn about diseases he has the descriptions given in the "straight" textbooks, while to help him to learn (or look up) the diseases that cause particular symptoms there are books which give the differential diagnosis of separate main symptoms.

THE MECHANISM OF DIAGNOSIS

What happens in the doctor's mind when he is faced with a patient? This will depend on his experience, on his book knowledge, and on his mental endowment; but the diagnosis will be made in one or all of the following ways.

(1) The patient's story and the results of physical examination may bring into action the subconscious process of immediate recognition of the disease. The diagnosis here is made in the same way as we "diagnose" the identity of our friends—i.e., without conscious formulation of reasons but with a high degree of confidence and accuracy. This capacity for recognition diagnosis is the invaluable possession of the doctor who has had much experience in practice and has profited by it.

(2) The doctor may recall descriptions from books or from memories of practice of several diseases that might fit the patient's story. This process of recalling to consciousness the diseases that enter the differential diagnosis is not usually a logical effort but relies on the storehouse of the memory to "throw up" several likenesses to the present patient. That it is far from being the infallible result of an act of volition is suggested by the experience that more things are missed through not being thought of, and so not looked for, than through not being known. The doctor will try to hold in his mind's eye the descriptions of the diseases he has "thought" suitable for consideration in his differential diagnosis, and to see which best fits the patient's case as he has elicited it. In no case will his patient have *all* the described symptoms of any of the textbook diseases, because they are collective descriptions. The individual case presents usually but a tattered fragment of the full-blown composite picture of the disease described in the textbook.

This task of assessing the significance of all the patient's symptoms together and relating them to a disease is extremely difficult. Theoretically the doctor could go through the descriptions of diseases in his straight textbook—i.e., review it from cover to cover to find the description that most nearly fits his patient. But in practice one cannot re-read a textbook for each patient.

(3) The doctor may take a main or significant symptom or sign, and, using it as an intellectual straw to cling to, or start from, in a sea of memories and observations, he may review the diseases that could cause it. He may do this for several of the patient's symptoms in turn, perhaps using a book on the differential diagnosis of main symptoms to help him. If he uses a book like French's *Index* he will find his fingers in different pages on which are given lists of causes of those of his patient's symptoms he tries to look up. To find the disease names that occur every time under each separate symptom as shown in different parts of the book may be far from easy, even with pencil and paper to hand. To hold the several lists

of possible causes of each of the patient's different symptoms and signs in mind at once and logically to select those causes that best explain—i.e., are common to—the largest number of his symptoms is beyond the capacity of most minds.

However differential diagnosis is approached, our literary tools will not enable us to recall without fail all the diseases that could be the causes of the symptoms and signs, taken together, of each particular patient. The inadequacy of these tools is inherent in the structure of the page as the unit holder of data, owing to its rigidity—i.e., its inability to present the relevant data in the order or pattern that may be required. What is needed is a device which will answer the question "What are the possible causes of the group of symptoms and signs I have elicited from my patient?" Theoretically a giant table containing hundreds of vertical columns of symptoms and signs and hundreds of horizontal rows of diseases would suffice, but such a table would be as big as the wall of a room and far too unwieldy for practical use.

The reason why no such device has been found is that the only commonly used fact-holder has been the book or a card, both of which hold the facts as symbols on a page. The continuous use of the page for thousands of years makes it unnecessary to speak of its advantages for recording. Yet we may conceive that the book, and particularly its unit the page or card, may not be the ultimate form of record. Though some of the defects of the bound book are obviated by the loose-leaf ledger or card system, even cards have the limitations inherent in their structure. In narrative records side-by-side comparison of groups of data is impossible, and the table on a single page or folding sheet is a sign that a vague want is felt for devices to display any required relationships. Unfortunately if one makes a table big enough to include as much data as would occupy a whole book of narrative type, the thing becomes utterly unmanageable. For any particular problem we have in mind, the table is cluttered with irrelevant data that obscure the data and their relationships that we are trying to trace.

Apparatus

The solution offered here is a mechanical table with hundreds of removable columns which allow the manipulation at will of any chosen groups of qualitative data. It is a supplement to books and a mechanical aid to certain types of logical thinking.

The device consists of a frame to one side of which is fixed a category reference index. In the index the categories (in this instance diseases) are listed one beneath the other (in the prototype in alphabetical order). A space is provided in the frame into which fit a number (8 in the prototype) of detachable members of strip form which are inserted with their longitudinal axes parallel to the category reference index. Each detachable member carries a reference to the symptom or other attribute concerned—e.g., haemoptysis—and on its exposed surface is graduated (or written on) at right angles to its longitudinal axis in all those places which (when the member is in position in the frame) align with a category (disease) in the index in which the symptom the strip represents is known to occur. There may be hundreds of detachable strip members which are conveniently stored in a separate index ready for use when wanted. They can each represent any chosen single attributes—e.g., symptoms, signs, age-incidence, and sex-incidence of diseases.

The prototype contains about 300 diseases. This list when typed is about 4 ft. 3 in. long. By photographic reduction this was made into a scale about 2 ft. 3 in. long. The scale can be reduced still more, so that the list of 300 diseases is only 18 in. long. The symptom members are made of obeche wood (*Triplochiton scleroxylon*). In the diagram the symptom members are numbered, but in practice it is preferable for the name of the symptom to be printed on each one.

To obtain classification of a number of attributes to a particular category or categories, the appropriate members are taken out of the store and inserted one beside the other in the frame. It will then be seen that each symptom has its own spectrum or pattern of causation. It will be also seen that in some places two or more of the spectral lines lie adjacently against the same disease, with the result that on the apparatus it looks as if a single straight horizontal line has been drawn across several or all of the symptom units opposite that disease. Our patient's disease must be one of these diseases that would account for all or most of his symptoms. These can be seen literally at a glance. One can also see at once which disease would explain some of his symptoms but not others. Roughly, the diseases with the longest horizontal composite lines against them will be those we should consider as possible diagnoses in our particular patient whose symptoms we earlier fitted into the machine. Such a preliminary review of the range of diagnostic possibilities and probabilities could precede and to some extent guide the physical examination and investigations. However, if desired, sign strips or units can be made on the same principles as the symptom strips and the whole case can be put into the machine for analysis and consideration. Although in the prototype the spectral lines have been used, it would be possible to use adjectives, figures, or other symbols instead—e.g., on the cough unit bar, instead of a simple linear spectrum,

one could have adjectives such as brassy, gander, and stridulous, in the appropriate places—i.e., opposite diseases to which they are applicable. It is intriguing to find how many causes the apparatus can suggest for one or two of a patient's symptoms or signs, and how, as more and more of the patient's symptoms are inserted, the range of possibilities rapidly narrows.

Discussion

What does the apparatus described do? It tells us what diseases could account for any particular group of symptoms we care to put into the machine. Its programme of symptoms and signs is potentially as great as the repertoire we decide to give it. A book will not arrange data in the way required for the solution of particular individual problems, and for this reason the man who merely knows the books by heart cannot apply the knowledge he has to particular problems. His associational ability to extract and associate information from different parts of the book is of a low order.

Limitations of Apparatus

The machine can only suggest which diseases a particular patient may have, and so give the doctor some jumping-off points in thought from which he can go on to consider the most likely diagnosis or what further observations he needs to help clarify the issue. The apparatus will also indicate some points against certain diagnoses that may have spontaneously occurred to the observer. It is not a substitute for any of the human faculties needed in the difficult art of differential diagnosis. All it can do is to assist, and so perhaps improve on, the workings of the unaided ordinary mind in certain parts only of the process of diagnosis. Any diagnostic aid, whether book, list, or other device, can never be the sort where one puts in a penny and out comes the diagnosis, because no apparatus will ever be able to take a proper history, examine the patient intelligently, and possess clinical judgment.

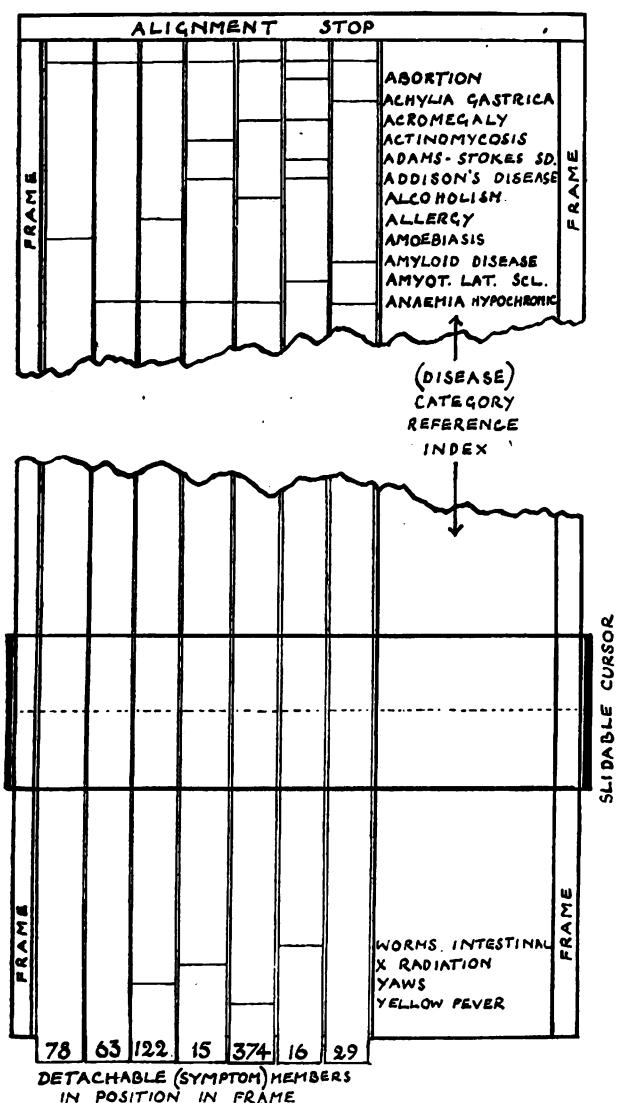
Logically the apparatus can be said to have the purpose of stating the inclusion or exclusion of classes in reference to one another, especially in demonstrating the relationships of overlapping classes. Thus, when we say "This patient has a cough" we could be considered logically to be saying "This patient is a member of the class of all coughers." The "class of all coughers" will be distributed among many groups of ill people who have the different diseases of which cough forms a part. Other classes of persons with other symptoms will overlap the class of all coughers in so far as they occur in the same diseases as cough. To put the matter more traditionally, the symptom strips represent grouped data about certain qualities, attributes, or characteristics of the diseases or other entities listed in the reference category index.

Summary

Books and card indexes have shortcomings inherent in their unit, which is the page. When we use them as fact-holders they impose on us rigidity in the arrangement of data.

A physical aid to thinking, which may be called the group fact manipulator or associator, is described.

The apparatus allows the free manipulation at will of prefabricated groups of data for the solution of classificatory problems in medicine and other subjects. If the symptoms of a particular patient are put into the device, it will indicate at a glance the range of differential diagnostic possibilities. It is a supplementary aid and in no way a substitute for books, knowledge, experience, or clinical judgment. Like any tool it can be misused; but time may give it a useful, though limited, place in teaching and practice.



REMPLOY

FROM A CORRESPONDENT

No other industrial concern has quite so curious a problem to solve as Remploy Ltd.; or is more exposed to political cross-fire. Cannon to right of them, cannon to left of them, fairly describes the situation. On the one hand are those who say that Remploy factories should be purely a social service for the severely disabled, giving them somewhere to work and to feel they are earning a living. On the other are those who think that the country cannot afford sentimental luxuries, that it is cheaper to support these men and women in idleness on public-assistance funds, and that anyhow with proper management Remploy factories could be made to pay their way.

If Remploy factories could in fact be made to pay their way, of course, most of their critics would be silenced. Most of them, however, run at a loss, anyhow on paper; and according to industrial experts they always will, though the degree of loss may be reduced in time. Partly because these severely disabled people tire easily, partly because they are more often away sick than healthy workers, and partly because it has not always been possible, so far, to keep them supplied with steady runs of work, they have not been able to achieve and maintain more than a third of the output of workers in ordinary industry. The overhead costs of running a factory, however, go on all the time, whether the employees are working fast, slowly, or not at all. That is the crude financial problem—though only one aspect of it. There are others, and there are many other sides to Remploy; so we should look more closely at what they are doing, what they have done already, and what they hope to do, before assessing even the financial loss or gain.

RAPID EXPANSION

Remploy Ltd. was formed in 1945, under the Disabled Persons (Employment) Act, 1944, as a public corporation financed by Treasury funds, to provide employment for people on section II of the Disabled Persons Register—that is, for people so severely disabled that they are unable to work under ordinary industrial conditions. It has thus no choice about the type of person it employs.

In the nine years since it was founded Remploy has opened 90 factories; indeed all 90 were in action within seven years of the start. It has been much criticised for forging ahead so fast, instead of proceeding more cautiously and learning by experience; but it had no choice. The pressure on it—from Ministries, local authorities, and the public—was so great that it was obliged to set up factories much faster than it wished, or thought advisable. Between March, 1949, and March, 1950, for instance, it set up 26 factories.

There are at present some 6000 people employed by Remploy. The number of disabled on section II of the register who were still unemployed in January, 1954, was 5592; so the factories have not yet absorbed all the available labour from their pool. Some of these disabled unemployed, however, are doubtless unemployable; some live too far from the factories; and some will not be fit for factory work, though they may be able to do work at home. Remploy has already begun to organise homework schemes on a small scale, and is so far employing 137 people in this way.

The disabilities of Remploy workers include those due to injuries and amputations, congenital malformations, arthritis, diseases of the digestive and genito-urinary systems, diseases of the heart, circulatory system, and lungs (including pulmonary tuberculosis), skin diseases, ear and eye defects, organic diseases of the nervous system (including epilepsy, disseminated sclerosis, and poliomyelitis), mental defect, neurosis and psychoneurosis, and many others.

The average age of the workers is high compared with that of workers in ordinary factories, for most of them have tried and failed to make a living in open industry, many have been unemployed for years before entering the service of Remploy, and some have never worked before.

An analysis made in November, 1952, showed that 64% of the men were over 40, and 42% were over 50; more than a quarter were over 55. The women were relatively younger—only 26% of them being over 40, and only 10% over 50; but only about 350 women are employed.

On entry, most of the workers are quite unskilled in the trades Remploy has to offer them, and they have to be trained. Again, many of them have psychological difficulties associated with their disability, or with long unemployment. Moreover, idleness—as anyone who has been obliged to try it for any length of time well knows—corrupts the will to work. Again, when Remploy started, its workers were not entering long-established factories with a team spirit and a social life of their own; these things have had to be built up gradually. To begin from scratch, with employees who know nothing of each other, or of the work, is never an easy task; and the disabled, being as human as the rest of us, have among them old-soldier types who will do as little as they can for the money, and sea-lawyers who can air a minor grievance with a wealth of rhetoric. The number of such characters varies with the place in which the factory is set: some areas breed tougher types than others. Fortunately most of the workers in any of the factories are glad to find themselves in productive work again, and taking home a pay packet instead of collecting an allowance.

MATERIALS AND MARKETS

The problems in management which the workers present are at least equalled by the practical and industrial problems which Remploy has to solve. Thus it has to provide its factories where the disabled are chiefly grouped, not where the demands of industry could best be served. In some places it has been possible to take over Government premises, or to rent a factory; but quite often Remploy was obliged to build, and this has been expensive. The goods to be made have to be within the compass of the workers, not too tiring or heavy to handle, not exposing sick people to extra industrial risks (such as dust risks), and not likely to cause annoyance to any section of open industry by cutting across its lines of production. Remploy tries never to undercut the market price: its goods are sold at commercial rates, and sell on their merits. Materials have to be available in sufficient quantity; and steady markets are needed so that there shall be no "waiting time" in the factories. Morale is a delicate plant of slow growth, easily struck down, and the man who comes to the factory and does nothing for days on end may reasonably suppose that he is living on the nation's charity. He may also feel that when the next job comes along he had better spin it out. Both ideas hinder production.

With so many answers to find it is small wonder that Remploy has not always found the right ones. Its greatest difficulty has been in securing long runs and continuity of production.

Knitwear has proved a great success in these ways, and one at least of the group of six factories doing this kind of work has shown a profit. Cardboard-box making is also relatively successful, though here delays in getting some kinds of appropriate material have proved troublesome. Light engineering, and electrical assembly work, have in these days permanently good markets; and the "preservation, identification, and packing" (P.I.P.) of other manufacturers' goods for transport or export also provides steady work. There is a limited demand for such things as school and hotel furniture and bedroom suites; and surgical footwear and appliances are slow and expensive to make (whoever makes them). Other trades offered by Remploy include mattress-

making, printing and bookbinding repairs, strapmaking, textile sewing, the making of equipment for the Forces, and brush-making.

WORKERS ON PRODUCTION

One difficulty in the London area is to find suitable factories. The following brief account of three of them gives some idea of the degree to which Remploy has overcome its difficulties.

I
The first, set in an industrial estate in a busy London suburb, is in an old factory, rented for this purpose, and not fully suited to its task: the windows are not large enough and the lighting system—by modern standards—is poor; but it is roomy and warm. It employs about 90 men in making orthopaedic footwear, callipers, tripod walking-sticks, crutches, 'Polythene' splints, and luggage straps. Their average age is 46. Their work was beautifully finished (this was true of all the work seen in Remploy factories), and in particular the orthopaedic footwear they were making was much lighter and more supple than that usually inflicted on the lame: many disabled patients know from experience where the orthopaedic boot pinches—or rather, how much it can weigh.

Great difficulty was experienced, at first, in getting the local hospitals to give this factory's work a trial. It was only when one hospital's supplier was snowed under with work that Remploy was given an order for a pair of shoes: the work was not only well done, but was done within a very few hours, and this hospital now always gives the factory a proportion of its orders for orthopaedic footwear. The men in the orthopaedic workshop were all cheerfully busy at the time of the visit, but some of those in the woodwork department were idle: orders had temporarily run out. It was evident that the men found this as unsatisfactory as the management—the difference in mood in the two workshops was noticeable.

II

The second factory, well to the east of London, in the dock area, takes about 110 men. No fewer than 18 of them are epileptics; and the medical officer of the factory—a general practitioner working part-time—remarked on the good effect of steady work on these patients. Many of them have lost job after job because of their fits. When they have had 3 or 4 fits on the factory premises without any attempt being made to get rid of them, they cheer up wonderfully, and as a rule their fit-rate falls considerably. This factory makes laminated furniture from wood veneers, turning out a great variety of pieces, from chairs and school furniture for the London County Council, to television tables. There are continuous markets for some of these goods (television tables seem to be a strong line at present). Others do not sell so freely, and some take long to make.

Much of the work requires a fair amount of active movement, or quite long periods of standing. Though none of the men questioned admitted to feeling tired, it seems likely that their output may have been slowed by fatigue. They have, however, a factory medical officer who is interested in methods of reducing fatigue, and ingenious in inventing devices for the purpose. They also have a good first-aid attendant, one of their own number who has been a bomb-disposal sergeant, whose concern for their well-being evidently gives them great confidence.

The men in this factory included some who were unstable, and at times inclined to violence. Remploy does not discharge workers because of troublesome behaviour except as a last resort, and after long months of trial and retrial; even then the discharge is made at the topmost level by the executive director. This ensures for the disabled the security they need; but it does not make any easier the task of management.

III

The third factory, in the suburb of a coastal city, employs only tuberculous disabled: Remploy has seven of these "special" factories scattered about the country. This one was built for its purpose, and while it is light, airy, and equipped with a good canteen (and a very good cook) it is short of storage space. It makes cardboard boxes, a commodity which cannot be compressed, and stacks of finished work stand about in every available corner, awaiting removal.

This factory, which will take 55, has 41 workers at present, 20 of them women. Most of the work is done sitting down, and it is neat skilled work, very suitable, it seems, for these people. Here again there is a good deal of machinery, but of course of a much lighter type, and more easily attended than that required in making furniture.

There was a cheerful pleasant atmosphere about the factory, where men and women were working together. They work hard and are keen on the job, but they tire towards the end of the day. Some attend the neighbouring hospital at intervals for pneumothorax refills or other treatment, and they are fatigued when they return. Most work full-time however; only 9 work half-time (four hours daily). The output here is better on the average than for many Remploy factories; and the manager hopes that as manual nimbleness improves, and as orders become continuous and steady, output will improve even more.

SOME FUTURE PROSPECTS

The managers of these three factories were of totally different types: what they had in common was an ability to get on with their workers, and a thorough knowledge of their own industries. They face at close quarters the problem which confronts Remploy as a whole: how to get each of their workers to contribute as much as he can without driving him to do more than he should. Remploy was established for the good of these disabled people, not to make a profit, so the managers probably err on the side of caution. One reasonable way of encouraging a man to do his best is to offer him a bonus on his output; and a bonus system has been introduced into one factory, making mattresses, with good success in stepping up production. But it would not do to introduce a bonus system in a factory which has much waiting time.

The first thing to ensure, then, is that Remploy makes goods for which there is a constant demand. This was pointed out by the Select Committee on Estimates¹ in 1952. The committee also made some useful suggestions on the organisation of sales on a trade basis instead of a geographical basis; but Remploy already had this in mind, and it has now been done, with advantage. Remploy also now has a managing director as well as an executive director and a financial director. These and various other changes have made it possible for Sir Robert Burrows,² the chairman, to note in his annual report a reduction of £62,613 on the previous year's loss.

Nevertheless, the loss for the year was high—nearly £2,380,400—and Remploy has plans for reducing it next year. Some of the factories are to be turned over to work which can command steadier markets, such as the assembling of electrical equipment, knitwear, and the making of elements for steam irons (which promise to be very popular). The cardboard-box factories can supply the containers for such small objects, and the P.I.P. factories can pack and dispatch them. With such steady lines it will probably be possible to introduce bonus systems into more factories, and so encourage production. Moreover, every year Remploy workers become more skilled in their trades, and newcomers are now entering factories with a good team and social spirit. Homework schemes, too, will be extended, and these should bring good returns because there are few overhead charges. A central sales showroom is to be opened at Cricklewood, and the export trade, which has just begun, will be developed. All these measures should help to bring down costs.

COSTS

Remploy workers get three-quarters of a normal full-time wage, even though their output is only a third of normal. This rate has been agreed with the trade unions. At present, as Sir Robert Burrows put it, the cost to each of us of employing these 6000-odd disabled people is 11½d. per head per year. It seems little enough looked at in this way; and there are some hidden advantages we get for our subscription which we all ought to take into account. Thus by March, 1953, Remploy had already returned some 1435 people to open industry: it had acted, in fact, as an unofficial reablement service. Again, though it would cost less, on paper, to pay these workers

1. Training, Rehabilitation, and Resettlement. London: H.M. Stationery Office, 1952.
2. Remploy Ltd., Annual Report 1952-1953.

from public-assistance funds, that would not allow for additional costs in sickness benefit likely to be needed by disabled people out of work, with nothing but their ills and failure to think about. The country, moreover, benefits by purchase-tax on Remploy goods sold, and by income-tax from the workers—figures which do not appear in the balance-sheet. Finally, some of the costs which do appear are merely figures on paper: thus, if a factory belongs to the Government, and Remploy pays rent for it, has money done more than circulate through a closed channel? Such rentals, however, help—on paper—to swell the figure for Remploy's trading loss.

Experts seem agreed there must be some financial loss on this project. Against this must be set its value, in mental and physical health and in self-respect, to the individual disabled person. We are willing to help these people at some cost to ourselves, and though we might do it a little more cheaply in other ways, the financial saving might not be worth the waste of spirit.

AMERICAN COLLEGE OF PHYSICIANS

FROM A CORRESPONDENT IN THE U.S.A.

As president of the Royal College of Physicians of London, Sir Russell Brain was the guest of honour at the 53rd annual meeting of the American College of Physicians, held in Chicago from April 5 to 9. He spoke on Cervical Spondylosis and on Problems of Cerebro-vascular Disease, and he also lectured to the students and faculty of the University of Illinois College of Medicine. On less formal occasions he managed to astonish the few who still believe that "Britishers don't have a sense of humour."

The American College of Physicians was founded in 1915 by Dr. Kurt Stern and was patterned by him after the Royal College in London. Its fellows are selected from physicians in the United States, Alaska, Hawaii, Canada, Mexico, and the Caribbean Islands. The governing bodies consist of officers, regents, and governors. The officers and regents are an executive body and are chosen from former governors. Each governor represents the fellows of his State, province, or territory in North America, and, with governors from the United States Federal Services they number 67.

Election to fellowship in the American college usually comes after a three-year apprenticeship as an associate, and the fellowship is conferred each year by the president at the annual convocation.

Because the fellows are scattered over a continent and its islands, the headquarters in Philadelphia has never developed into a professional and social centre. To overcome the geographical problems, the American college holds small regional meetings and a large annual meeting in one of the important medical centres of North America. Here, each year, fellows, wives, and families congregate for a week of lectures, clinical and television demonstrations, panel discussions, and clinicopathological conferences. Besides these offerings and visits to local medical schools and hospitals, the main business of the college is transacted and a social programme is organised for the fellows and their guests.

The most important function of the college is the annual convocation. This year the processional of the officers, regents, governors, newly elected fellows, and distinguished guests was led by the president, Dr. LeRoy Sloan, professor of medicine at the University of Illinois. He conferred fellowships on 200 new fellows and masterships on four fellows. He presented the John Phillips memorial medal to Dr. Donald Van Slyke for his many contributions to clinical chemistry, and the James D. Bruce memorial medal to Dr. David Marine for his work on endemic goitre. He then conferred honorary fellowships on Prof. U.S. von Euler, of Stockholm, and on Sir

Russell Brain. In conferring the latter Dr. Sloan spoke movingly of the close ties between the American and London colleges, and he indicated that these bonds were to be further strengthened. At the end of the ceremony, Sir Russell Brain asked for the floor, and presented a gift from the Royal College of Physicians. This was a replica of the caduceus presented in 1540 by John Caius and carried ever since by the presidents of the Royal College. This was, Sir Russell believed, the first time that a president of the Royal College of Physicians had ever carried out official duties in the United States, and he was delighted to be at the convocation and to deliver in person the following message:

"We, the President and Fellows of the Royal College of Physicians of London, meeting in Comitia on January 28th, 1954, send by the hand of our President greetings to the American College of Physicians. Our two Colleges are united by a common tradition in medicine and by the constant interchange of new knowledge. We welcome this opportunity for strengthening the ties of friendship which already exist between many physicians in our two countries, and we offer to our sister College every good wish for her continued prosperity."

This message and the gift of the caduceus were greeted with obvious pleasure by the members of the American college; and when the processional withdrew from the convocation hall we noticed that Dr. LeRoy Sloan was carrying the caduceus in his hand. It is to be hoped that future presidents will carry on the tradition he has started.

PAY OF CIVIL SERVICE DOCTORS

THE pay of three grades of medical officer in the Civil Service has now been revised, and the new scales are to operate retrospectively from Jan. 1, 1952. They are:

Grade	Age	(basic pay plus addition)		Salary Scales
		Old scale	New scale	
Basic grade	35 ..	1331 5 0	..	1500
	36 ..	1382 10 0	..	1575
	37 ..	1433 15 0	..	1650
	38 ..	1485 0 0	..	1725
	39 ..	1536 5 0	..	1800
	40 ..	1600 0 0	..	1900
Senior medical officer	41 ..	1675 0 0	..	2000
	42 ..	1750 0 0	..	2100
	43 ..	1825 0 0	..	2200
Principal medical officer	..	\$1900 × 100 - \$2100	2200
		\$2250	2300

The negotiations which have led to this conclusion have been carried out by the Civil Service Medical Officers Joint Committee, composed as follows:

Dr. A. J. OWSTON (chairman); Dr. E. A. GREGG, Dr. A. MACRAE, Dr. D. P. STEVENSON, and Dr. H. K. COWAN (British Medical Association); Dr. N. R. BEATTIE, Dr. A. F. ALFORD, and Dr. E. MARTIN (Ministry of Health Medical Staff Association); and Dr. A. I. G. MC LAUGHLIN, Dr. J. H. MURDOCH, Dr. A. B. WALKER, Mr. STANLEY MAYNE (secretary), and Mr. T. H. PROFITT (Institution of Professional Civil Servants). As from the beginning of this year, the Ministry of Health Staff Association has brought its membership within that of the Institution of Professional Civil Servants.

The new scales are provisional in that both the committee and the Treasury remain free to put different proposals before the Royal Commission on the Civil Service. "This particularly applies to the rates of pay for senior and principal medical officers the increases in which both sides regard as purely token." Neither the recent increases in the salaries of hospital doctors nor any other change in the remuneration of medical work outside the Civil Service will be made the basis of a claim to the Treasury before the Royal Commission's report is published; but this in no way limits either party's freedom to use any such factors in its submissions to the Royal Commission, or to use any other new considerations in fresh representations either before or after the Royal Commission has reported.

The scale now agreed for the basic grade is not to be regarded as establishing any particular relativity between that grade and any non-medical grade in the Civil Service.

In England Now

A Running Commentary by Peripatetic Correspondents

ONE of the pleasures of Professor Aird's film on the *Conjoined Twins of Kano* lay in following the investigations which established, before operation, which structures did and which did not connect the infants. Simple palpation was most important, but radiological, electrocardiographic, and radioactive isotopic methods also provided essential information. As a physician, I may say that I think that surgeons often have a lot to teach us in the use of direct, intelligent step-by-step elucidation of clinical problems. But surgeons have no monopoly. The morning after I saw the film I went to the garage in my car, which was making a new noise, like water running into a deep cistern. Not very loud, but I feared what it might portend, and like a mother with her child I wanted reassurance. Nevertheless I behaved correctly and consulted the vehicle's usual attendant, although I knew his liking for gloomy prognosis. He listened. "Specialist job," he said.

The specialist was of middle age and below medium height, clothed in an immaculate white gown like those worn by some doctors in hospitals in France. He asked me what was the matter. "It's the noise," I said, "transmission, I think." He listened there and here. "Probably magneto or water pump. Can you spare five minutes?" "Well, yes, but I can't spare half an hour. I have to go to hospital." "When we say five minutes we mean only six," he replied with a smile—a model for every consultant who wishes to temper authority with humour.

Two assistants in brown overalls arrived, towels were draped over the mudguard and in no time the fan-belt was off. I started the engine, the noise had gone. "Yes, magneto or water-pump. Joe, would you mind fetching the stethoscope? The telescopic one as well as the other. Thank you so much. And Bill, would you put the fan-belt on again?" The monaural telescopic and the binaural ordinary one arrived. The ear-pieces of the latter looked just like mine, except that the nickel plate was not flaking off and the rubber tubing was clean. The chest-piece, if I may so call it, bore a narrow metal rod about six inches long. The specialist applied its tip here and there systematically, with the engine running. "Yes," he said, removing the stethoscope, "water-pump. Now we'll order the replacement and you bring her in on Monday."

I should not push the surgical analogy too far, but I must admit that I paid no fee for the consultation and expect a whopping bill for the operation.

* * *

It is all very well for you, Sir, to affirm editorially that "enteric infections due to bathing beyond reasonable doubt are few," but you have not attempted to answer the really ticklish question of when a bather can be said to have bathed beyond reasonable doubt. Any wretched member of the party who gets up early may appear before breakfast looking virtuous and wringing out a wet bathing suit for all to see, but such evidence is obviously suspect. Unfortunately no-one has really ever defined the borderline between paddling and bathing. I would put the line at the pubis. The shock I get when the first wave splashes my perineum is something quite distinct from paddling, but if one retreats at this stage I'm afraid there is still reasonable doubt about the bathe. Some would accept a wet abdomen; others demand a wet neck or even wet hair; but no doubt, allowing for enteric, the editorial criterion would demand total immersion with a good swallow of sea water.

* * *

I often breathe a sigh of relief that Jim Dale and his partner seem to cope so effectively with the ailments of Parkwood Hill; Mrs. Mountford would be off my list after the first quarter. I should hate to be called in to attend the Huggetts, and if the Archers lived a bit nearer they would find me very short-tempered with Philip at times. But no practice can thrive on such a negative philosophy, so there are now seven new names on my list since the cards for the Grove Family arrived this month.

You know how it is when you take on a new family; you tend to make a snap judgment of their relative nuisance values to the practice. The Grove household shows all the signs of being another matriarchy, with weekly anarchical fugues, so the prognosis seems likely to follow the basic patterns of petticoat rule. Grandma's autocratic hold is getting shaky and it obviously won't be long before I am digging the Authorised Officer out of bed to cope with the old girl's senile dementia. Mrs. Grove is shaping up pretty fast to take on Grandma's crown while it is still warm.

Both Mr. and Mrs. Grove carry enough middle-aged spread to make constant demands for 'Dexedrine' a dead cert within the next six months, and I suspect that Mrs. G. is going to be rather tiresome to steer through her looming menopause on account of the psychosomatic factors in the household.

Mr. Grove suffers from the initial disability of not being master in his own house, and if I can manage to sustain him from anxiety neurosis I rather fear that he will throw a duodenal ulcer on us.

On the whole I feel confident that I can grapple with the more mature members of the Grove Family, but the kids would make any G.P. wonder if they are worth their capitulations. That scrounger Jack reminds me of my Service days; M and D for you, my lad! And let's hope that the Army knocks a bit of sense into you where your father has obviously failed. Pat is going to be hard to convince that a lot more early nights and a lot more protein in her lunches would be better than burning the candle at both ends. I won't be able to do much for her shallow mind, but I really would like to keep tubercle out of her apices until the penny drops and she settles down. Daphne is my main hope despite her tender years. I think I shall have to take her into consultation to get the low-down on the rest of the family. And then there is Lennie—the sooner we ship him and his behaviour problems off to the nearest child-guidance clinic the better, otherwise the poor tax-payer will have to find another £6 10s. a week to keep him in an approved school.

Well, there they are, seven little cards beaming at the kindly executive council, seven more wrinkles to furrow a practitioner's weary brow, seven more peripheral grey hairs. Look in and see for yourself the wealth of clinical material while I try and find an easier way of earning a living.

* * *

The other evening, on my return home from work, late and exhausted, my wife said: "You know, doctors are paid too much." I digested this awhile, and after due thought replied: "I think you mean that teachers are not paid as much as they should be?" "Exactly."

Ruminating upon my correct interpretation of her remark I came to the conclusion that she probably needed a new evening dress. To confirm the diagnosis, I remarked: "By the way, you know it's three years since I had a new suit? Do you think I can go on much longer in this one?" "Well, you are whole-time, and you're an S.H.M.O. . . ." I accepted both rebukes, and at that moment the B.B.C. announced the magnificent award to hospital staff. "There you are," says she, "you'll get at least £50 more: surely you aren't so mean as all that?"

During the past week she has ordered: (1) a new car at £550; (2) an evening dress at £31 10s.; (3) an alteration to her fur coat at "approx. £28"; (4) a new shirt for me at £3 3s.

* * *

My assistant and I bent over the foul-smelling post-mortem. The surgical registrar who was looking on fished his pipe out of his pocket and lit it. But presently it was too much even for him and he walked out. As the door closed behind his back, my assistant heaved a great sigh of relief. "Thank goodness," he said, "that fellow has taken his pipe away."

* * *

Clinician: Why are you looking at those skin biopsies?
Pathologist: I'm trying to sex them by this new-fangled idea of studying the nuclear chromatin.
Clinician: Then you will issue a Skinsey report I suppose?

Letters to the Editor

TUBERCULOSIS IN ADOLESCENCE

SIR.—The recent Ministry of Health circular,¹ to which you refer in your leader of April 17, calls for action.

Some may think that we have hardly reached the point when tuberculosis can be dealt with on epidemiological lines like smallpox or typhoid fever; but all will agree that new and greater effort is called for in many branches of our anti-tuberculosis organisation. A vigorous drive is certainly needed to diagnose the disease more often in its earliest stages.

I have been impressed, in recent years, by the finding of adult-type disease in school-children who happen to have been examined by mass radiography. The disease in adolescence has a strong tendency towards inevitable deterioration if energetic measures are not taken. If the disease in young people is not dealt with at an early stage, treatment will, in most cases, be demanded in later years when the chances of success may be much reduced.

Among 14-year-olds mass radiography reveals 1.1 new cases of active tuberculosis per 1000 boys and 1.7 per 1000 girls,² but the method has so far only been applied in a patchy way. Has not the time arrived to extend the use of mass radiography in young people towards the end of their school careers? Such a proposal is hardly new, for a scheme of this sort was advanced in 1936 by Wingfield and Macpherson.³

Another recent Ministry circular,⁴ which gives local authorities powers to inoculate 13-year-olds with B.C.G. vaccine, points the way. Local authorities who implement the new scheme will find that approximately 40% of children have already been infected with tuberculosis. It is very much to be hoped that these children will be promptly radiographed, for it is certain that they will provide a useful harvest of early cases of pulmonary tuberculosis, many of adult type. Obviously, all the cases which may be revealed by mass radiography will be in this 40% who are already tuberculin reactors. It is likely that, taking one year of age only (say, 13 or 14), a single careful examination would bring to light 18 new cases of active tuberculosis in every million of the population (approximately 13,000 children at, say, 1.4 per thousand); and it would only be necessary to radiograph approximately 5000—the 40% known reactors. It is to be hoped that local authorities and regional hospital boards will consider what this would mean in their own areas and decide that it is both practicable and worth while.

Pulmonary tuberculosis of adult type in young people has, in the past, generally been so scattered that few can claim much experience with this age-group. My colleagues and I have recently reported⁵ on 116 such cases treated in a sanatorium for long periods and subsequently followed up for an average of over six years. Collapse therapy was used extensively, but antibiotics were not yet available. Selected cases did well with an artificial pneumothorax, but the over-all results left much to be desired. Long-term investigation of a more recent series would probably show greater improvement with modern chemotherapy. So far, however, there can be no final decision on the most effective therapy. Many adolescents will certainly require sanatorium treatment, perhaps combined with antibiotics and collapse or resection. Treatment should be undertaken only in

centres where adequate education can be given. Possibly some youngsters may be allowed to continue, under expert supervision, at ordinary schools. Special registers of these cases should, in any event, be compiled in appropriate areas so that they can be followed up in groups large enough for helpful analysis. In this way knowledge would be gained not only of the disease in school-children, but of its often insidious development in young adults.

High Wood Hospital for Children,
Brentwood, Essex.

F. J. BENTLEY.

SPREAD OF INFLUENZA IN THE HOUSEHOLD

SIR.—The paper from Cirencester by Dr. Hope Simpson and Dr. Sutherland in your issue of April 3 is a most interesting example of the information which can be gathered by careful observations on that fundamental epidemiological unit—the family or household. The success of timing of the occurrence of cases of an infectious illness as a means of proof of the mode of contagion must, however, depend upon the accuracy of the recognition of each infection. The latter, in turn, calls for a recognisable clinical phenomenon as an accompaniment of infection, or else must be based upon laboratory findings.

Diseases such as measles, which exhibit characteristic rashes, thus afford good material for analysis, and it is hardly surprising that the actual occurrence of cases in the family agrees so well with the predicted numbers based upon a person-to-person chain of infection.

Similar observation on cases of influenza is handicapped in two ways: firstly, by the occurrence of other febrile respiratory diseases resembling influenza but not due to the influenza viruses; and, secondly, by the known frequency of subclinical infection as a result of exposure to influenza viruses. The first difficulty would be likely to obscure the findings by inflation of the figures for the number of cases in the household, whereas the second one might prevent the expected wave of secondary cases because of the exhaustion of susceptibles by this mode of infection. Whether or not these arguments are valid as an explanation of the irregularity of the influenza data presented by Dr. Hope Simpson and Dr. Sutherland, it would seem necessary to urge the need for laboratory confirmation of the occurrence of infection in future studies of this kind. Nevertheless, the variable pattern of behaviour of influenza, as judged on a purely clinical basis such as the authors describe, is in keeping with the variable epidemiological pattern seen in the community as a whole, and also, may it be added, with the remarkable variability of the characters of the causative viruses and of the still-undefined human properties of susceptibility or resistance to their attack.

University Department of Medicine,
The Royal Hospital,
Sheffield, 1.

C. H. STUART-HARRIS.

TREATMENT OF VARICOSE ULCERS

SIR.—I would like to support Mr. Murley (April 10) in his criticisms of some of Mr. Lee's suggestions (April 3) for the treatment of "varicose" ulceration. Arterial spasm plays a very small part in the causation of the vast majority of varicose ulcers, a fact which was well demonstrated by Brewer¹ of Liverpool. In his series he proved by arteriovenograms that the ulcer which was due to arterial spasm was rare. It is in this small group that sympathectomy, or the alternative of injection of the femoral artery with tolazoline, might possibly give some benefit. It is to be hoped, however, that Mr. Lee will confine sympathectomy and injection of the femoral artery to this rare group and that the remainder will receive the accepted treatment, whose benefits we all understand so well.

1. Brewer, A. C. *Lancet*, 1951, II, 177.

1. Prevention of Tuberculosis. Circular H.M.(54)30.
2. Report of the Ministry of Health, 1952.
3. Wingfield, R. C., Macpherson, A. M. C. *Brompton Hosp. Rep.* 1936, 5.
4. Circular 324/B.C.G., 1953.
5. Bentley, F. J., Grzybowski, S., Benjamin, B. *Tuberculosis in Childhood and Adolescence*. London, 1954.

Compression treatment is the sheet anchor in the treatment of varicose ulceration. This fact has been shown to us throughout the ages, especially by Thomas Baynton in the eighteenth and Benjamin Brodie in the nineteenth centuries. Recently we have to thank Bisgaard for calling our attention to the immense value of physiotherapy, and Cockett and Elgan Jones² for simplifying what they term so aptly "the ankle blow-out syndrome." The skill in healing thrombotic ulcers lies in the correct timing of when to use these three cardinal factors in treatment. As a rule, compression will give us a slim and healed limb; massage will then still further improve the leg; and finally the removal of the "short-circuited circulation" above and around the ankle will complete the treatment, even though in certain cases a changed "way of life" may be required.

London, W.1.

R. ROWDEN FOOTE.

REMUNERATION OF HOSPITAL MEDICAL STAFF

SIR.—I have been wondering why I am pleased with the recent award of pay increases to hospital medical staff, while so many of my colleagues feel that it is not enough. I have now realised that when I became a tuberculosis officer in 1941 my income was £600–800 per annum, and now, though graded S.H.M.O., it will be £1500–1950—a betterment factor of 150%. There must be others with a similar experience.

Clearly, some redistribution of income within the profession has been taking place, and viewed dispassionately this would not seem to be a bad thing. The justification for very large incomes for consultants in the past was surely in the lean years, during which their incomes varied from nothing as a houseman to the odd hundred or two as a registrar later on. The path has been made easier, though perhaps, as a result, the competition is now fiercer. Surely the demand for 100% increase for everybody is unrealistic and would only perpetuate the injustice to the lower-paid ranks. The negotiators have done well, in my opinion, to distribute the available sum where it will be most appreciated.

When we compare ourselves with the general practitioners, there is room for disappointment, especially as the hospital medical staff award is not retrospective to 1948. But again, as you say in your leader of April 10, future experience will show whether the correct balance will be found, and sufficient recruits attracted to all sides of the profession. The Cinderella of the health service now is Public Health, and every effort should be made to help our colleagues there in this just claim.

Liverpool, 18.

WILLIAM D. GRAY.

SIR.—The majority of S.H.M.O.s occupy posts carrying full clinical responsibility, and in fact work as consultants. We must have considerable value as "cheap labour" in the National Health Service. Unfortunately, we have little or no bargaining-power, and our posts could easily be filled by registrars in search of financial security. Could this be why we have received an increase in our rate of pay of 15·4% as against 23·5% for the consultants?

Queen Alexandra Hospital,
Cosham, Portsmouth.

A. M. READ.

SIR.—Surely we are all agreed that the award which junior hospital doctors have just received is ridiculously inadequate. It is neither retrospective nor untaxed, and bears no relation to the increase in the cost of living since 1948.

If this award goes unchallenged we shall probably receive another £75 or £100 in 1960! It is understandable that each section of the profession has its own economic interest at heart, but if these token awards are to be stopped, the B.M.A., in its proper rôle of a trade union,

2. Cockett, F. B., Elgan Jones, D. E. *Ibid*, 1953, 1, 17.

must press the claims of each section of the profession as a whole, and refuse piecemeal settlements, such as the Danckwerts award, which leave the claims of other sections of the profession unsettled.

Only when this happens will we be able to reject these awards, knowing we are in a strong enough position to do so.

Norwich.

J. M. BROWNIE.

SIR.—Now that salary increases for hospital medical staff and consultants have been finally agreed on, is it not high time National Service medical officers' pay was increased? Recent Service increases expressly omitted National Servicemen.

One reason that National Servicemen are not paid so much as their Regular contemporaries is to try to persuade some to apply for permanent commissions; but we, especially those who are married and trying to build up some sort of home, have to exist in comparative penury. There are no allowances in lieu of married quarters (no accommodation is provided for National Service medical officers) and the marriage allowance is less (two-thirds) than for Regulars.

At one time the rates of pay of house-officers and National Servicemen may have been adjudged to approximate (with the perquisites available to some house-officers the difference was greater), but now this can no longer be true, especially for any who held senior house-officer posts prior to call-up.

NATIONAL SERVICEMAN.

REPAIR OF LARGE HERNIA

SIR.—Your issue of Feb. 20, containing Professor Stock's account of the use of nylon mesh in the treatment of inguinal hernia, has just arrived.

"The use of implants of foreign material," he says, "is almost as old as the history of operations for hernia . . . but most attempts have failed because of undesirable tissue reactions and sepsis." Surely there is only one type of tissue reaction to the introduction of any sterile foreign material into the human body—an aseptic inflammatory response that may or may not proceed to pus formation irrespective of actual infection introduced at the time of operation. Indeed, the essence of all operations of this type is the induction of just this type of response, with the production of a strong fibrous wall which, it is hoped, will take the place of the weakened muscles in the posterior inguinal wall.

Perhaps the greatest weakness of all "implant" operations, applied to indirect inguinal hernia, is that they concentrate attention on the repair of the posterior inguinal wall, instead of on the re-creation of a functioning internal ring. But, as Ogilvie pointed out many years ago, in indirect hernia the primary site of weakness is not the posterior wall but rather the stretched, weakened internal ring. Professor Stock does not say how many of his "ten patients with inguinal hernia" actually had indirect hernia, but he implies that his operation may be used equally well for either direct or indirect. Surely there is a distinction to be made between the two.

He adds that "if the testis is abnormal or there is a thick hydrocele sac, orchidectomy is usually performed," which is a curious statement in this context. If an indirect hernia has reached such a stage that the internal ring and the posterior inguinal wall cannot be functionally re-formed, then the prospect has to be considered of complete closure of the canal, usually (though, as Aird points out, not necessarily) with orchidectomy. This, like all other forms of herniorrhaphy, does not guarantee against recurrence; and the patient, as well as the surgeon, must weigh the relative advantages which orchidectomy and complete closure of the canal offer. But in the treatment of hernia, it is the hernia that determines the necessity or otherwise of orchid-

ectomy, and not the state of the testis, let alone the state of the sac or tunica. To say that orchidectomy is usually done "if the testis is obviously abnormal" is surely irrelevant in this context: to say that it is usually done if "there is a thick hydrocele sac" is a little radical. When else would one do an orchidectomy for hydrocele?

Inexpensive, ubiquitous, malleable, and indestructible, nylon may be; and it is perhaps some comfort to know that when we have shuffled off our mortal soles the immortal uppers will still live on: but will they help my hernia?

Methodist Mission Hospital,
Ilesha, Nigeria.

H. J. WRIGHT.

IDENTIFICATION OF DRUGS

SIR.—We are interested in the letter from Dr. King, in your issue of April 10.

This company manufactures its tablets with an identification mark, and we issue, on request, details showing which marks coincide with which drugs. Furthermore, in our advertisements in the medical press, we often show a picture of the actual tablet so that doctors may become familiar with the marking on the tablet. We know that some other manufacturers adopt somewhat similar policies.

Bayer Products Ltd.,
London, W.C.2.

L. M. SPALTON
Director.

TREATMENT OF DEAFNESS

SIR.—In your issue of March 13, Mr. Robin warns the medical profession and its hard-of-hearing patients against "claims made for improved hearing by re-education methods."

It seems that he has, once again, confused the purely physical ability to hear with hearing in its broadest sense—namely, the ability of the cerebral cortex to interpret and respond to the auditory signals it receives from the ear in the course of daily hearing.

It is hard to say why Mr. Robin wishes to give your readers the impression that auditory training is said to improve the patient's physical ability to hear, when no such claim has been made. The very term implies that auditory re-education deals solely with cortical hearing. Obviously there is no simple, single, "scientific" test or measurement for a complex function which embraces a wide variety of auditory achievements such as recognition, discrimination, reaction-time, and memory for an endless variety of sounds received under dozens of different conditions, and which, in the hard-of-hearing, is further governed by fear, doubt, fatigue, lack of confidence, and even personality change.

Yet Mr. Robin demands that these aspects of hearing, and any change therein, be gauged by tests designed solely for gauging physical change in the peripheral auditory mechanism. Without such "scientific proof," he says, there can be no improvement in hearing, even though the patient's relations, associates, or employers state freely that it is very evident that the patient hears better. When confronted with such evidence, Mr. Robin mistakes cause for effect and seeks refuge in the suggestion that the patient's ability to "listen" has improved, even though we have painstakingly shown him that the improvement included sounds and conversations for which the patient could not possibly be listening.

As an aural surgeon, Mr. Robin must recall that the rather unscientific "social adequacy index" was adopted to assess hearing improvement in fenestrated cases, simply because pure tone and speech audiometry too often failed to portray the clinical results.

At this unit we assess improvement by what, in our opinion and long experience, is the most comprehensive way of depicting the results of auditory rehabilitation—the hearing disability questionnaire. This lists and indicates graphically the patient's stated ability before and after re-education for: conversation across a desk and a room, round a table, and in groups; speech and sounds other than speech (bells, buzzers, sounds from behind him, and from room to room); telephone, television, radio, confidential tones, whispered speech, and so on. Mr. Robin makes no mention of this in his letter. It might interest him to know, and to inquire why, the results of rehabilitation of the orthopaedically handicapped

are also assessed and recorded in such homely and "unscientific" terms as "turning over in bed," "combing and brushing the hair," "drinking from a glass," "walking up and down stairs," "striking a match," and so on.

The tone of his letter implies that auditory re-education is a worthless quackery whose "principle needs medical and scientific investigation before the practice is recognised as of true value," when in fact its use, both with and without hearing-aids, has long been practised in many of the most important auditory rehabilitation centres of the world.

Mr. Robin's motives are not to be questioned, but it is to be regretted that he has seen fit to voice his opinion publicly and dogmatically on the worth of a very specialised field of endeavour—after only a half-hour's exposure to it. In seeking to protect the hard-of-hearing public from being exploited, he has only succeeded in directing them away from the type of help they so sorely need. We trust that this letter will be able to undo the harm.

Ardente Audiology Unit,
London, W.1.

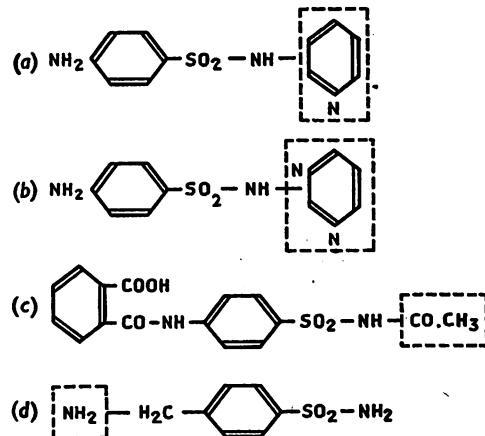
ELIZABETH CHADWICK.

CHEMICAL STRUCTURE OF SULPHONAMIDES AND THEIR EFFECT ON PERISTALSIS

SIR.—The effect of phthalylsulphacetamide on intestinal peristalsis was mentioned in your journal last year¹; so I am writing to draw your attention to some experiments done in Germany. These have shown that the action of various sulphonamides on peristalsis is closely related to their structure.

Enders^{2,3} and Kleibel^{4,5} have found that certain groups of sulphonamides inhibit peristalsis, apart altogether from their antibacterial action in intestinal infections.

Sulphathiazole ('Cibazole,' 'Eleudron'), sulphapyridine ('Eubasine'), and phthalylsulphathiazole ('Taleudron') inhibit peristalsis in experimental concentrations of about 1 : 2000, which should be attained with a dosage of 8–10 g. daily in the human subject. Their chemical structure shows a benzolsulphonamide group attached to a ring containing a single N-atom (fig., a). If benzolsulphonamide is combined in a molecule with a ring carrying a double N-atom (b), as in sulphapyrimidine ('Debenal') or sulphadiazine, or if this ring is replaced by



an aliphatic chain (c), as in sulphacetamide ('Albucid'), sulphaguanidine, and phthalylsulphacetamide, peristalsis is inhibited only at an experimental concentration of about 1 : 500, which would require a dosage of 36–40 g. daily in man. In other words, the quantity needed to inhibit peristalsis has to be four times as great.

1. *Lancet*, 1953, i, 831.

2. Enders, A. *Dtsch. med. Wschr.* 1951, 76, 1404.

3. Enders, A. *Dtsch. med. Wschr.* 1951, 76, 1404.
Arch. exp. Path. 1943, 201, 366.

4. Kleibel, F. *Dtsch. Z. Verdau. Stoffwechselkr.* 1952, 12, 257.

5. Kleibel, F. *Ibid.* p. 183.

6. Henning, N. *In von Bergmann, Frey, and Schwiegk's Handbuch der Inneren Medizin.* Berlin, 1952: vol. III, part 2, p. 37.

Finally there is another sulphonamide, aminomethylbenzolsulphonamide ('Marfanil'), which has been shown both experimentally and clinically to excite peristalsis instead of inhibiting it. This preparation differs from those previously mentioned in having an NH₂ group joined to its benzole ring by a methyl group (*d*). It is interesting to note that it also differs from the others in its effect on intestinal bacteria.

These actions were demonstrated on the gut of rat and guineapig, and they did not persist longer than one hour. Desensitisation may thus be ruled out.

Medical Polyclinic,
Würzburg University.

FRANZ KLEIBEL.

THE RECENT BURN

SIR.—Correspondents have lately discussed the desirability of leaving blisters intact when dealing with minor burns in industry. I have found that undiluted 1% electrolytic sodium hypochlorite solution, applied immediately in the form of a compress, prevents the formation of blisters; or if they have already formed on a recent burn, they are quickly reduced. Since the skin remains unbroken, there is absolutely no risk of infection with this method; moreover, it takes very little time, and pain is much reduced. If the skin is broken, the hypochlorite should be diluted to form an isotonic solution.

London, W.1.

M. MARGARET DURRANT.

TREATMENT OF THYROTOXICOSIS WITH POTASSIUM PERCHLORATE

SIR.—We should be grateful if you would allow us to add a postscript to our article of April 10. We there described a patient whose gastric symptoms became much worse when her treatment was changed from methyl thiouracil (50 mg. daily) to potassium perchlorate (100 mg. daily). The dyspepsia disappeared when she was put back on methyl thiouracil, but reappeared a second time when potassium perchlorate was given. She was known to have a diaphragmatic hernia, and we concluded that perchlorate was probably irritating an already inflamed gastric mucosa.

Further experience with this patient makes this conclusion unlikely.

After another period on methyl thiouracil the gastric symptoms again increased, and became incapacitating. They mainly occurred when she went to bed at night, and consisted of severe epigastric pain and vomiting. These symptoms were only partially controlled by outpatient therapy and she was admitted to hospital. After a few days' treatment by posture, diet, and alkalis the symptoms rapidly subsided, and we took the opportunity of testing the effect of potassium perchlorate under controlled conditions.

For four consecutive 5-day periods she was given tablets of identical appearance, labelled A, B, C, and D, to be taken twice daily. Tablets A and C contained lactose only, tablets B and D contained 200 mg. of potassium perchlorate. The content of the tablets was not known to the patient, the nursing staff, or the clinical clerk who recorded the symptoms daily. During the 20-day test period only one attack of epigastric pain and vomiting occurred. This happened while she was taking tablet A (lactose). At the time of the test potassium perchlorate clearly did not irritate her gastric mucosa, although gastric symptoms had recently been present and the mucosa might be expected to be in a sensitive state. It seems probable that the exacerbations of dyspepsia twice observed in the past when she was taking potassium perchlorate were not caused by the drug.

This was the only case, out of 108, in which there seemed to be good evidence of gastric irritation by potassium perchlorate. Since further experience has shown that this evidence was probably misleading, it now seems unlikely that potassium perchlorate will prove to be a gastric irritant, although this possibility must still be kept in mind.

University College Hospital
Medical School, London.

M. E. MORGANS
W. R. TROTTER.

METHYL PENTYNOL AS A HYPNOTIC FOR OLD PEOPLE

SIR.—Most elderly patients require some artificial aid to sleep, but the range of suitable hypnotics for routine use is very limited. The drugs commonly used include paraldehyde, chloral hydrate, sodium bromide, the traditional "Mist. Three-fifteens," and—most widely used of all—the barbiturates (mainly the "medium-acting" and "short-acting" ones). For old patients nearly all these hypnotics have some disadvantages.

I would like to report a trial of a comparatively new hypnotic drug, methylpentynol ('Oblivon'). Although its chemical structure bears superficial resemblances to paraldehyde and to methyl alcohol, methylpentynol is a separate drug in its own right. Methylpentynol (methylparafynol in U.S.A.) is a simple unsaturated aliphatic carbinol, 3-methyl-pentyne-ol-3, having the structural formula: CH₃:C(C(CH₃)₂)(OH).CH₂.CH₃.

The literature on this drug has been reviewed¹ but, with the exception of a limited study of the drug in fifty-two psychiatric patients aged 61 and over,² the usefulness of methylpentynol as a mild hypnotic for the elderly has received little attention.

All the patients studied were aged 65 years or over. The report is based on a series of ninety-four patients, of whom thirty-two were aged 65–74, forty-three aged 75–84, and nineteen aged 85 or more. There were twenty-eight men and sixty-six women. All were general hospital patients and were under continuous observation, day and night. The great majority had required regular dosage with other commonly used hypnotics, with variable effect and for varying periods, up to the time of beginning methylpentynol treatment. Only those who received the drug continuously for a minimum period of 7 days or more were included in this study: thirty-eight patients received the drug nightly for 21 days or more, and twelve for 42 days or more. The minimum total dosage was 6.7 g., the maximum 144 g. The longest trial was in a man aged 76 who received a total of 144 g. over a continuous period of 72 days.

Method of Administration.—The unit dose of methylpentynol is 250 mg., and this was incorporated in one drachm of elixir specially prepared by the manufacturers. Any drug, if sufficiently soluble in water and not objectionable in taste, is more conveniently given to old people in liquid form rather than as tablets or capsules. The crude drug, methylpentynol, is a volatile liquid with a vile burning taste, far worse than paraldehyde, and it was therefore originally dispensed in capsules. For the purpose of this study, however, it was incorporated in an elixir, which disguised its taste. The most effective dose was 4–6 drachms (1.0–1.5 g.). Smaller doses seldom had a hypnotic effect, and larger doses had no added advantage. Altogether, forty-four patients received a dose of 4 drachms nightly for periods varying from 7 to 59 days; forty-eight were given a nightly dose of 6 drachms for periods of 7 to 49 days, and twelve were given a dose of 8 drachms nightly for periods ranging from 12 to 72 days.

Assessment of Efficiency.—The effectiveness of the drug on each individual was observed by doctors and by senior nurses, who also recorded every half-hour during the night whether or not the patient was asleep. Special charts were used and records were kept every night while the drug was being given. After the trial, the hypnotic effect for any night was noted as "good" if after the dose had been given the patient had been asleep within 1 hour, and had remained asleep for at least 5 hours. The response was noted as "poor" if sleep was broken, or had not ensued within 2 hours of giving the drug, regardless of the duration of sleep. In any particular patient, the drug was said to have been "efficient" if a "good" night's sleep was obtained on 70% or more of the nights on which it was given.

Results.—In sixty-one of the ninety-four patients (64%), the drug was found to be "efficient." Its prolonged use gave no troublesome side-effects, and there has been no evidence of addiction. When the hypnotic effects wear off, patients remain quietly sedated and do not become restless or noisy, so there is usually no need to repeat the dose during

1. *Brit. med. J.* 1953, ii, 435.

2. May, P. R. A., Ebaugh, F. G. *J. Amer. med. Ass.* 1953, 152, 801.

night, and excessive drowsiness next day is thereby avoided. The hypnotic action is a mild one, and the drug will not produce sleep in the presence of pain or acute mental disorder.

Thus, methylpentynol was found to be an efficient hypnotic in almost two-thirds of these patients. It appears to be a useful drug for elderly patients needing a mild hypnotic; and it is apparently safe and free from troublesome side-effects.

I should like to thank Dr. A. G. Anderson, Dr. A. W. Hendry, and Dr. W. R. Gauld for permission to include patients under their care in this investigation. I am also indebted to members of the nursing staff at Glenburn Wing, Woodend General Hospital, Aberdeen, for their willing co-operation. Methylpentynol elixir was supplied by British Schering Ltd.

Geriatric Unit,
Royal Infirmary,
Perth.

RONALD G. SIMPSON.

MOUTH-PIECE FOR USE WITH PNEUMOFLATOR IN RESPIRATORY PARALYSIS

SIR.—In your issue of Dec. 12 Dr. Beaver and Dr. Gillatt described a cheap and simple improvisation of a mouth-piece for use with lung inflators. It was devised to take the place of the face-mask which is commonly used with these machines in maintaining artificial respiration. In this hospital we have had long experience in methods of artificial respiration, particularly for poliomyelitis, and we were fully aware of the difficulties encountered when using the face-mask in the conscious patient. Since the description of this mouth-piece was published, we have had the opportunity to give the mouth-piece (and modifications of it) an extensive trial in two intelligent adult patients. Both were loud in their praises for a device which they could accept with great comfort where previously, with face-masks, they were anxious, even alarmed, and almost certainly under-ventilated at times, even when the mask was being applied correctly.

Western Hospital,
Seagrave Road,
London, S.W.6.

W. HOWLETT KELLEHER.

NURSING BY THE MOTHER

SIR.—This correspondence has arisen out of the subject of cross-infection in hospitals, raised by the Pickerills in their article of Feb. 27; but I would like to add these comments in support of Dr. Lowenfeld's letter of April 10. She emphasises (1) the structure and organisation of the hospitals in which children are treated; (2) reconsideration of the training of nurses who will care for them and study of the ways in which help of the mother can be enlisted; (3) the value of play in recovery from illness. Homesickness and, above all, boredom work against recovery, and play is the only palliative.

There are many who agree that small children admitted to hospital should be accompanied by, and nursed as far as possible by, their mothers, but rather few, I fancy, who have found it easy to put into practice. This is where structure comes in. In most modern children's units and adapted old wards, the cubicles are too small to accommodate both mothers and children; the bathing and lavatory arrangements for the mothers are makeshift, and there is no sitting-room, dining-room, or telephone for them.

If it became known to the public that arrangements were adequate and that mothers were expected to go to hospital with their babies and keep in touch with home from this outpost, the neighbours would feel their obligation to step into the breach more binding than they do at present—in the south of England, at any rate.

Our nursing-staff difficulties are going to increase, not diminish, and although children usually get a better deal than adults when shortage is acute, the staffing of wards at night often reaches dangerously low limits.

On the second point—"Reconsideration of the Training of Nurses" (and doctors, I would add)—it is often felt, if

not actually declared, by those who have charge of sick children in hospital that the parents of a child are not good for it. The child may be brought in in a dirty condition; the hair may have nits; a distressing emotional scene occurs at each visiting-time; or the feed the baby was having may be "a bit out" by ordinary calculations; and, as if any further proof were required that the parents are to blame the child under proper nursing gets well, gains weight, looks rested, and, above all, looks clean. Is it surprising that nurses and doctors see little to change in the time-honoured method of taking over completely from the mother? When we admit a child to hospital, mentally we nail a notice over its cot or on the door of its cubicle—Under New Management.

At present, nurses in training hardly notice the parents in the picture. They certainly cannot have an opportunity of seeing mother and child as one, and they are rather too young to have a serious interest in the mother's character and competence. Ward sisters, on the other hand, have to develop what may be called critical sympathy with the mothers, and some have a special gift for it.

The new orientation will make big demands on them in that it requires much further study and the sacrifice, to some extent, of the bond they would normally have with the child. Having seen it begin to work in a paediatric unit (in spite of the structure being unsuitable), I am moved to write this letter.

Department of Paediatrics,
Stoke Mandeville Hospital,
Aylesbury.

DERMOD MACCARTHY.

THE HOSPITAL MAKES FRIENDS

SIR.—The letter by "Registrar in Teaching Hospital" (April 10) illustrates the difficulty of conveying in writing a precise point of view. Writing as a psychiatrist, I assumed that, by the wording of my letter of March 10, it would be clear to your readers that I was not a general practitioner. I wonder whether it is not a common fault for people to interpret what they read in terms of their own problems.

At one clinic at which I worked before the late war, we had a weekly case-conference to which all concerned were invited. I feel this made for co-operation between the clinic and the general practitioner, as well as between other social services connected with the welfare of the patient.

Bishop's Stortford,
Hertfordshire.

D. N. HARDCastle.

A WORD WANTED

SIR.—With Dr. Apley's search for the best antonym to "retrospective" (April 10), I have that sympathy which comes from failure, partial or complete, in a similar quest. In my own attempt,¹ I finally settled for "prospective," not too happily, since this word has acquired connotations other than that desired. In my private vocabulary at the time, I used "Promethean" and "Epimethean" to make this contrast; and I just wonder if a transfer from upper to lower case might not supply Dr. Apley's needs, and those of others. The words "promethean" and "epimethean" are euphonious, they suit the desired meaning, and they have no taint of that hybrid origin which has kindled so much etymological flame.

Department of Medicine,
The Royal Infirmary, Manchester, 13.

D. A. K. BLACK.

SIR.—"Prospective" seems right. Præspective might be better, but we have "predestined" and "prescribed" and recently "pre-selective"; and American "pediatricians" would certainly omit the "a."

Bristol.

ALLAN MCFARLAN.

SIR.—Dr. Apley's difficulty seems to have been answered this very week by no less an authority on the

¹ *Lancet*, 1953, i, 305.

use of words than Sir Winston Churchill. In a reply to Mr. Shinwell on a question concerning the atom bomb, he said : "I endeavour to allow my thoughts to play in retrospect as well as in prospect over all my acts."

Perhaps that too gives us a clue to the approach we should adopt to both forms of research.

Thornton Heath,
Surrey.

S. G. HAMILTON.

PATHOLOGISTS AND PNEUMOCONIOSIS

SIR.—I hate prolonging this already rather long correspondence any further, but I find Dr. Fletcher really hard to please.

Last time (March 20) he blamed the absence of a pathological classification for missed post-mortem diagnoses, and he dismissed the pathologists' approach to the problems involved for that reason. This time (April 3) he finds that the greatest source of sampling error in post-mortem statistics is the failure of all possible cases to reach the necropsy table.

As far as the intra-vitam certified cases are concerned, the necropsy is obligatory by law and the procedure is foolproof. As for the non-certified cases, the times when a coalminer would hesitate to mention his chest troubles for fear of losing his job are long gone. At present, it would mean a failure on the part of the coalminer, his dependants, his trade union, and—dare I mention it?—his doctor if the case is not fully investigated before or at least after death. The first two parties would be activated by the prospect of a pension and the other two by the wish to do their job; all that is required is a phone call to the coroner.

In these circumstances, while I agree that even this quadruple failure may happen as an occasional and deplorable occurrence, I feel it is rather hard of Dr. Fletcher to consider that it does so frequently. His statement implies a censure on G.P.s in colliery practices, and I doubt that they deserve it.

Dr. Fletcher mentions the concept of "pulmonary dust disease." I agree with him there, but, as long as the present Acts are based on a different definition, such considerations, valuable though they are, cannot form the basis of our actions.

Dr. Joules (March 27) tells me that at the necropsies of the 4500 fog victims in London in December, 1952, no fog was present in the lungs. While I have no wish to dispute this, I wish to point out that, according to the U.S. Government Report on the Donora fog disaster in 1948, sulphur compounds were found in the lungs of the victims at necropsy. So on that occasion at least, fog was present in the lungs.

Finally, in my original letter I asked for co-operation from other practitioners working in coalmining areas. I repeat my plea, for I feel that progress in the research into industrial dust disease will not come from recriminations and fault findings, but from co-operation and mutual assistance.

Abertillery, Monmouthshire.

K. TRIGER.

CONTROL OF DENTAL CARIES

SIR.—I would like to add a few remarks about the control of dental caries, particularly since Dr. Burgess and Dr. Burton, in their article of April 10, discuss "Beginning at the Beginning." Although prevention does not apparently concern the G.P. directly, the principles of prevention are very much interwoven with many aspects of his work.

An excessive intake of carbohydrate is blamed for the production of caries, and I believe rightly so; but, in addition to the local effects, it may affect the "protein pool" of the body and incidentally the "organic turnover" of not only the teeth but other structures.

In the prevention of caries the introduction of one factor, say fluorine, may raise the level of resistance to a satisfactory

height, but we do not know what it may do to resistance to other types of bacteriological invasion or equivalent forms of stress.

By aiming at calcium intake, have we pinpointed the mineral constituent, and by the recommendation of milk have we given an impression which overemphasises it as a "good food"?

Coming back to the carbohydrate intake, there are several factors involved: (a) the family feeding pattern; (b) the generally accepted habits of the circle in which we move; (c) the difficulty of restricting sweet consumption in one's own children without making them feel too different from their friends; (d) the feeding difficulties of early life and the easing of tension when sweeter foods are given because "after all a child as active as that must have something to keep going"; (f) an understanding of diet, especially from the point of view of breaking the habits produced by temporary stresses. Finally, the conversion of "diabetic hyperinsulinism" and its cravings to a normal metabolic pattern is probably not the least of the problems.

These remarks are not levelled in criticism; I am merely trying to show, if possible, how wide the problem of dental caries is.

Clapham, Yorkshire.

J. A. FARRER.

SAFER HYPOTENSION

SIR.—Much interest has been focused in recent months not only on the advantages but on the dangers of the use of hypotensive techniques in surgery.¹⁻³ With the methonium compounds the degree and duration of the blood-pressure falls are often variable and not always easily reversed. It would seem from reports on the use of 'Arfonad'^{4,5} that, because of its short action, this agent makes the use of hypotension a more controllable and hence a safer procedure. In our opinion, and that of others,¹ the safety of this technique can be further increased by combining it with hypothermia, thereby lowering the metabolism and oxygen requirements of the brain.

We have used the combination of hypothermia and hypotension (with arfonad) in a small series of selected neurosurgical procedures, and the results have been very satisfactory. These were operations for aneurysms and vascular tumours which would have proved difficult, if not impossible, with orthodox methods of anaesthesia. Hypothermia, and the drugs used in its production, will lower the systolic blood-pressure to about 100 mm. Hg, this fall being reinforced when required by the use of arfonad.

Hypothermia is produced by surface cooling using a modification of a technique already described.⁶ All adult patients are given 50 mg. of chlorpromazine by deep intramuscular injection about one hour before anaesthesia is induced. This is combined with pethidine and/or promethazine, depending on the degree of consciousness. On arrival in the anaesthetic room, patients are prepared for operation in the usual manner, very small doses of thiopentone being required. Surface cooling with ice bags is then commenced, and any tendency to vasoconstriction, as shown by a sharp fall in skin-temperature, is overcome by the intravenous administration of further doses of chlorpromazine. The largest dose of this drug that we have used to date is 95 mg.

The light anaesthesia maintained with nitrous oxide-oxygen, together with the chlorpromazine, with or without trichloroethylene, has completely eliminated shivering. With this technique it has always been possible to reduce the rectal temperature to 32°C (89.6°F) within one hour of the first application of ice. All active cooling is then stopped and the temperature falls slowly during the operation to about 30°C (86°F).

1. See *Brit. med. J.* Feb. 6, 1954, p. 324.

2. Davison, M. H. A. *Anaesthesia*, 1953, 8, 255.

3. See *Ibid.* p. 263.

4. Anderson, S., McKissock, W. *Lancet*, 1953, ii, 754.

5. Kilduff, C. J. *Ibid.* Feb. 13, 1954, p. 337; Scurr, C. F., Wyman, J. B. *Ibid.* p. 338.

6. Dundee, J. W., Gray, T. C., Mesham, P. R., Scott, W. E. B. *Brit. med. J.* 1953, ii, 1237.

The arfonad is given by continuous infusion of a 0·1% solution, similar to the method of Scurr and Wyman.⁶ A very slight head-up tilt (5°–10°) is used during operation.

The outstanding difference between this technique and those previously described is the small amounts of arfonad required to reduce the systolic blood-pressure to 60 to 70 mm. Hg. A drip rate of 5 to 10 per minute is rarely exceeded, 100 to 150 mg. of arfonad being the usual requirements for 3 to 4 hour operations. In one case a "pressure floor" of 70 mm. Hg systolic could not be passed by increasing the drip rate, and this only delayed the recovery. Tachycardia has not been observed in any case, presumably because of the hypothermia.

It is our aim to return the systolic blood-pressure to 90 to 100 mm. Hg before closure of the dura mater, and in this we have always succeeded. A rise of 15–20 mm. Hg occurred within 5 to 10 minutes of stopping the arfonad. Irrespective of the degree of bleeding, a bottle of blood or 'Intradex' is given quickly at this stage, resulting in a similar rise in the pressure. In the one instance where these measures were not sufficient, a 1 : 1,000,000 *l*-noradrenaline drip quickly rectified matters, and it was discontinued after 20 minutes.

No active attempts are made to restore the normal body-temperature at the end of the operation, and temperatures of 35°–37°C are attained within 6 to 8 hours, with a gradual return of normal blood-pressure.

Reduction in bleeding resulting from controlled hypotension has opened up new fields in the realms of plastic, E.N.T., and neurosurgery. In every case, however, one has to weigh the dangers of severe bleeding at operation and those which may result from the prolonged period of low blood-pressure. We feel that while arfonad is probably the greatest advance that has been made since the technique was introduced, its combination with hypothermia should rob controlled hypotension of many of its undesirable sequelæ.

Department of Anaesthesia,
University of Liverpool.

Regional Neurosurgical Unit,
Liverpool.

JOHN W. DUNDEE,
ITHEL LL. FRANCIS
C. B. SEDZIMIR.

SHOE DESIGN AND THE GREAT TOE

SIR.—May I, an outsider, join your discussion of shoe design?

I take the view that the normal environment of the foot is unshod on a yielding and uneven surface (sand, earth, &c.), so I have designed a shoe that will simulate this environment as closely as possible. First, a plaster impression of the foot is taken, with the foot bearing no weight but in a weight-bearing attitude, and from this a plaster model is made. The shoe is moulded directly on this model, the hypothesis being that the foot should design the shoe, not that the shoe should design and deform the foot.

The outside of the shoe is made of soft leather with a flexible rubber sole. The inside will fit every curve of the dorsum and the plantar surface of the foot. The insole will be rounded at the heel and metatarsal area, built up to the long arch, and even built up under the toes to aid them in their grasping action and also prevent the foot from sliding forward.

In the moulded shoe the entire plantar surface of the foot will help carry the body-weight: heel, long arch, five metatarsal heads, five toes, and even the webbed areas under the toes.

In the conventional woman's shoe the body-weight is carried by the base of the heel and the second, third, and fourth metatarsal heads. Because of the pointed shoe, the great toe is forced medially during walking, causing all the weight to be carried on the middle metatarsal heads with the subsequent formation of corns and callosities and deformities of the toes—the most serious of which is hallux valgus. In men, where the shoe is wider, but not wide enough, the most common condition is the callosity under the first and fifth metatarsal heads.

I have observed excellent results with shoes made in this way. Corns and callosities have completely disappeared within six to eight weeks. Within a year after wearing the shoes, many toe deformities begin to correct themselves; but it is too early to say what will happen to chronic deformities. At all events, pain is relieved immediately.

Philadelphia, U.S.A.

H. T. LOVITZ.

SIR.—I was interested to read in your issue of March 27 a letter from Dr. Haines and Mr. McDougall. But I must disagree with their statement that, although flat shoes have become popular since the war, "they seldom appear in fashion magazines." My own company, in common with other leading manufacturers of flat shoes, publicise them extensively in fashion magazines and women's magazines. We also find that the fashion magazines often discuss our flat shoes in their editorial columns.

Selby Shoes Limited,
London, W.1.

J. F. H. HINTON.

AUTOHÆMOTHERAPY IN HERPES ZOSTER

SIR.—Two leading textbooks say of herpes zoster: "The course of the eruption is uninfluenced by treatment."¹

"Nothing will check the disease."²

Yet this is a severe affliction, which causes long-lasting neuritis and pain in the affected part, and, if it attacks the cornea, the result may even be loss of the eye.

In the past forty years I have treated many cases of herpes zoster by intramuscular injection of the patient's own blood, and when this treatment has been started in the first two days it has always checked the disease. The most dramatic improvement has been in herpes of the eye, and I believe that I have saved many eyes.

Using a 5-ml. syringe, 5 ml. of blood is withdrawn from a vein in the bend of the elbow and is injected into the deltoid muscle of the same arm. It is as well to repeat this injection of the patient's own blood the next day. Of course, in addition, the pain-relieving remedies should be used—i.e., aspirin, phenacetin, codeine, or pethidine—and an aperient should be used to counteract the constipation they cause.

This autohaemotherapy is simple and without risk. It should be given as soon as the illness is recognised. Unfortunately it is not much good three weeks later when the neuralgic pains cause so much distress.

London, W.1.

V. NESFIELD.

3-D. IN MEDICAL ILLUSTRATION

SIR.—In your issue of April 10, you note (p. 787) an article of Dr. J. G. Robson and myself which appeared in *Anesthesia* and which was illustrated by stereoscopic anaglyphs.

In his editorial comment the editor of *Anesthesia* expressed the belief that "it is the first time that this type of stereogram has been used in a medical journal." In this comment he may strictly be correct, since I believe that there are several processes for producing these stereograms, though the final result of them all appears rather similar. Your note is a little more general however, and I think it would be unfair if your readers gained the impression that this is the first occasion on which stereograms by any anaglyphic procedure had appeared in a medical journal, because in a supplement to the November, 1953, issue of *Medicine Illustrated* there appeared some anaglyphs by Mr. P. Hennessy and Mr. J. Hardman.

This sort of confusion readily arises when a technique is new, and I apologise for occupying your space with

1. Conybeare, J., Mann, W. N. *Textbook of Medicine*. Edinburgh, 1952.
2. Taylor's *Practice of Medicine*. London, 1936; p. 1000.

a rather minor matter. It would, however, be a pity, through misunderstanding, to cause irritation to those concerned.

Department of Anesthetics,
The Medical School,
Newcastle upon Tyne.

E. A. PASK.

BILIGRAFIN IN CHOLECYSTOGRAPHY

SIR.—I have read the annotation on 'Biligrain' in your issue of April 17 with interest. I am at present working with samples of biligrain kindly supplied by Messrs. Schering A.G. of Berlin.

I have found the substance entirely satisfactory, fulfilling all the claims mentioned in your annotation, save that I now have to record a severe reaction. This occurred in an apparently healthy man of 72 years, suffering only from suspected gall-bladder disease and not at that time jaundiced.

The injection of biligrain was slowly given intravenously. After 30 ml. had been injected the patient complained of a pricking sensation in the anus, and injection was immediately discontinued. Four minutes later, he suddenly lost consciousness. He was pulseless with stertorous breathing, pallid complexion, cyanosis of the extremities, and an imperceptible radial pulse. There was urinary incontinence. Resuscitation was achieved with the aid of continuous oxygen, injections of nikethamide ('Coramine'), antazoline ('Antistin'), and adrenaline. After 15 minutes, the patient regained consciousness and his subsequent recovery was uneventful.

One previous case of collapse is quoted by Hornykiewytsch and Stender¹ but no details are given.

Cambridge.

M. W. P. WARD.

THE BOMBS

SIR.—Many people will be grateful for your leading article last week. The established facts about the bomb reduce to tragic absurdity the arguments of statesmen and military leaders that the world must, to preserve peace, devote itself to preparing for war. Homicide on a scale approaching this has hitherto been possible only when millions of people have been persuaded that their duty or interest lay in supporting war, and the act of war demanded that these millions should throw themselves into movement. The hydrogen bomb makes it possible, for the first time in the history of the world, for a few men in positions of power to dispense with the consent and active support of their people in waging war. Neither fear of retaliation nor any moral considerations will restrain the desperate. Indeed, the decision to use the first atom bomb appeared to many people then, and to far more since, to have no moral justification.

You praise our profession for the part some members of it have played in urging upon the world the paramount need for humanity to outlaw the mass murder which is at present condoned in war. Professor Haddow, to whose courageous letter in the *Times* you call attention, has suggested that scientists all over the world, profiting by the international status of science, should meet to appraise the human situation created by the existence of the hydrogen bomb, and set themselves to devise policies to prevent its manufacture. This is obviously a proposal of great value and I suggest that all of us have a duty to obtain for it the support of our professional organisations.

I should like to remind my colleagues that there is an organisation of doctors in this country which exists to study this great dilemma—namely, the Medical Association for Prevention of War. Under the auspices of this association, Prof. C. F. Powell, F.R.S., and Dr. Comfort will be addressing a meeting on the hydrogen bomb at Friends' House, Euston Road, London, N.W.1, at 7.30 p.m. on Wednesday, April 28.

DUNCAN LEYS.

¹. Hornykiewytsch, T., Stender, H. S. *Fortschr. Röntgenstr.* 1953, 79, 293.

SIR.—There is one aspect of the hydrogen bomb which few medical men will fail to recognise—it is the mental patient's weapon *par excellence*. Atomic research in the United States (we cannot speak for Russia, which keeps its own counsel) has long since passed from the sphere of weapon research into that of abnormal psychology. In such a context, it is hard to place confidence in the consideration that no sane authority will destroy itself. The sane man may say "If that man hits me I will hit him": the sane but cruel man, "If that man hits me, I will kill him and his whole family." But there is a recognisable and pathognomonic ring about the proposition "If that man hits me, I will burn down the house and kill us both." It leads naturally on to the further proposition "That man is going to hit me: I will burn down the house and kill us both to forestall him." To say that the policy of "massive retaliation" already exemplifies this state of mind is a medical, not a political, judgment—to those who remember the utterances which came from a certain burning Chancellery, the cravings for *Götterdämmerung*, for the deliberate mistake, for the opportunity to smash everything, are dangerous and present realities in both medicine and politics.

The paranoia of nations, being shared out, as it were, between a large number of normal, and a few abnormal, but directing, individuals is always diluted with normality, with some humane responses to which we can appeal. In both the major atomic powers today, it is largely so diluted. From the psychological standpoint, the traditional rigidity of Russia seems less menacing today, and in the context of this weapon, than the traditional hysteria of the United States. Both powers are subject to the pressure of world public opinion. I believe that a forthright and total renunciation of such weapons by our own country would have great psychotherapeutic value; it might help us to avoid the paralysis of public attitudes by guilt-feelings over the last atom bombs, which has affected the United States, and it would enormously raise our domestic morale and our external moral authority. This is a case where British opinion might without arrogance act as therapist. In spite of the propaganda of malicious people, we have no great fear or hatred of either side. We have few McCarthy's or Berias to handicap us. The responsibility of reconciliation is one which we can all accept, and which the medical profession should be proud to lead. It is our only hope, after all, of surviving the century.

Loughton, Essex.

ALEX COMFORT.

Parliament

Fewer Dentures

In the House of Commons on April 15, replying to Mr. R. E. Winterbottom who raised the question of the number of dental technicians, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the Ministry believed there were more of these workers than there was work for them to do. In 1948, 437 people applied for apprenticeships, and in 1949, 1205 people applied. In 1950, when many of these apprentices were not yet trained, 5 million dentures were supplied under the National Health Service. But in 1953 only 2 million dentures were supplied, and she thought that this figure would be the average annual demand for some years. If the service was a success fewer, and not more, technicians would be needed for people would look after their teeth and keep them longer. In the last quarter of 1953, 380,000 dentures were supplied; in the first quarter of 1954, 394,000. The effect of the treatment charges had been a vast increase in conservative work, particularly among children and adolescents. There was no desire to cheapease on this service, but the Minister was convinced that there were enough technicians to deal with the situation. There

were between 200 and 250 technicians employed in the hospitals, and all except about 80 were in the teaching hospitals. At present the Whitley Council was drawing up an apprenticeship scheme for the training provided in hospital and local-authority laboratories.

QUESTION TIME

Hospital Consultants

Mr. A. A. H. MARLOWE asked the Chancellor of the Exchequer what consultations had taken place between the Treasury and the Ministry of Health on the expenses of hospital consultants employed in the National Health Service which were not deductible for income-tax.—Mr. J. A. BOYD-CARPENTER, financial secretary to the Treasury, replied: Hospital consultants are, like other employees, assessable under schedule E, and the same rules for expenses apply to them as to other taxpayers. I see no reason to propose legislation giving them preferential treatment. The general question of what expenses are admissible to such taxpayers is within the terms of reference of the Royal Commission.

Replying to a question, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the number of consultants employed by regional boards in England and Wales who had transferred from whole-time to part-time service was 42 in 1951, 61 in 1952, and 46 in 1953.

N.H.S. Charges

Replying to questions, Miss HORNSBY-SMITH said that N.H.S. charges were introduced in 1952. The number of prescriptions dispensed by chemists in February, 1954, was 19,203,000, compared with 21,645,000 in February, 1953.

Public Health

Poliomyelitis in Denmark

Denmark had a formidable outbreak of poliomyelitis in 1952, when the attack-rate of the paralytic form in Copenhagen was 106 per 100,000 population. Hamtoft¹ has now compared the experience in 1953 with that in the preceding year.²

The epidemic of 1953 was surpassed only by those of 1952, 1944, and 1934. Between the outbreaks of 1952 and 1953 notifications fell to the lowest level about May 1,

POLIOMYELITIS IN DENMARK, 1952 AND 1953

Area	January, 1952, to April, 1953				May, 1953, to December, 1953				1952 + 1953 : paralytic cases per 100,000 population	
	Paralytic cases		Non-paralytic cases		Paralytic cases		Non-paralytic cases			
	Total	Per 100,000 population	Total	Per 100,000 population	Total	Per 100,000 population	Total	Per 100,000 population		
Copenhagen, metropolitan area	1289	106	1631	134	53	4	147	12	110	
Rest of country	1271	41	1694	55	521	17	672	21	58	
Total Denmark	2560	58	3325	76	574	13	819	19	71	

and for the purpose of assessing the two outbreaks this date is taken as the dividing-point. The most striking difference between the two epidemics is in the relative distribution of cases between Copenhagen and the rest of the country, shown in the accompanying table. Whereas in 1952-53 the attack-rate of paralytic poliomyelitis was nearly three times greater in Copenhagen than in the rest of the country, in May to December, 1953, the rate in Copenhagen was only a quarter of that in the rest of the country. Furthermore, "The counties

The estimated cost to the Exchequer of dental treatment for these months was £1 million and £800,000 respectively.

Hydrocortisone Supplies

Replying to a question, Miss HORNSBY-SMITH said that production of hydrocortisone in this country started only recently. The supplies now available to hospitals receiving cortisone would be increased as the need arises.

Welfare Food Service

Replying to a question, Major GWILYNN LLOYD GEORGE, Minister of Food, said that about 97% of those entitled to obtain milk or 'National Dried Milk' under the welfare foods service did so. The quantities of the vitamin supplements taken up in 1953 expressed as a proportion of the full entitlement were as follows: orange juice 29·4%; cod-liver oil 23·8%; vitamin tablets 32·6%. The percentage of persons who obtained the vitamin supplements was higher than these figures suggested, because many did not take their full entitlement.

Contamination of Citrus Fruits by Thiourea

Mr. JOHN PARKER asked the Minister of Food what action was being taken to safeguard the public from thiourea poisoning in oranges imported from Spain. Major GWILYNN LLOYD GEORGE replied: Local authorities in whose areas such oranges have been reported have been approached with a view to their taking appropriate action. As a result they have warned merchants against further importation. The Spanish authorities have also warned all their fruit-inspection offices that the complete prohibition of the export of such oranges to Great Britain must be strictly enforced.

which showed the greatest number of cases in 1952 practically escaped the epidemic in 1953, while the counties not stricken by the epidemic in 1952 showed large numbers of cases in 1953."

England and Wales in 1953

The Registrar-General publishes this week further details³ for England and Wales in 1953; he had already given some provisional figures in an earlier return.⁴ The estimated home population of England and Wales at Dec. 31 was 44,186,000—an increase of about 420,000 since the census in April, 1951. On the basis of the death-rates for 1952, it is reckoned that the expectation of life of a boy at birth is now 67·06 years and of a girl 72·35 years. On the basis of the death-rates for the years 1901-10, the expectations were 48·53 and 52·38 respectively. In an analysis of the causes of death, it is noted that the number of deaths from accidental poisoning continues to rise, reaching 659 in the first nine months of 1953, compared with 586 during the corresponding nine months of 1952. The number of suicides increased in the same period from 3299 to 3641. A comparison of death-rates of children under one year of age in the September quarter of 1953 shows that the rate of 22 per 1000 related live births compared with the following rates in other countries: Netherlands 19, Australia 25, U.S.A. 26, Scotland 28, France 33, Italy 64.

The School Lavatory

In his 1953 report to the City of Oxford Education Committee, Dr. J. F. Warin comments on the continuing failure of some of the schools to remedy obvious defects in sanitary arrangements. Provision of bolts on lavatory doors, lavatory chains, and brackets for toilet-paper and a supply of paper, cost little and are too often lacking. "The key personnel in this matter are the head teacher and the caretaker." Dr. Warin again emphasises the need for schools to play their part in training children in cleanly habits—for which a sufficiency of properly equipped lavatories (with wash-basins) is essential. "The experience of most head teachers has been that provided conveniences are kept in good order and supplied with toilet paper on proper brackets then care is exercised by the children."

3. The Registrar-General's Quarterly Return for England and Wales. Quarter ended Dec. 31, 1953. H.M. Stationery Office. Pp. 32. 2s.

4. See *Lancet*, Jan. 30, 1954, p. 260.

1. Hamtoft, H. *Dan. med. Bull.* 1954, 1, 12.

2. See *Lancet*, 1953, ii, 196.

Notes and News

A CANADIAN COLLEGE OF GENERAL PRACTICE

LAST year, at a meeting of the Canadian Medical Association, it was decided to set up a college of general practice "within Canadian organised medicine" with the following aims:

- To establish an academic body with broad educational aims.
- To arrange for undergraduate teaching by and for general practitioners.
- To arrange for the presentation of postgraduate education for general practitioners.
- To arrange for research in general practice.
- To arrange for publication of original articles by general practitioners.
- To arrange for hospital staff appointments for general practitioners.
- To provide suitable recognition to members in the field of general practice.
- To do all things necessary to maintain a high standard in general practice.

The college will be officially inaugurated at the meeting of the association at Vancouver in June. Applications for membership should be sent to the College of General Practice of Canada, 244, St. George Street, Toronto 5, Ontario.

DANISH BULLETIN

Denmark, with just over four million inhabitants, makes a contribution to medical knowledge out of proportion to its size; but, since the Danish language is understood by less than 1% of the people of the world, the extent of this contribution may not always be apparent. Accordingly a new monthly bulletin in English,¹ sponsored by the Danish Medical Association, medical schools, and national health service, should prove especially valuable. Its purpose is to survey Danish medicine by means of original articles, short communications, and annotations; and an article in the first issue is referred to in our public-health section this week. The bulletin will be sent without charge to subscribers to *Ugeskrift for Læger* and, on request, to medical institutions.

RENÉ SAND MEMORIAL

THE International Conference of Social Work is opening a memorial fund to commemorate the life and work of Prof. René Sand, its founder, who died in 1953.

Professor Sand, who held the chair of social medicine in the Free University of Brussels, was a former secretary-general of the League of Red Cross Societies, and had also shared in the foundation of the World Health Organisation. He was at the time of his death president of the International Hospital Federation.

It is proposed that the memorial fund shall be used to award a biennial prize for "outstanding service in social welfare or social medicine." Contributions may be sent to Mr. G. E. Haynes, the president of the conference, 26, Bedford Square, London, W.C.1, or to the secretaries of the national committees of the conference.

THE UNMARRIED MOTHER

A PAMPHLET by a Roman Catholic social worker² gives a brief but comprehensive survey of the social and moral causes of illegitimacy and the measures for prevention and alleviation of the suffering caused to women and their illegitimate babies. Written from the Roman Catholic viewpoint, its approach is sensible and practical, and due tribute is given to the work of other bodies.

University of London

On March 19 the Graham medal was presented to Prof. G. R. Cameron, F.R.S.

University of Glasgow

On June 16 the honorary degree of LL.D. will be conferred on Prof. J. H. Dible, Sir John McNee, and Prof. G. I. Strachan.

Royal College of Physicians of London

Dr. J. Forest Smith will deliver the Croonian lectures on Tuesdays, May 4 and 11, at the college, Pall Mall East, S.W.1, at 5 p.m. His subject will be Nutrition and Child Health.

1. Danish Medical Bulletin. Subscription £1, \$3, or equivalent; payable to Ejnar Munksgaard, 6, Nørregade, Copenhagen.
2. The Unmarried Mother and her Child, by MARY WALSH, Catholic Truth Society, 38, Eccleston Square, London, S.W.1. Pp. 21. 4d.

National University of Ireland

Mr. Patrick Fitzgerald has been appointed associate professor of surgery at University College, Dublin. Dr. Paul Cannon has been appointed professor of physiology, and Dr. Fergus O'Rourke professor of zoology, at University College, Cork.

The degree of M.D. has been awarded to A. P. Barry.

Royal College of Obstetricians and Gynaecologists

On Friday, May 21, at 5 p.m., at the college, 58, Queen Anne Street, London, W.1, Mr. Ian Donald will deliver the Blair-Bell lecture. He is to speak on Atelectasis Neonatorum.

Institute of Dermatology

Two semi-permanent exhibitions are being shown at the institute during the summer course. The first, from May 3 to 22, by Dr. J. O. Oliver, will be on Animal Parasites in Diseases of the Skin.

Royal Sanitary Institute

The annual health congress of this institute is to be held at Scarborough from April 27 to 30, under the presidency of the Earl of Feversham.

Diabetic Association

The scientific meeting of this association will be held at University College Hospital Medical School, Gower Street, London, W.C.1, on July 16 and 17. On July 16, at 2.30 p.m., Dr. K. Hallas-Møller will deliver the Banting lecture, on the New Insulins. Those who wish to read communications should write to the association, 152, Harley Street, London, W.1.

Where to Practise

The Medical Practices Committee have revised the classifications of areas for England and Wales. A doctor who is proposing to enter practice should apply for up-to-date information from the executive council of the district before taking steps to secure surgery and waiting-room accommodation.

Medical Art Society

This society is holding an exhibition at Walker's Galleries 118, New Bond Street, London, W.1. Until May 8 it will be open from 10 a.m. to 5 p.m. (Saturdays 10 a.m. to 1 p.m.).

Association of Social Workers

This association is holding a course at County Hall, Westminster Bridge, London, S.E.1, on May 28, and 29, on the Social Worker and the Group Approach. The first session will take place at 6 p.m. on Friday, the 28th. Further particulars may be had from the conference secretary, Silverbeck, Stanwell Moor, Middlesex.

National Society of Children's Nurseries

A conference on the Needs of the Family in a Changing Society is to be held on Friday, May 7, at 10.30 a.m., at County Hall, Westminster Bridge, London, S.E.1. The speakers will include Prof. Fraser Brockington, Dr. Alice Stewart, and Dr. D. W. Winnicott. Further particulars may be had from the secretary of the N.S.C.N., 45, Russell Square, W.C.1.

Prizes for Clinical Research

A year ago the South West Metropolitan Regional Hospital Board decided to offer prizes to encourage "minor items of clinical research" (see *Lancet*, 1953, i, 249). The following awards for 1953 have been announced:

Up to 3 prizes of £100 each for consultants and S.H.M.O.s.—Dr. M. Hamilton, formerly psychiatrist (S.H.M.O.), Springfield Hospital (treatment of paranoid psychoses); Dr. A. M. Read, assistant chest physician, Portsmouth chest clinic (ventilatory defect following treatment by artificial pneumothorax); Dr. D. A. J. Williamson, consultant paediatrician, Southampton, Winchester, and Treloar groups (epidemiological and clinical survey of ascariasis).

Up to 3 prizes of £100 each for senior registrars, registrars, etc.—Mr. G. Bennett, D.O.M.S., senior registrar, Southampton Eye Hospital (etiology and surgical treatment of glaucoma); Dr. G. S. Crockett, senior medical registrar, Lambeth Hospital (measurement of pulse-wave velocity in the human subject); Dr. C. Donovan, formerly psychiatric registrar, St. James' Hospital, Portsmouth (plasma-ascorbic-acid response in psychotics).

Up to 3 prizes of £100 each for house-officers.—Mr. A. O. Wilson, F.R.C.S., formerly house-surgeon, Royal Hants County Hospital (absence of fluid and electrolyte disturbances in patients undergoing partial gastrectomy and given limited amounts of fluid intravenously after operation); Mr. M. Wynyard, F.R.C.S., formerly house-surgeon, St. James' Hospital, Balham (anatomy of the big toe with regard to the long saphenous nerve).

A similar competition is being held this year and particulars will be sent to group medical committees in the region.

Medical Association for the Prevention of War

In collaboration with Science for Peace, this association has arranged a meeting on the Hydrogen Bomb. This will be held on Wednesday, April 28, at 7.30 p.m. at Friends' House, Euston Road, N.W.1, and the speakers will be Prof. C. F. Powell, F.R.S., of Bristol, and Dr. Alex Comfort. The address of the association is 291, Burntwood Lane, S.W.17.

Davidson Clinic, Edinburgh

A summer school on Conscience and Psychology is to be held at the clinic, 58, Dalkeith Road, Edinburgh, 9, from July 28 to Aug. 3.

Research Board for the Correlation of Medical Science and Physical Education

This board has given the William Hyde award (£300) for 1952 to Miss P. C. Colson, the general secretary to the Central Council of Physical Recreation.

Sister Kenny's Contribution to the Treatment of Poliomyelitis

Dr. M. E. Knapp, of the Elizabeth Kenny Institute, Minneapolis, will speak on this subject at Queen Mary's Hospital for Children, Carshalton, on Monday, May 10, at 5 p.m. Further particulars will be found in our advertisement columns.

Institute of Hospital Administrators

The annual conference of this institute is to be held from May 6 to 8 at Oxford. The subjects chosen for discussion are: The Patient as the Centre of the Hospital; Cooperation with other Services in Treating the Patient; and Patients' Complaints and Criticisms. Further particulars may be had from the secretary of the institute, 75, Portland Place, London, W.1.

French Documentary Film on Cancer

Sir Stanford Cade will introduce this film when it is shown at the Institut Français, 15, Queensberry Place, London, S.W.7, on Wednesday, May 12, at 8 p.m.

The film was made by Etudes Cinématographiques, under the direction of Dr. Pierre Thevenard of the Institut Pasteur, as part of the anti-cancer campaign. The 13 sections include cartoons, laboratory work with animals, acted scenes, and interviews with successfully treated patients. Tickets may be had from the scientific office of the French Embassy, 22, Wilton Crescent, S.W.1.

Association Internationale pour l'Étude des Bronches

The fourth congress of this association will be held at Geneva on June 5 and 6, under the presidency of Prof. André Montandon. The subjects chosen for discussion are: Blood-supply of the Bronchi, Classification of Bronchial Adenomas, and Surgical Treatment of Bronchial Dilatation. Further particulars may be had from the secretary of the congress, Clinique Universitaire d'Oto-Rhino-Laryngologie, Hôpital Cantonal, Geneva, Switzerland.

Human Milk Bureau.—With the help of Queen Charlotte's Maternity Hospital, London, Camera Talks (23, Denmark Place, W.C.2) have produced a filmstrip illustrating the work of the hospital's milk bureau.

Appointments

FIELD, C. M. B., M.D. Belfast, M.R.C.P., D.C.H.: consultant paediatrician, South Belfast H.M.C.
KLEIN, DOROTHY, M.B. Edin., D.O.BST.: asst. m.o., Southend-on-Sea.
RICHARDSON, J. D., M.D. Lond., D.P.M.: consultant children's psychiatrist, South Lincolnshire.
ROONEY, JEAN F. W., M.B. Dubl., D.C.H.: asst. school m.o., Bedale & Northallerton area.
SEWELL, T. P., M.D. Manx., D.P.H.: deputy county m.o.h. and deputy school m.o., Lancashire.
WATSON, JEAN M. I., M.B. Leeds, D.O.BST.: asst. maternity and child welfare m.o. and school m.o., Derbyshire.
WESTON, J. W., M.R.C.S., D.T.M.&H.: asst. pathologist (s.n.m.o.), Halifax hospitals group.
YOUNG, R. J., M.D. Belfast, M.R.C.P.: consultant paediatrician, Londonderry and north west area of Northern Ireland.

Sheffield Regional Hospital Board:

BATES, T. J. N., M.B. Dubl., D.P.M.: senior asst. psychiatrist, Saxonvale Hospital, Radcliffe-on-Trent.
CONN, HERBERT, M.D. Berlin: senior asst. psychiatrist, Kingsway Hospital, Derby.
LUMLEY, W. T. C., M.B. Lond., D.O.M.S.: asst. ophthalmologist, Chesterfield Royal Hospital and associated school ophthalmic clinics.
MONTFENNY, ISABELLE G., M.R.C.S., F.F.A.R.C.S., D.A.: consultant anaesthetist, Sheffield R.H.B. and United Sheffield hospitals.
OSTROWSKI, T. M., M.B. Polish School of Medicine, Edinburgh: senior casualty officer, Beckett Hospital, Barnsley.

Diary of the Week**APRIL 25 TO MAY 1****Monday, 26th**

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Section of Odontology.* Mr. R. L. Hartles, B.Sc.: Carbohydrate Degradation in the Mouth.

HUNTERIAN SOCIETY

7.30 P.M. (Talbot Restaurant, London Wall, E.C.2.) Mr. W. R. Le Fanu, M.A.: Hunter-Baillie Manuscripts.

MANCHESTER MEDICAL SOCIETY

9 P.M. (Medical School, University of Manchester.) *Section of General Practice.* Dr. W. E. C. Thomas: Obstetrics in General Practice.

Tuesday, 27th**ROYAL SOCIETY OF MEDICINE**

8 P.M. *Section of Medicine.* Prof. Max Rosenheim, Dr. S. J. de Navasquez, Dr. J. M. Stansfeld: Chronic Pyelonephritis.

ROYAL STATISTICAL SOCIETY

6 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) *Study Circle on Medical Statistics.* Discussion of Working Party Report on Assessment of Need for Clinical Services.

SOCIETY FOR ENDOCRINOLOGY

5.15 P.M. (1, Wimpole Street, W.1.) Dr. Gregory Pincus: Pathways of Steroid Synthesis in Animal Organism.

Wednesday, 28th**RENAL ASSOCIATION**

4.30 P.M. (41, Portland Place, W.1.) Mr. I. H. Griffiths: Renal Arteriography. Dr. Robert Gaunt: Studies on Experimental "Eclampsia-like" Syndrome.

Thursday, 29th**ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2**

5 P.M. Mr. I. P. Todd: Elective Surgery in Management of Diverticulitis of Colon. (Hunterian lecture.)

UNIVERSITY OF LONDON

5 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. E. L. French (Melbourne): Epidemiological Aspects of Murray Valley Encephalitis.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1

8 P.M. Prof. J. K. Robertson, F.R.S.C.: An Experiment in Medical Education.

INSTITUTE OF LARYNGOLOGY AND OTOLGY, 330, Gray's Inn Road, W.C.1

5.30 P.M. Prof. F. C. Ormerod: Aspects of Sinusitis.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S.E.5

5.30 P.M. Dr. Pinous: Steroids in Ageing.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY

8.30 P.M. (11, Chandos Street, W.1.) That Quackery Plays a Useful Part in Medicine Today. For: Dr. M. Marcus, Dr. S. H. Chazen. Against: Dr. D. Preiskel, Mr. I. Preiskel.

MANCHESTER MEDICAL SOCIETY

4 P.M. Prof. Bruce T. Mayes (Sydney): Could Eclampsia Disappear?

UNIVERSITY OF ST. ANDREWS

5 P.M. (Medical School, Small's Wynd, Dundee.) Mr. W. M. Dennison: Advances in Surgery of Infancy and Childhood.

Friday, 30th**ROYAL SOCIETY OF MEDICINE**

4.30 P.M. *Section of Epidemiology and Preventive Medicine.* Dr. John Gordon (Harvard): Epidemiologic Method in Modern Perspective.

8 P.M. *Section of Radiology.* Dr. E. W. Emery: Three Years' Use of a Cobalt Unit. Dr. D. Verel: Radioactive Phosphorus in Treatment of Polycythaemia Rubra Vera. Dr. F. E. Neal: Radioactive Phosphorus in Treatment of Fungoises.

FACULTY OF RADIOLOGISTS

4 P.M. (Royal College of Surgeons, Lincoln's Inn Fields, W.C.2.) Prof. D. W. Smithers: Rotation Therapy.

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12

2 P.M. Prof. A. G. R. Lowdon: Surgical Management of Intestinal Obstruction.

4 P.M. Dr. J. E. Caughey (New Zealand): Hypopituitarism.**INSTITUTE OF LARYNGOLOGY AND OTOLGY**

3.30 P.M. Mr. W. D. Doey: Indications for Tonsillectomy.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, W.1

7.30 P.M. Dr. Neville Mascall: *Trichomonas vaginalis.* (Presidential address.)

Births, Marriages, and Deaths**BIRTHS**

CHALMERS.—On April 16, at St. David's Hospital, Cardiff, to Doreen, wife of Dr. T. M. Chalmers—a son.

GIBSON.—On April 11, at The Shiel, Elgin Road, Weybridge, to Graeme (Galbraith), wife of Dr. Eric Gibson—a son.

HELSBY.—On April 12, at Liverpool Maternity Hospital, to Joyce, wife of Raymond Helsby, F.R.C.S.—a daughter.

MARIAN.—On April 14, to Biddy Kingsley Pillers, M.B., wife of Denis H. Marian, F.R.C.P.—a son.

THOMAS.—On April 13, at Plas Bowman, Caernarvon, to Nansi Wyn (née Owen), wife of Dr. R. Garym Thomas—a daughter (Amanda Claire).

DIET AND CORONARY DISEASE

J. B. DUGUID
M.D. Aberd.

PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF DURHAM

THE prevalence of coronary thrombosis in recent years has revived interest in the problem of atherosclerosis, and the question of diet as a factor is now receiving a great deal of attention. We have been so impressed by the fact that arterial lesions can be produced in animals by adding cholesterol to their food that we have been disposed to accept the diet hypothesis almost without question, and to infer from it that fatty foods are a cause of coronary disease. Nevertheless the incidence of coronary disease did not seem to decline in this country during the war when our intake of fats was restricted; nor, for that matter, do rabbits with cholesterol lesions tend to die from coronary thrombosis.

In connecting coronary disease with diet we have, I think, oversimplified the problem and taken too much for granted. We have assumed that atherosclerosis represents a single disease process referable to some particular combination of causes, whereas it can now be shown that lesions which go by that name may be the outcome of at least two different processes, with causes which may be quite unrelated to one another. This point, although mentioned as a possibility by White and Ferrero (1949) and by Shillingford (1952), has never been clearly brought out; but unless it is taken into account it is hardly possible to judge where diet may come into the picture. Let us compare, for example, the common form of coronary atherosclerosis with the lesions produced in rabbits by cholesterol feeding. Here I shall repeat, with fresh materials, a demonstration already made (Duguid 1946), because it illustrates certain principles which must be kept clearly in mind.

Coronary Atherosclerosis

The term atherosclerosis refers to a lesion of variable morphology but with two essential characters—namely, fatty change and fibrous thickening of the intima. Sometimes the one character is predominant and sometimes the other; but, in the form of coronary disease with which we are mainly concerned, fibrous thickening is the outstanding one, involving, as it often does,

extreme narrowing of the vessel; and this, as I shall show, is a feature of crucial significance.

When the coronary arteries from cases of long-standing cardiac infarction are examined, occasional examples of canalised thrombi are found in which the affected vessels have two or more channels instead of a single lumen (fig. 1). In these it will often be noted that the fibrous tissue which separates the channels, and which obviously represents organised thrombus, merges with the intima so that the two are indistinguishable. Further, if serial sections are made, a point is reached where the channels unite to form a single lumen; and there it is found that the same organised thrombus extends along the vessel as an inner lining which looks like a fibrous over-growth of the intima (fig. 2). The thrombus has in fact become part of the intima, and the appearance is that of a thickened artery.

The same thing happens with mural thrombi, which are much commoner than these producing total occlusion. When a mural thrombus forms in an artery it becomes covered with endothelium so that it is incorporated in the vessel wall, with the result that when it is subsequently organised it forms a fibrous thickening of the intima. Since most mural thrombi, before being completely organised, undergo fatty degeneration—sometimes with atheromatous softening and ulceration—they acquire all the characters of atherosclerotic plaques, and we thus learn that some of the lesions we classify as atherosclerosis are in fact organised, or partly organised, mural thrombi. It should of course be understood that most mural thrombi are very small, consisting of no more than microscopic layers of fibrin; but these, when laid down repeatedly one on top of another, can give rise to considerable thickenings of the vessel walls; and this appears to be the sequence of events in many examples of atherosclerosis.

These observations have now been confirmed in one way or another by a number of observers including Harrison (1948), Heard (1952), Geiringer (1951), McLetchie (1952), and Crawford and Levene (1952), and we may safely take it that thrombosis is one factor in the pathogenesis of atherosclerosis. That this has been overlooked in the past is due, I think, largely to the presence of fatty changes. We have not been accustomed to associate these with thrombosis, and their presence has prevented us from recognising the thrombi as such.

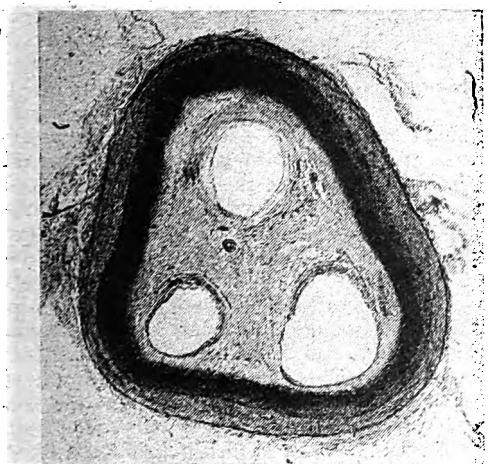


Fig. 1.

Canalised left coronary artery from man of 61 who had an infarct of his left ventricle of about 2 years' duration. (Frozen section : Sudan IV and haemalum. $\times 12$.)

In fig. 1 the lumen is occupied by a mass of fibrous tissue which represents an organised thrombus with three separate channels.

In fig. 2, from a point less than 1 mm. distant, the channels have joined to form a single lumen while the thrombus now appears as a fibrous thickening of the wall.



Fig. 2.

Nevertheless fatty changes can be shown to be an almost constant feature of mural thrombi, not only in the arteries but in the heart, including endocardial vegetations, and "in venous thrombi of all kinds," as Cohnheim long ago remarked. The fats, which vary in amount, are presumably derived from the lipids present in the blood when the thrombi are formed.

Cholesterol Sclerosis in Rabbits.

It is generally assumed that arterial thrombosis depends on some underlying lesion of the vessel wall, and a common example in the larger arteries is fatty change. To see whether cholesterol lesions would lead to thrombosis in rabbits Dr. I. Rannie and I have recently repeated the classical feeding experiments and studied the lesions in various stages of development. Rabbits were given 1.5 grammes of cholesterol daily in addition to their ordinary diet and killed after periods ranging from six weeks to more than a year. No mural thrombi were found, but much useful information was obtained from the experiments.

By the end of the sixth week there were changes in the aorta and pulmonary arteries consisting of small deposits of cholesterol-bearing phagocytes (foam cells) in the subendothelial layer of the intima, chiefly near the openings of branches. By the twentieth week the lesions were usually widespread and severe, with great accumulations of foam cells in the intima, often swelling the vessel wall to many times its normal thickness. In the superficial zones the foam cells were deposited in layers of variable thickness, with layers of spindle cells between forming a kind of stroma. In the deeper zones there was often complete disorganisation, the foam cells having disintegrated, leaving atheromatous masses of cholesterol and other fatty debris in their place. In rabbits allowed to survive more than a year the cholesterol had mostly disappeared, leaving dense fibrous thickenings of the intima, so that the condition could with every justification be termed atherosclerosis.

Our findings (Rannie and Duguid 1953) agree in general with those of other observers, but our interpretation embodies a somewhat unorthodox conception. It should be explained that authorities have differed in their views on the process by which cholesterol gets into the walls of the arteries. Duff (1936) and Hueper (1944) believed that it is precipitated from the tissue fluids and taken up by the intimal phagocytes, whilst Altschul (1950) thought that it is absorbed from the circulating blood into the lining endothelial cells and carried by them into the intima. In 1941 Leary put forward the view that in rabbits with hypercholesteræmia foam cells, probably derived from the liver, circulate in the blood and adhere to the arterial walls, which they then actively invade. Our findings supported this in all but the last particular. We saw convincing evidence that the cells in question were present in the blood and adhered to the vessel walls, but we came to the conclusion that instead of invading these, they simply become covered with endothelium and were thus passively incorporated in the same way as mural thrombi. In our view the advanced lesions were formed by successive deposits of foam cells heaped one on top of the other, with occasional layers of endothelial cells laid down between. The atheromatous foci were produced by the breakdown of older and more deeply buried deposits.

The Endothelial Reaction

The important point to be gathered from the foregoing comparative study is that atherosclerosis can arise by two different processes; mural thrombosis on the one hand, and the deposition of lipids, or lipid-bearing cells on the other. This alone should make us cautious in assigning causes. Two further points are I think worth recording although they are contingent on our own

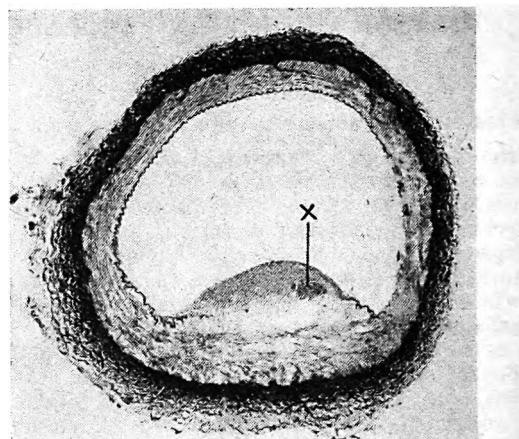


Fig. 3.—Dog's femoral artery into which a silk thread (x) has been inserted and then passed down the lumen. The thread is surrounded by organised thrombus which has been incorporated in the intima to form a fibrous thickening. (Paraffin section : Weigert's elastic tissue stain. $\times 20$.)

interpretation. The first is that in both processes the mechanism, in so far as the arteries are concerned, is the same; solid matter is deposited on the intimal surface and in due course covered with endothelium and incorporated in the intima. That this is a natural reaction of arteries to the presence of solids in their lumen can be shown by inserting a silk thread into the femoral artery of a dog. The thread becomes fixed to the intimal surface with fibrin and the whole mass covered with endothelium and organised, so as to produce a fair imitation of an atherosclerotic nodule (fig. 3) but with silk instead of fat in its centre. The reaction provides an effective means of disposal of undesirable solids from the blood-stream.

The second point is that in none of the processes are the thickenings the result of changes in the original tissues of the vessel wall, as visualised in the current conception of atherosclerosis. All are products of substances deposited on the intimal surface; and thus, if our interpretations are correct, we may take it that atherosclerosis is not a specific disease but merely the common end-result of a number of different pathological processes with different causes.

The Pathogenesis of Human Atherosclerosis

The development of cholesterol lesions has been demonstrated in rabbits, but there is reason to believe that something of the same kind occurs in man, although not necessarily as a result of diet. The "xanthomatous" deposits which appear in the arteries in familial hypercholesteræmia are probably the exact counterpart of the rabbit lesion, but they are too rare to be of much account in the pathology of atherosclerosis. A much commoner lesion of similar morphology is the so-called superficial fatty streaking which occurs in the aortas of young subjects. This consists of deposits of fat-laden cells in the subendothelial layers of the intima, chiefly around the openings of branches, producing an appearance so like the early cholesterol lesions that it is difficult to avoid the conclusion that the same process is involved.

Similar changes are seen in older subjects; but in them they tend to be obscured by advanced atherosclerosis and are therefore difficult to interpret. All observers will agree, however, that in human atherosclerosis changes take place which cannot be put down to thrombosis; and some of them, we may suppose, are of a primary fatty nature, analogous to the cholesterol lesions of rabbits.

Thus we may take it that in man there are two pathogenetically distinct forms of atherosclerosis, and

before arriving at any conclusions as to causation we must have some means of distinguishing them and assessing their relative incidence. Unfortunately most of the lesions we find in human arteries are of long standing, and have passed through a succession of changes which obscures their origin; but sometimes certain distinguishing features persist, and one of them is narrowing.

Arterial Narrowing

The narrowing of arteries in atherosclerosis is a feature which has puzzled observers for the past century. If we accept the long current view that the condition represents a degeneration of the vessel walls, then narrowing seems paradoxical. Arteries are especially constructed to withstand a high internal pressure which is constantly pulsating, and it is their elasticity * which enables them to dilate and recoil again to their original size at each pulse wave, without becoming progressively distended. Any change which weakens them or reduces their elasticity must therefore cause them to give way and dilate rather than become narrowed. Yet in atherosclerosis they are often narrowed almost to the point of occlusion and, as I have reasoned (Duguid 1949), it is difficult to explain this on any other grounds than thrombosis or embolism. When a thrombus forms in an artery it occupies the lumen from the outset and so narrows the blood-stream; and, although in due course it becomes part of the vessel wall, it does so at the expense of the lumen. In this process there is no weakening of the vessel, but merely a reduction of its effective lumen; and, although the thrombus may subsequently shrink, and the lumen become widened again, narrowing must, for a time at least, be the rule.

With the cholesterol lesions it is different, because in them there is no sudden reduction of the lumen but merely a gradual silting up of the walls with foam cells. This must have the effect of reducing their elasticity,

and so we find the rabbit's arteries dilated when they are loaded with cholesterol (fig. 4). An exception to this is sometimes provided when small arteries and arterioles become plugged with foam cells, as may happen in the myocardium. In vessels of small calibre a few such cells are often enough to occlude the lumen and bring about a condition equivalent to embolism, but it is usually in very small branches that this occurs and the effects are negligible. When the larger coronary arteries are the seat of cholesterol deposits, dilatation is the rule; and this is one of the most significant points brought out by the experiments. It has always been assumed that fatty changes lead to narrowing of the arteries by increasing the intima so that it encroaches on the lumen, but the cholesterol lesions show that this is not what happens. Thickening of an artery merely impairs its resilience and leads to dilatation. The only process likely to reduce its lumen is one arising in the lumen itself, such as thrombosis or embolism, and we may therefore take it that, where a coronary artery is narrowed by a fibrous thickening of the intima, thrombosis is the most likely factor.

Narrowing as a Feature in Human Atherosclerosis

Thirty years ago pathologists were inclined to look on atherosclerosis—or atheroma as it was then called—as a minor lesion, universal in old age, and only occasionally attended by serious consequences such as cerebral haemorrhage. In course of time, however, its association with gross myocardial infarction came to be more widely recognised, and today it is regarded as one of the most deadly of lesions, because it leads to narrowing of the coronary arteries with impairment of the cardiac circulation and a tendency to sudden death from thrombosis. Yet these effects are by no means a constant feature of the condition. In old people we often see extreme atherosclerosis with widespread destruction of the arteries but little or no narrowing, and conversely we occasionally find points of extreme narrowing in arteries which are otherwise not very severely affected. There are, in fact, two forms of atherosclerosis—one in which there is narrowing, and which is consequently a highly dangerous condition, and another in which the tendency is rather in the opposite direction.

It would be convenient if we could correlate these two forms with what we have learnt of the pathogenesis, and so infer that all lesions with narrowing were thrombotic, and all others were of a primary fatty nature; but this we cannot do, because thrombotic lesions do not always remain narrowed. Thrombi shrink as they become organised, and arteries which have been narrowed become widened again—sometimes to beyond their original size. Moreover, it is only when thrombi are large in proportion to the vessels they occupy that narrowing is much in evidence. The great majority of mural thrombi consist of no more than microscopic encrustations of fibrin which are too thin to reduce the lumen appreciably. They may if laid down repeatedly on top of one another, give rise to considerable thickenings; but these do not encroach on the lumen to any extent, because such thickenings, by reducing elasticity usually lead to dilatation, and this more than compensates for any encroachment. Thus the arteries of aged people are commonly dilated although many of the lesions in them are obviously thrombotic.

Narrowing is therefore by no means a constant feature of arterial thrombosis; but nevertheless when present it is a fairly sure sign of that process, and, since it is only when there is narrowing that atherosclerosis is likely to be dangerous, it follows that thrombosis is the one factor of importance in fatal coronary disease. When we consider all the possible ways in which thrombosis may be influenced by diet we shall cover a large part of this very involved problem.

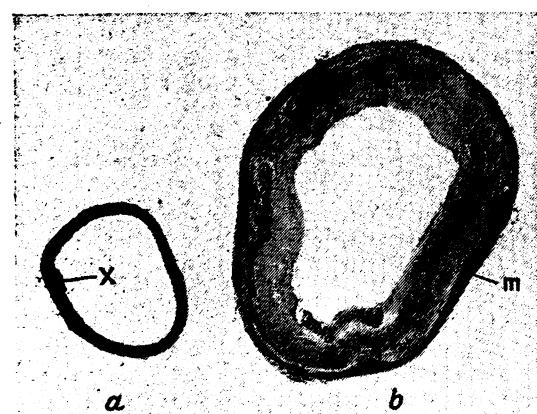


Fig. 4—Ascending aortas from two rabbits illustrating the dilatation which results from cholesterol-loading. (Frozen sections: Sudan IV and haemalum. $\times 6$.)

(a) Aorta from rabbit weighing 2800 g. which was on cholesterol treatment for 7 weeks. One small deposit of foam cells is seen at (x) the vessel being otherwise normal. Almost the whole wall consists of medial coat, the intima comprising no more than a single layer of endothelial cells.

(b) Aorta from rabbit weighing 2200 g. after $9\frac{1}{2}$ months' cholesterol treatment. Most of the wall consists of thickened intima; the media, which is greatly stretched, is represented by the thin dark line (m) at the periphery. (It should be explained that the contrast in diameter is probably somewhat accentuated by post-mortem contraction in the more normal vessel, the thickened vessel being fixed in the position of maximum dilatation by the almost rigid intima.)

* It should be explained that the term elasticity as applied to arteries does not refer to the so-called elastic tissue in their walls but to the resilience of the walls as a whole.

Thrombosis and Diet

There are two ways in which diet may conceivably play a part in arterial thrombosis. Firstly it may, by affecting the coagulability of the blood, increase the tendency to clotting; and secondly, by causing fatty changes in the arteries, it may promote mural thrombosis.

The first possibility has recently been suggested by Fullerton, Davie, and Anastasopoulos (1953) who showed that the alimentary lipæmia which follows fatty meals is accompanied by an accelerated clotting-time in vitro. The same was also found by Waldron, Beidelman, and Duncan (1951). As Fullerton and his co-workers point out, a factor of lipid nature is concerned in blood coagulation, and an excessive intake of fat may perhaps increase it. It is well however to recall that there is also a lipid-inhibiting factor in coagulation; and the probabilities may thus cancel out. We do not yet know whether an accelerated clotting-time in vitro actually signifies an increased tendency to thrombosis, and any hypothesis of this kind is difficult to put to the test; but we may justifiably take the evidence of cholesterol experiments, since it is on them that the diet hypothesis mainly rests; and, as it happens, they provide no confirmation. In none of the rabbits were arterial thrombi to be found, in spite of the fact that cholesterol—the substance most frequently cited as the dangerous food constituent—was greatly in excess in the blood. We can only await further information on this point, especially with regard to the phenomenon of coagulation in other species.

The second possibility—that diet may lead to mural thrombosis by damaging the arterial walls—is of course the root of the diet hypothesis. Fatty lesions have long been regarded as the cause of mural thrombosis, and Rannie and I undertook the feeding experiments in the hope that we might demonstrate thrombi in relation to the cholesterol lesions and so bring these into line with coronary disease. But in this we were disappointed. Despite extreme disorganisation of the vessels, there were never any fibrin formations, and we were forced to conclude that neither an excess of cholesterol nor the consequent arterial lesions were in themselves sufficient to promote thrombosis in rabbits.

Nevertheless there can be little doubt that in man arterial lesions play a part in the development of mural thrombosis, for we almost never find such thrombi without some underlying fatty change. Some of the fatty changes are themselves secondary products of thrombi; but others are almost certainly of a primary nature, and, if not dependent on diet, are at least related to some disturbance of the fat metabolism. Superficial fatty streaking of the aorta is probably in this category, and it is not infrequently attended by fine fibrinous encrustations on the aortic surface (Duguid 1948). It can hardly be put down to diet, since it is mostly found in young subjects who have died from acute febrile conditions in which an excessive intake of rich foods is unlikely; but as I have said, lesions of a very similar kind can be seen in older subjects and some of them may be of dietary origin. We know that old people tend to have abnormal lipids circulating in their blood after heavy meals, and they may perhaps get into the arteries and lead to thrombosis. Such is of course the conception on which the diet hypothesis is based, and it is one that cannot be entirely discounted; but it leaves out of consideration one point of paramount importance with regard to vascular thrombosis, and that is its inherent variability.

Factors Governing Arterial Thrombosis

We have seen that the cholesterol lesions do not lead to thrombosis in rabbits, and this is quite in keeping with what we frequently find in man. Few observers can have failed to be impressed with the fact that there

may be widespread atherosclerosis of the aorta and other vessels, even with ulceration, and yet little or no thrombosis. We have been given to understand that the rapidity of the blood-stream in the larger arteries limits fibrin formation, and this is perhaps to some extent true; but when on occasion we find quite large mural thrombi in these same vessels, in people who have been active up to the time of death, speed of blood-flow does not seem to be the whole explanation.

To anyone who tries to produce arterial thrombosis in animals by injuring the arteries it becomes evident that there are refractory states, in which thrombi will not readily form, even with severe damage, and irrespective of the speed of the blood-flow. There are also states in which thrombi, having formed, rapidly disappear; and it would seem that there are factors in the blood—possibly anticoagulant substances, or possibly fibrinolysins as suggested by Mole (1948)—which in favourable circumstances control fibrin formation, and so make arterial lesions potentially less dangerous.

On the other hand there are the converse states, which may be described as thrombophilic. In cases of sudden death from coronary thrombosis I have several times noticed that the thrombotic process was not confined to the site of occlusion in the one coronary artery, but was widespread and prominent in the aorta and other vessels. This suggests that, when the fatal occlusion occurred, some thrombogenic influence, more powerful and generalised than mere local damage to the vessel walls, was at work; and this I believe is the factor we must aim at controlling if we are to reduce the incidence of coronary disease.

Undoubtedly intimal lesions are a contributing factor in mural thrombosis; but they are not the controlling factors, for there is no consistent correlation between the severity of the lesions and the size of the thrombi. Sometimes quite large masses of fibrin are formed on lesions which seem comparatively insignificant, and vice versa. It is obviously not the underlying lesion but some factor in the blood that determines how large the thrombus shall be, and that is what counts in so far as vascular impairment is concerned.

The Danger of Fatty Lesions

In the past we have looked on coronary thrombosis as a complication of atherosclerosis, but we must now regard it as a factor in this condition. Where there is much narrowing of an artery there is usually evidence of recurring mural thrombosis; and, while we may suspect that the process arises in the first place on some primary fatty lesion, its subsequent progress is simply a succession of one mural thrombus leading to another. Thus if a primary fatty change comes into the picture, it may be only at the initial stage, and long before the disease has begun to assume dangerous proportions.

With these considerations in mind one is less inclined to attach much importance to the presence of fatty changes. As Geiringer (1950) and others have shown, such changes are an almost constant feature of the aorta from childhood onwards, and we know that they are compatible with long life. They may, it is true, provide the foci in which thrombi develop, when conditions are set for thrombosis; but their severity seems to be a matter of minor importance. Fatal thrombosis is more likely to occur in a coronary artery which is narrowed by a dense fibrous thickening as in (fig. 2) than in one which is very fatty.

The Basis of the Diet Hypothesis

The idea that atherosclerosis is connected with diet arose out of an impression that fatty changes in arteries were prevalent in diabetics, gouty persons, alcoholics, and fat people who had presumably lived well; but we now know that some of the fats which appear in athero-

sclerosis are products of thrombi and are therefore secondary. Since they are probably derived from the lipids present in the blood when the thrombi are formed, it is not surprising that they should be prominent in diabetics and others who are prone to lipemia. They may in fact be related to diet and yet have nothing to do with the cause of atherosclerosis.

In more recent years the mainstay of the diet hypothesis has been the cholesterol experiments. The fact that arterial lesions can be produced by giving an excess of a normal metabolite seems to put the hypothesis on an unassailable footing until we examine it critically. When we do so we merely find that to produce the lesions far more cholesterol is needed than is ever likely to be derived from a normal human diet, and that when produced these lesions are not of the kind which leads to vascular insufficiency.

The hypothesis therefore rests on slender foundations, and we have, I think, allowed ourselves to be too much influenced by it in our approach to the problem of coronary disease. Certainly much valuable information about the metabolism of fats has been collected, but before we can apply it to coronary disease we must be clear in our minds as to what we mean by that term. If we simply mean fatty changes in the coronary arteries, then we refer to a condition which is almost universal in adults. It may perhaps be related to diet, although there is no clear evidence on that point, but it is not the condition responsible for cardiac impairment and sudden death.

This problem will remain confused until it is more generally recognised that there are two different forms of atherosclerosis involving different pathological processes. They may present similar histological pictures, and they are often indistinguishable, but they are vastly different in their causes and effects. The form with which we are mainly concerned is the one which leads to coronary occlusion, and we know that in this form thrombosis is the important factor. It is possible that diet may have some effect on thrombosis, since nutrition must be a factor in most biological processes; but, when there are so many other important factors to be considered, there is a danger in allowing ourselves to be led too far along this line of approach by what may be a misleading hypothesis.

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"I should like to suggest that intelligent behaviour may admit of differences in kind as well as in degree. For me, intelligent activity consists in grasping the essentials in a given situation and responding appropriately to them. This can scarcely claim to be a definition and it is certainly not precise. I prefer 'intelligent activity' to 'intelligence' because I wish to avoid the suggestion of some one trait which an individual simply possesses, to a greater or lesser extent. I use the word 'activity' in its widest sense, not necessarily implying activity which is overt at the time."—A. W. HEIM, *The Appraisal of Intelligence*, London, 1954, p. 29.

AUGMENTED RESPIRATION AN EMERGENCY POSITIVE-PRESSURE PATIENT-CYCLED RESPIRATOR

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THE principle of augmented respiration—in which spontaneous respiratory effort is amplified—has already been discussed, and the servo respirator used for the purpose has been described (Donald and Lord 1953). Experience has shown, however, that in treating respiratory difficulties in the newborn there is also need for an emergency type of apparatus which can be brought into action more rapidly. The servo respirator is not always readily available, and the staff who can handle it have to be mustered. Moreover, in spite of our efforts to forecast the likely course of events, with the help of radiography (Donald and Steiner 1953) and spirometry, delays often arise from the difficulty of deciding whether the baby really needs to be put in the servo respirator. When signs of respiratory distress develop—usually soon after delivery—it is far from easy to say whether spontaneous recovery is likely to take place; and in some cases a series of cyanotic attacks may be the first warning of trouble.

Of the 28 infants so far treated with the servo respirator, those whose treatment began before the age of three hours have done much better than those treated later.

In table I asphyxial deaths include cases of atelectasis (with and without hyaline membrane formation), and cases of intraventricular haemorrhage, which is nearly always the result of asphyxia (Claireaux 1953b), and then operates as a secondary cause of further asphyxia. In 7 cases the infants were non-viable, being of less than twenty-eight weeks' gestation; and, since there was no question of their maintaining respiration, treatment was started without delay. Hence they all appear in the group in which treatment was started before the age of three hours. In this group 1 viable child died of hyaline membrane, and in this instance the respirator had failed mechanically.

To cover delays in preparing the servo respirator or to meet respiratory emergencies we clearly needed a respirator which could be operated at once via a mask, with the child still in its cot or incubator.

Our routine treatment of a cyanotic attack consists in pharyngeal, oesophageal, and gastric aspiration, with administration of gastric oxygen; but, if the child does not quickly revive, a respirator is used. Intubation of premature or very sick neonates is not well tolerated, and, without intubation, positive pressures applied to the face without regard to the timing of the child's respiratory efforts tend simply to drive air or oxygen down the oesophagus into the stomach. If on the other hand, a positive pressure is applied synchronously with contraction of the diaphragm in inspiration, it closes the

TABLE I—RESULTS WITH SERVO RESPIRATOR (28 CASES)

Weight (lb.)	Age under 3 hours 10 + (7) cases		Died from other causes	Age over 3 hours 11 cases		Died from other causes
	Lived	Died from asphyxia		Lived	Died from asphyxia	
-2	0	(2)	(4)	1	0	0
2-3	4	1 + (1)	0	1	1	1
3-4	4	0	0	1	2	1
4-5	1	0	0	0	1	1
5+	0	0	0	0	1	0
Total	9	1 + (3)	(4)	3	5	3

Figures in parentheses indicate preivable foetuses of less than 28 weeks' gestation.

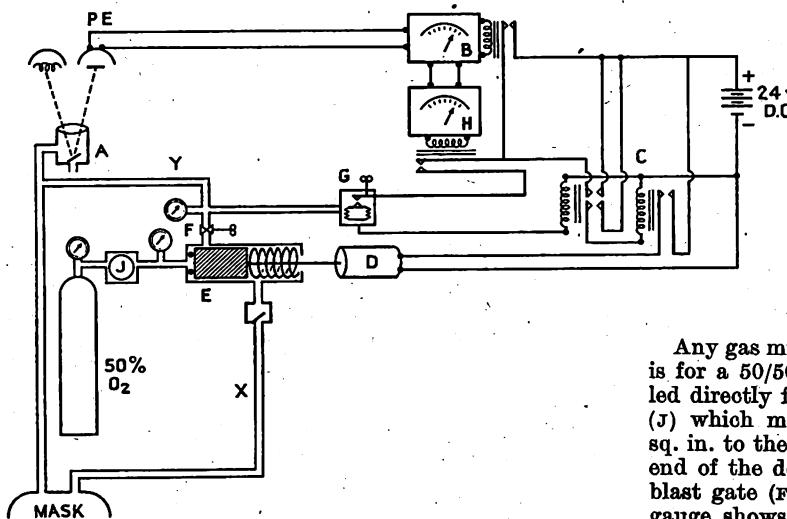


Fig. 1—The electrical circuit.

lower end of the oesophagus and allows the gases to take their intended route to the lungs—which alone are likely to achieve rapid oxygenation of the blood. The principle of augmented respiration therefore applies.

The Apparatus

For short-term emergency treatment we now use a positive-pressure patient-cycled respirator—known locally as "the puffer."

As in the servo respirator, the triggering of intermittent pressures is achieved by a photo-electric mechanism, in which the flap of the inspiratory valve consists of a mirror (A) (figs. 1 and 2) whose slightest movement deflects a light-beam from a photo-electric cell (P.E.). The beginning of an inspiratory effort thus causes a change in voltage output from the cell. This is amplified (B) to operate the electromagnetic relay system (C) which controls the solenoid (D). The solenoid moves the piston valve (E), which not only closes off the exhaust pipe (X) from the face-mask but opens the delivery pipe (Y) through which a suitable gas mixture is fed under direct pressure to the face-mask. A blast gate (F) adjusts the rate of flow of gas. By means of an aneroid switch (G), which interrupts the circuit, pressures are prevented from exceeding a pre-set maximum.

The amplifier (B) includes the refinement of a "paralysis time" circuit which introduces a refractory phase and allows the amplifier to pass on only the first impulse from the photo-electric cell and to reject all others over a pre-set period—usually about a second. This prevents false and repetitive triggering.

A "hold-in" time circuit (H), in this case an 'Elcontrol Weld Timer' switch, is also necessary to keep the solenoid in action for a predetermined period after each triggering—in case sufficient pressure is not built up to operate the aneroid switch (G). H and G are connected in series so that the circuit shall be interrupted by the aneroid pressure cut-out switch or by the hold-in timer, whichever operates first. In other words, if the maximum permitted pressure is achieved before the hold-in time has expired, the solenoid will be inactivated, the spring behind the piston valve will shut off the supply of compressed gas mixture, and the expiratory pipe will be opened; but if (perhaps

because the mask does not fit) the pre-set pressures are not achieved within the hold-in period, the time switch will first interrupt the supply of gas. This prevents the solenoid from holding the piston valve in the open position which would otherwise continue indefinitely and waste the gas mixture.

The hold-in time and the paralysis time must not be allowed to overlap, and the former must be adjusted not to equal or exceed the latter.

Thus at the completion of each cycle, the apparatus is ready to respond to the next triggering from the inspiratory valve.

Any gas mixture can be supplied. Our usual preference is for a 50/50 mixture of oxygen and nitrogen, which is led directly from a cylinder to a pressure-reducing valve (J) which maintains a delivery pressure of 1.8 lb. per sq. in. to the piston valve. The pressure at the proximal end of the delivery pipe to the mask is adjusted by the blast gate (F) to about 30 cm. of water. A manometer gauge shows the pressures achieved in the mask itself, and these are usually about 15 cm. of water, though different pressures can be achieved at will. The mask is simply a soft rubber U.S. Army resuscitation mask applied *upside down* so that the baby's chin fits into the apex which would normally lie over the bridge of an adult's nose. The base of the mask lies over the baby's forehead, and with a very little practice almost any size or shape of face can be satisfactorily fitted. The mask can be lightly held in place by spreading the fingers round the sides.

The aneroid switch controlling the maximum permitted pressure, and the "hold-in" and "paralysis" times seldom require adjustment, and all that is necessary in a given emergency is to switch on the apparatus, turn on the gas supply, and (having aspirated the pharynx) apply the mask to the face—the whole operation taking no more than a minute.

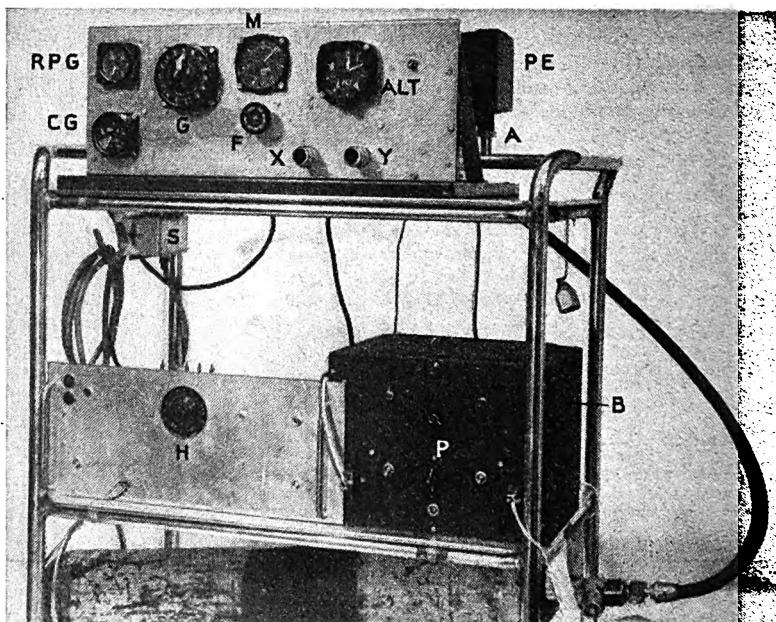
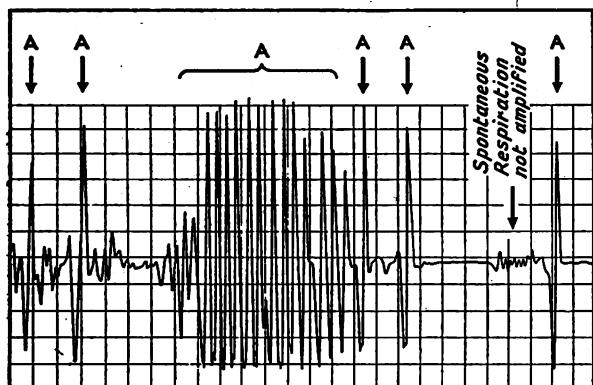
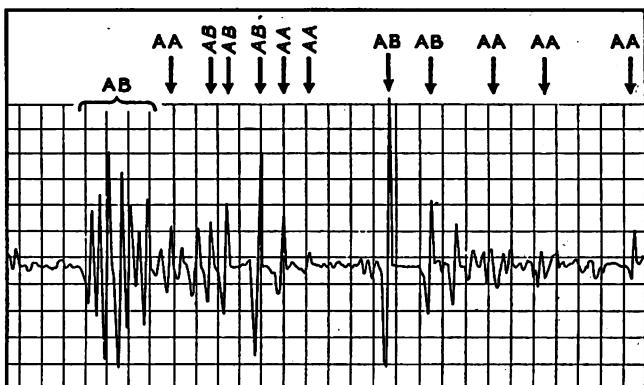


Fig. 2—Photograph of the puffer respirator.

- A. Inspiratory mirror flap valve.
- P.E. Photo-electric cell box.
- B. Amplifier.
- ALT. Altimeter barometer.
- X. Exhaust pipe } to mask.
- Y. Delivery pipe } to mask.
- F. Blast gate.
- G. Aneroid cut-out switch.
- P. Paralysis-time controls.
- H. Hold-in time control.
- M. Manometer (cm. H₂O X 10).
- C.G. Cylinder gauge.
- R.P.G. Reduced pressure gauge.
- S. Switchbox.



(a)



(b)

Fig. 3 (case U.C.)—Tracings obtained with Smyth anemometer. (a) Spontaneous respiration amplified at A with puffer. (b) AA = non-triggered amplification. AB = patient-triggered amplification.

If the baby has stopped breathing altogether, and for the moment there is no respiration to amplify, an occasional pinch and release of the delivery tube (γ) is sufficient to trigger off a surge of positive pressure to the mask. This has none of the advantages of augmenting respiration; but when the baby does take a breath, even though small, that breath will instantly be increased.

Fig. 3 shows that much greater ventilation is achieved when spontaneous respiration is amplified than when gases are supplied under pressure without regard to the child's own respiratory efforts. This tracing was made at University College Hospital by Dr. Norman Smyth who applied his nasal anemometer apparatus underneath my mask. It gives an indication of the rate of flow of gas through the nostrils.

Application in the Adult*

Although the apparatus was originally intended for babies, my colleagues in the department of medicine of the Postgraduate Medical School, Dr. Russell Fraser and Dr. Charles Fletcher, encouraged me to adapt it for adult use. This was done quite simply by fitting alternative large-bore delivery pipes. It was not long before an opportunity arose for treating an adult, and I am indebted to Prof. Ian Aird for permission to describe the following case.

The patient, a woman aged 62, had a straightforward cholecystectomy. A curare derivative was used to obtain relaxation, and after the operation, which lasted just over an hour, spontaneous respiration did not return, despite intravenous injection of nikethamide, atropine, and neostigmine. For more than five hours artificial respiration was continued by rhythmic squeezing of the bag of the anaesthetic machine, and during this time a total of 8.5 mg. neostigmine methyl sulphate and atropine gr. $\frac{1}{12}$ was given. After three and a half hours feeble spontaneous respiration began, but it was inadequate without continued assistance and a cabinet respirator was sent for.

About five and a half hours after the operation, while the arrival of the cabinet respirator was awaited, the puffer was applied, the patient's spontaneous respiratory efforts being sufficient to operate the sensitive trigger mechanism. Her colour at this time was somewhat grey. After five minutes' treatment with the apparatus an adequate depth of respiration was achieved, and this was maintained thereafter spontaneously. The corneal reflex returned and half an hour later she was returned to the ward showing signs of regaining consciousness. The systolic blood-pressure now dropped precipitately to 60 mm. Hg, but her general condition responded to routine resuscitative measures. Convalescence was complicated by a small pulmonary embolus after the first postoperative week, but was then straightforward.

In this case the use of the apparatus was immediately followed by return of adequate spontaneous respiration.

The patient was not intubated at the time, and if, as I think probable, she was suffering from prolonged pulmonary underventilation, with accumulation of carbon dioxide, her recovery may well have been due to removal of this carbon dioxide with the help of the apparatus.

Results in the Treatment of Neonates

Up to the end of 1953, 25 cases had been treated with the puffer. Of these, 4 were also (and mainly) treated with the servo respirator and therefore appear in table I. The remaining 21 cases are analysed in table II.

It is our practice to keep the puffer standing by, adjusted and ready for immediate action in cases of severe prematurity or where attacks of respiratory failure threaten. Certain members of the nursing staff in the Premature Baby Unit at Hammersmith Hospital are now capable of handling the apparatus well and have repeatedly been able to restore satisfactory respiration and oxygenation before medical help arrived.

It must here be repeated that the apparatus is not used without first thoroughly aspirating mucus from the pharynx.

NON-SURVIVING CASES

Intraventricular haemorrhage was the predominant cause of death in 4 of the 14 non-surviving cases and hyaline membrane was also present in 2 of them. One had a tear of the tentorium. Except in one of the cases demonstrating hyaline membrane in marked degree, all lobes of the lungs floated at necropsy. In 3 of the above cases the period of gestation was less than twenty-eight weeks and the infant was therefore not viable.

Atelectasis with hyaline membrane was responsible for death in a further 5 cases, in 2 of which intraventricular haemorrhage was also a contributory factor. In a 6th case hyaline membrane was present but the primary cause of death was intrapulmonary haemorrhage.

The following case is worth quoting because a mild degree of pulmonary damage was sustained.

TABLE II—RESULTS WITH PUFFER ALONE (21 CASES)

Weight (lb.)	Lived	Hyaline membrane	Intraventricular haemorrhage	Hyaline membrane and intraventricular haemorrhage	"Asphyxia" unspecified	Intrapulmonary hemorrhage
-2	0	0	(1)	(1)	0	0
2-3	3	1	0	(1)	0	1
3-4	1	1	1	1	1	0
4-5	2	1	0	1	0	1
5+	3	0	0	0	0	0
Total	9	3	1 + (1)	2 + (2)	1	2

*A fair copy of my prototype apparatus is now being developed by British Oxygen Company Ltd.

Figures in parentheses indicate preivable fetuses of less than 28 weeks' gestation.

Case Lo2.—The second of twins; breech delivery at thirty weeks' gestation; birth-weight 2 lb. 10 oz. At birth lively and pink, but signs of inspiratory recession of the chest wall developed within half an hour. Radiographs taken at one hour, six and a half hours, and eighteen hours showed the evolution of signs which we have come to associate with the development of hyaline membrane. The child was treated repeatedly with the puffer and then transferred to the servo respirator from which it was removed at the age of thirteen and a half hours because its condition then seemed satisfactory. One hour later, however, its condition was again very poor. It was repeatedly aspirated, and revived with the puffer.

After replacement in the servo respirator, the child appeared to progress fairly well throughout the day until one of the valves in the apparatus jammed. The puffer was now connected with the head chamber in order to supply positive-pressure assistance. Meanwhile the faulty valve was repaired.

All went well thereafter until the age of twenty-four hours when a series of cyanotic attacks recurred. At twenty-five hours the child was again breathing very well without augmentation. During the next four hours the colour gradually deteriorated but the respirator was not switched on again because the breathing appeared to be fairly regular. At twenty-nine and a half hours the child died in a prolonged apnoeic attack which both machines operating simultaneously failed to modify.

At necropsy there was severe emphysema of the left lung. Four large bullæ were present in the posterior medial margin of the left upper lobe and there were numerous smaller emphysematous bullæ throughout this lobe. The use of servo respirator and puffer simultaneously may have been responsible for the emphysema. Dr. Claireaux, who performed the necropsy, did not regard the emphysema as the cause of death and he reported extensive hyaline membrane. There was no pneumonia.

There were 3 cases in which the cause of death could not be definitely determined other than as "asphyxia." One of these infants weighed only 1 lb. 6 $\frac{3}{4}$ oz. and, having been treated in the servo respirator as well, is included in table I. Pulmonary aeration was no more than moderate in all of them, but all lobes of the lungs floated at necropsy. The usual picture histologically was that of areas of atelectasis alternating with areas of over-distension.

SURVIVING CASES

Of the 11 infants who survived, 2 were also treated in the servo respirator and therefore appear in table I instead of in table II. The largest weighed 5 lb. 8 $\frac{1}{2}$ oz. and the smallest 2 lb. 6 oz. The indications for treatment were the appearance of severe and increasing inspiratory recession of the thoracic wall, the development of apnoeic and cyanotic attacks, or very shallow and infrequent breathing associated with clinical signs of cyanosis. As these babies survived it is impossible to discuss the underlying pathology treated.

Case Na. Weighing 2 lb. 6 oz., was delivered in a nursing home at thirty weeks' gestation and was admitted aged eighty minutes. The condition deteriorated at three and a half hours and multiple cyanotic attacks necessitated the use of the puffer intermittently at each attack during the first three days of life. Radiographs showed fine miliary stippling of the lungs which became more conspicuous and coarser by ten hours but cleared by sixty hours. At the age of twenty-three days the child developed pneumonia but recovered and has since done well.

Case Va was delivered spontaneously face to pubis at thirty-nine weeks' gestation and weighed 4 lb. 15 oz. The condition at birth was one of shock and the child was intubated. Positive pressures were applied endotracheally by the usual routine method for sixty minutes without spontaneous respiration becoming established. The puffer was then used and the child quickly recovered and did well thereafter. Possibly a very lucky coincidence.

Case Oa.—Breech delivery at thirty-two weeks; birth-weight 3 lb. 5 oz. Inspiratory recession and grunting respiration were soon apparent. The puffer was used repeatedly during the first six hours of life, during which time trip

spirometry showed considerable improvement from 420 ml. to over 700 ml. per min. The child thereafter did well.

Case Lo1 was the first of twins born precipitately at thirty weeks' gestation. Birth-weight 2 lb. 7 oz. Pethidine had recently been given to the mother. The child was apnoeic and obviously narcotised, and nalorphine ("Lethidrone") 0.5 mg. was given into the cord. This revived the child, but its colour remained blue and there was considerable inspiratory recession. The puffer was then used and its colour improved at once. Progress thereafter was uninterrupted.

Nalorphine greatly contributed to the successful outcome here. In the following case it was given belatedly.

Case Go.—Birth-weight 2 lb. 12 oz. Rapid delivery three and a half hours after morphine had been given to the mother because of mixed accidental antepartum haemorrhage. At birth the child was flaccid and grey and took only occasional gasps. Gastric oxygen had no apparent effect. The puffer was thereupon used—without much immediate benefit, for the respirations were infrequent. Nikethamide 0.25 ml. was injected intravenously, with transient benefit, and treatment with the puffer was continued. At sixty minutes nalorphine (0.5 mg.) was injected, and regular but slow respiration was established at once. Treatment with the puffer was continued for another half-hour but the colour did not become really satisfactory until a high oxygen concentration was given by the apparatus.

In this case the Coombs test was strongly positive, and after a replacement transfusion the child did well. The nalorphine should have been given earlier.

Case Ee.—Normal delivery at thirty-seven weeks' gestation. Birth-weight 5 lb. 2 oz. This child did not appear to be breathing satisfactorily and at one hour fifty minutes the minute volume was only 330 ml. Fifteen minutes' continuous treatment was given with the puffer at the age of two and three-quarters hours. I was not present personally but my colleagues noted improvement clinically, and at four hours thirty-five minutes the minute volume was 550 ml. Progress thereafter was uneventful.

Case Bo.—Spontaneous premature delivery at thirty-one and a half weeks following premature rupture of the membranes for the preceding two and a half weeks. Birth-weight 4 lb. 2 $\frac{1}{2}$ oz. The child cried at birth but severe recession developed within four minutes. The colour was poor and treatment with the puffer was given intermittently with benefit. The signs of inspiratory recession gradually disappeared within a few hours.

The apparatus was here used intermittently to correct evident asphyxia. It is unlikely that it directly influenced the disappearance of the recession.

Case U.C.—Rapid delivery at term with foetal distress in the second stage. Birth-weight 5 lb. 8 $\frac{1}{2}$ oz. The child refused to take more than occasional gasps and its colour remained very poor.

Delivery had taken place at another hospital and I was asked to see the case because there were no signs of spontaneous improvement during three hours. I took the puffer with me, and treatment was started at approximately the age of four hours and maintained by my enthusiastic colleagues at this hospital for nearly three hours in spite of my gloomy forecasts. It seemed certain that the child had an intracranial haemorrhage and I doubted whether it was worth persisting. Dr. Norman Smyth, however, applied his anerometer under the face-mask, and fig. 3 is a sample of the tracings obtained. Ventilation appears to have been increased. The child slowly recovered and is now eleven months old and progressing normally.

Case Ar.—District delivery at approximately thirty-four weeks. Birth-weight 3 lb. It cried well at birth. On admission at three hours, the temperature was 96°F. Cyanotic attacks repeatedly occurred and intracranial bleeding was provisionally diagnosed. Nevertheless the puffer was used repeatedly to restore oxygenation and after the age of twenty-four hours no further cyanotic attacks occurred. Apart from subsequent difficulty with feeding the child has since done well.

The salvage of babies suffering from intracranial bleeding might be regarded by some as questionable;

but, since the diagnosis cannot be made with certainty before death, it is worth giving the child the benefit of the doubt, as these last two cases indicate.

Summary and Conclusions

Further experiences in augmented respiration showed the need for an emergency type of respirator as an ancillary to the main servo respirator.

A positive-pressure patient-cycled respirator, operated via a face-mask, is described and the results of its use are briefly reported.

The recovery of the surviving infants cannot necessarily be attributed wholly to the use of the respirator; but our observations have at least shown that, at the pressures normally employed, the treatment is harmless and temporarily beneficial. Its object is no more than to combat asphyxia for the time being and so allow the child time in which to achieve normal respiration if it is capable of doing so.

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HYPOCHROMIC ANAEMIA IN R.A.F.

RECRUITS

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IDIOPATHIC hypochromic anaemia in the male has been regarded as rare.

Wintrobe (1951) suggested that, if hypochromic anaemia was found in a man it was almost always caused by occult loss of blood, unless there had been a gastric operation.

Whitby and Britton (1950) describe the condition as exceedingly rare in males. Faber (1913), who first drew attention to this disease, reported 3 cases in males out of 20 cases; Davies (1931a) 4 cases in males out of 55 cases, and Witts (1930) 1 case; and Britton (1936) found 4 cases in males out of 66 cases.

Witts and Burgher (1934) published 26 cases in males, of whom 8 were aged less than thirty; they noted a tendency to immaturity in the lower age-group. Filo (1933) described eunuchoidism or underdevelopment of the genitalia with this type of anaemia in young males. Thomson (1943) found 9 cases of hypochromic anaemia in adolescent males, of whom 4 had splenomegaly.

Shorthouse and King (1951), who described 20 cases of hypochromic anaemia in army recruits, also discovered a tendency to immaturity and noted that the symptoms did not appear until after a few months' service.

This paper deals with 50 cases of hypochromic anaemia detected by routine blood examination of young men on entry into the Royal Air Force, which have been investigated and treated at this hospital. As all these men had recently undergone medical examinations to assess their fitness for military service and had all been passed grade 1, there is evidently some clinical difficulty in detecting the condition. The investigations were designed to attempt to answer the following questions:

- (1) What is the incidence of anaemia in R.A.F. recruits?
- (2) What types of anaemia are we dealing with?
- (3) What are the social background, symptoms, and clinical signs of anaemia in the young male?
- (4) How should these cases be treated?

Methods

Hæmoglobin values (oxyhaemoglobin method) were estimated in 1000 recruits in their first week of training. After this all of 3221 recruits entering the camp were screened by the copper-sulphate method. The total number of recruits examined was therefore 4221. Among these, 50 were found to be undoubtedly anaemic (Hb 12 g. or less per 100 ml.) and were admitted to a special ward for investigation and treatment.

The following determinations were made on 5 ml. of venous blood: (1) hæmoglobin (Medical Research Council grey-wedge photometer); (2) packed-cell volume; (3) red-cell count; (4) absolute values; (5) total and differential white-cell count; (6) reticulocyte-count; (7) erythrocyte-sedimentation rate (E.S.R.); and (8) blood fragility.

The following tests were also done as a routine: (1) fractional test-meal (combined alcohol and histamine method); (2) benzidine test (occult blood was tested for on three consecutive daily samples of faeces); (3) a mid-stream specimen of urine was examined for albumin, sugar, and deposit; (4) radiography of the chest; (5) total faecal fat (in many cases a four-day fat-balance test was made); and (6) examination of bone-marrow.

In the presence of gastric hyperacidity and a history suggesting peptic ulceration, or, if occult bleeding was detected, the whole of the gastro-intestinal tract was radiographed.

Findings

Of these 50 men with hypochromic anaemia 2 had bleeding from the gastro-intestinal tract and 1 acholuric jaundice. In the remaining 47 no cause of the anaemia was detected, and the condition must be regarded as idiopathic (table 1).

TABLE I—BLOOD FINDINGS

Case no.	Hb (g. per 100 ml.)	Hb* (%)	Packed-cell vol. (%) (normal average 47)	Red cells (million per c.mm.)	M.C.H.C. (%) (normal average 33)	Mean corpuscular volume (c.u.) (normal average 90)	White cells (per c.mm.)
1	4.9	33	28	3.8	18	74	8400
2	6.6	44	31	3.9	21	79	8400
3	6.9	46	31	4.0	22	78	5300
4	7.3	49	33	5.1	22	65	3000
5	7.4	49	33	4.2	22	79	9400
6	7.5	50	34	4.5	21	76	7400
7	7.6	51	33	5.2	23	63	7000
8	7.6	51	37	4.1	21	90	5100
9	7.6	51	34	4.3	22	79	3600
10	7.7	52	36	4.8	21	75	5200
11	8.0	54	34	4.9	23	69	7500
12	8.0	54	36	5.0	22	72	6000
13	8.0	54	35	5.3	23	66	5700
14	8.2	55	31	4.5	26	69	6000
15	8.3	56	33	4.4	25	75	5000
16	8.3	57	34	5.2	25	60	5400
17	8.5	57	34	4.7	25	72	4500
18	8.8	59	36	4.6	24	78	7600
19	9.0	60	35	4.7	26	74	3400
20	9.0	60	34	4.9	26	76	4800
21	9.0	60	38	4.8	23	79	5100
22	9.3	62	37	4.7	25	79	8300
23	9.6	64	35	4.7	27	74	4300*
24	9.6	64	35	5.1	27	69	5300
25	9.8	66	39	3.7	25	105	5400
26	9.8	66	42	4.9	23	86	6000
27	9.9	66	40	4.9	25	82	5000
28	10.0	67	38	4.4	26	87	7000
29	10.0	67	43	5.2	24	83	8300
30	10.0	67	40	5.3	25	73	7300
31	10.1	68	40	4.8	25	83	6800
32	10.1	68	38	5.0	27	76	7000
33	10.3	69	40	4.1	25	97	5800
34	10.3	69	39	4.9	26	80	8600
35	10.3	69	38	4.8	27	79	5100
36	10.3	69	41	4.2	25	97	6000
37	10.4	70	39	4.9	27	80	3300
38	10.6	71	37	4.2	29	88	6500
39	10.6	71	35	4.8	30	73	12,300
40	10.6	71	40	5.0	25	80	10,300
41	10.7	72	39	4.9	26	80	8200
42	10.8	73	41	4.8	26	85	5600
43	11.0	74	43	5.2	26	83	7100
44	11.0	74	39	4.9	28	79	6000
45	11.7	78	38	4.8	31	79	5800
46	11.7	78	39	5.1	30	77	6400
47	12.0	80	43	4.9	28	78	6400

* 100% = 14.8 g. per 100 ml.

THE PATIENTS

Incidence.—In 36 (0.9%) of 4221 R.A.F. recruits aged from eighteen to twenty the haemoglobin was less than 10.4 g. per 100 ml., and in the remaining 11 (0.2%) it was 10.4–12.0 g. per 100 ml. (table I).

Social Background.—The occupations of the recruits before enlistment did not appear to be significant, but this might well be expected in youths aged eighteen. The social classification of their fathers is a more reliable indication of their background :

Fathers' occupations	No. of patients
Unskilled	24
Semi-skilled	8
Skilled	2
Unemployed	7
Fathers dead	6

It can be seen that in most cases the fathers followed unskilled occupations and would come under social class IV or V of the Registrar-General's classification of the population. The number of fathers who, through either ill health or death, were not wage-earners, was high—13 out of 47.

Size of Family Unit.—The average number of siblings for each patient was three.

Geographical Distribution.—Most of the patients came from the North and Midlands, but the significance of this cannot be assessed without figures for the whole of the R.A.F.

SYMPTOMS AND SIGNS

Most of the patients had no symptoms at all, and only 1 had visited his family doctor because of symptoms caused by anaemia. 9 (19%) complained of breathlessness and tiredness of a very mild degree. Dyspepsia and diarrhoea were not complained of, even by those with achlorhydria. A family history of anaemia was reported by 2 patients, but without examining the blood of their parents and relatives this figure might be very misleading.

Their appetites were very good—a fact verified on the ward at mealtimes. Only 4 disliked meat and green vegetables or other iron-containing foods.

The unreliability of pallor of the skin as a sign of anaemia was confirmed, 34 out of 47 having no such pallor. Pallor of the conjunctivæ, gums, and nail beds were almost constant features. Flattening of the nails was seen in 11 (23%), but only 1 had definite koilonychia. The spleen was palpably enlarged in 2 but became impalpable after treatment. Most of the patients appeared dull and lifeless, and their facial expressions depicted easy fatigability. They were of all heights from 5 ft. 2 in. to 6 ft. 5 in. and most of them were built proportionately to their height; none showed signs of loss of weight. As a group they did not show immaturity or underdevelopment of the genitalia.

The 1 man (case 2, with Hb 6.6 g. per 100 ml.) who had significant symptoms before enlistment was a farm labourer aged eighteen and 6 ft. 3 in. tall who had been dismissed by his employer for not pulling his weight. On two occasions he had had severe dyspnoea while doing farm work. Treatment with an iron tonic had improved the dyspnoea on both occasions. Each attack of dyspnoea coincided with the threshing season, when an extra physical effort was required of him; during the rest of the year he had carried on with his farm work without symptoms. This case demonstrates how symptoms due to anaemia must be assessed according to physical effort required by the patient's occupation and other activities.

BLOOD FINDINGS

The low mean corpuscular haemoglobin concentration (M.C.H.C.) confirmed a state of iron deficiency, and some recruits were severely anaemic (table I). Wintrobe (1951) regards a M.C.H.C. of 22% or less as indicating extremely severe anaemia. In 10 patients the M.C.H.C. was 22% or less. Microcytosis was not found to be a prominent

feature, and the red-cell count was normal in most cases. Microcytosis and a low red-cell count may well be features of a long-standing case.

The appearance of the red cells invariably showed variation in staining, shape, and size. The more severe the anaemia the more pronounced were these findings and the greater was the percentage of cells affected. Elliptical red cells, seen in several films, disappeared after treatment and thus excluded elliptocytosis. Scanty stippling of the red cells was seen in a few blood films, but nucleated red cells were not seen. The presence of target cells and moderate anisocytosis with hypochromic anaemia seems to be a good indication to look for steatorrhœa (Cooke et al. 1948); several such cases have been seen in this laboratory.

The total white-cell count was normal, and there was no considerable granulocytopenia. The reticulocyte-count in most of the cases was significantly less than 1%, and in none did it exceed this figure. The platelets appeared normal in number, shape, and size. The E.S.R. and red-cell fragility were always normal.

BONE-MARROW FINDINGS

No published work on the marrow picture in this type of anaemia in young males could be found. Bone-marrow examinations were made in 37 patients. The method of taking the marrow, the staining, assessment, and terminology were those described by Israëls (1948).

The marrow was hyperplastic in 31 and normal in the remaining 6. Usually the lower the haemoglobin, the more hyperplastic was the marrow. The hyperplasia involved all forms of the normoblastic series. The normoblasts were smaller than normal and the cytoplasm reduced in quantity and basophilic in tint. Table II shows that the range found for the various types of normoblasts included a higher upper limit in all forms.

Hæmocytoblasts did not share in the hyperplasia in any marrow examined. In many films the increase was mainly in the pro-erythroblasts and early basophilic normoblasts. Megaloblasts were not seen in any film. The nuclei of many of the early basophilic erythroblasts were not absolutely typical of any stage in the normoblast series, but a megaloblastic nuclear pattern was certainly not present. Whether these cells could be classified as transitional megaloblasts is open to question (Innes 1949, Israëls 1951). Giant metamyelocytes were not seen in any film, and primitive white cells were not found to be increased in number.

In the haemoglobin range of 4.9–9.0 g. per 100 ml. the average myeloid/erythroid ratio was 1.9/1.0. In the higher haemoglobin range of 9.1–10.8 g. per 100 ml. the average ratio was 2.5/1.0. Usually the lower the haemoglobin, the more closely the myeloid/erythroid ratio approached unity. A ratio of 1/1 or less was never found, even in the severest anaemia.

The bone-marrow findings concur with Leitner's (1949) statement that only a moderate degree of normoblastic hyperplasia is usually found in iron-deficiency anaemia. Whitby and Britton's (1950) statement that normoblasts of various grades of maturity form 50% or more of the total nucleated-cell count was not confirmed in any case in this series.

TABLE II—NORMOBLAST SERIES

Forms	Normal range (%) (Israëls 1948)	Range found (%)	Average (%)
Pro-erythroblasts .. .	0.5–4.0	0.5–5.0	3.6
Early normoblasts .. .	1.0–5.0	2.0–11.0	5.6
Intermediate normoblasts ..	12.0–20.0	4.0–25.0	15.4
Late normoblasts .. .	6.0–10.0	4.0–12.0	7.0

TABLE III—RESULTS OF TEST-MEALS

	Achlorhydria (%)	Histamine-fast achlorhydria (%)	Normal acidity (%)	Hypo-chlorhydria (%)	Hyper-chlorhydria (%)
Davidson and Fullerton's (1938) series in females ..	64.9	45.6	17.5	14.6	3.0
Present series ..	62	43	25	13	

RELATION OF GASTRIC ACID TO ANAEMIA

Bennett and Ryle (1921), using the gruel test-meal, discovered 4 cases of achlorhydria (not histamine-fast) in 100 healthy medical students.

Lander and MacLagan (1934) found an incidence of 1% after the injection of histamine in a comparable series. Doig et al. (1950) found 1 case of histamine-fast achlorhydria in 134 students.

Fractional test-meals were given as a routine in the present series. 50 ml. of 7% alcohol was given, and 0.5 mg. of histamine was given if no free hydrochloric acid was found.

Table III shows the fractional test-meal findings in this series compared with Davidson and Fullerton's (1938) findings in middle-aged women, with idiopathic hypochromic anaemia. The incidence of achlorhydria and histamine-fast achlorhydria in the two series are virtually the same. In the present series hypo-chlorhydria was not separated from normal acidity; the dividing line is arbitrary, and the level of acid depends to some extent on whether alcohol or gruel is used. Davidson and Fullerton (1938) emphasised the importance of diet in the aetiology of achlorhydria.

In this series almost every patient had a good appetite, and most of them were taking a reasonable amount of meat, vegetables, and fruit. The findings of comparable incidences of achlorhydria in young men and middle-aged women suggests that the achlorhydria precedes the anaemia or else comes on early in the development of idiopathic hypochromic anaemia.

Davidson and Fullerton (1938) suggested that histamine-fast achlorhydria might not necessarily be permanent. Fractional test-meals were repeated in 13 of the present cases with histamine-fast achlorhydria, from six to ten weeks after the start of treatment, when the haemoglobin had returned to normal. 6 cases showed free hydrochloric acid—3 without histamine and 3 only after the injection of histamine. These findings are contrary to the generally accepted view on the irreversible nature of histamine-fast achlorhydria, and are hard to explain on any other ground than that of improvement in the blood haemoglobin, with consequent increase in oxygenation of the gastric mucosa.

Achlorhydria was present in 16 of 21 patients with Hb 9 g. or less per 100 ml., and in 13 of 26 patients with Hb more than 9.1 g. per 100 ml. Although the series is small, this suggests a relation between achlorhydria and the haemoglobin level. Davies (1931b) studied the gastric contents in cases of anaemia with achlorhydria, and found that gradually progressive stages of secretory failure may occur, and that a link between idiopathic hypochromic anaemia and pernicious anaemia, on the basis of failure in gastric secretion, might be postulated.

It is interesting to postulate that there may be two types of histamine-fast achlorhydria, which could be differentiated by histological examination of the gastric mucosa:

(1) *Congenital* (and perhaps familial).—The acid secretory cells either may not have developed in the foetus, or may be hypoplastic and unable to produce acid. If this type is

associated with iron-deficiency anaemia, treatment would not restore the secretion of acid.

(2) *Acquired*.—Some pathological process or processes may cause the oxyntic cells of the stomach to stop producing acid. The histological picture in the early stage might be quite different—i.e., no lack of development of the oxyntic cells. In this type early detection and efficient treatment may restore the secretion of acid. If, however, the anaemia is long-standing, as in typical idiopathic hypochromic anaemia of women, the prolonged anoxæmia might permanently damage the gastric mucosa, and treatment would not alleviate the histamine-fast achlorhydria.

Treatment

The cases reviewed here were all treated with intravenous iron ('Neo-ferrum,' Crookes) because oral iron therapy was slow and unreliable. Saccharated oxide of iron was given in a dosage of 50 mg. on the first day, 100 mg. on the second day, and 200 mg. daily thereafter until the total dosage prescribed had been given. The total dosage was calculated as 25 mg. for every 1% deficit of Hb, the aim being to increase the Hb to 15 g. per 100 ml. No extra iron was allowed for depleted stores. Slack and Wilkinson (1949) showed that, in chronic infections, more than 25 mg. per 1% deficit of haemoglobin was required, and a full response to this amount therefore helps to rule out chronic infections. Similarly, in idiopathic steatorrhœa and anaemias due to vitamin deficiencies, 100% utilisation of the iron administered would not be expected, because many patients would require folic acid, or the vitamin in which they were deficient, to restore the blood picture to normal.

The average daily increase in haemoglobin was 0.34 g. at ten days and 0.19 g. at four weeks. The utilisation of the preparation was 100%. In most cases a small reticulocyte peak developed between the sixth and the eighth days but never exceeded 4%. The height of the peak had no constant relationship to the initial haemoglobin level or the initial red-cell count. A reticulocyte-count of 2–3% after it had been less than 1% for several days was taken to be a definite reticulocyte response. A temporary erythrocytosis (packed-cell volume more than 50%) was noted in nearly every case and accounted for the M.C.H.C. reaching normal limits long after the haemoglobin. Untoward reactions were not observed in any patient. The technique of giving the iron was that described by Slack and Wilkinson (1949).

Although most of the patients had no symptoms, after treatment a sense of well-being, more energy, and a greater interest in life were admitted by almost every patient.

Conclusions and Summary

Idiopathic hypochromic anaemia is common in young males, and is the commonest form of anaemia in R.A.F. recruits. Of 50 cases of hypochromic anaemia found among 4221 recruits, 47 could be regarded as idiopathic.

Most of the 50 patients came from large working-class families.

Symptoms were rare, even with severe anaemia.

The incidence of histamine-fast achlorhydria in hypochromic anaemia in young men, is the same as in middle-aged women with this type of anaemia. The associated histamine-fast achlorhydria was reversible in 6 of 13 cases.

Early detection and treatment of the anaemia are important for the well-being of the gastric mucosa.

The bone-marrow findings showed that the typical picture is one of moderate normoblastic hyperplasia.

Treatment with intravenous iron was safe, efficient, and reliable.

After treatment nearly all the patients experienced a sense of well-being, more energy, and more interest in life than they had been accustomed to.

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PROLONGED ANURIA SUCCESSFUL MANAGEMENT BY CONTINUOUS INFUSION INTO THE INFERIOR VENA CAVA

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SUDDEN suppression of urine is of such varied aetiology that few clinicians have not observed it and been required to treat it. A few cases may be caused by obstruction of the urinary tract, but most are the result of shock during which renal damage develops. If cortical necrosis is complete, the prognosis is hopeless; but this must never be assumed, because, if the lesion is less extensive and the main damage is to the renal tubules, the outlook is quite good provided the appropriate treatment is started promptly and given with care and attention to detail.

Suppression of urine often develops when least expected and when treatment is very properly being directed towards the resuscitation of the shocked patient. Herein lies a danger. In his concern to restore and maintain an adequate circulation the doctor may miss by many valuable hours the early diagnosis of anuria and (of far greater importance) by over-enthusiastic intravenous therapy may so disrupt the patient's fluid and electrolyte balance as to prejudice ultimate recovery from the anuria. In such cases, and in some others deteriorating under treatment, complicated procedures—e.g., exchange transfusions (Dausset 1950), peritoneal dialysis (Frank et al. 1948), and the use of the artificial kidney (Kolff 1952)—

may be required; but, even so, conservative treatment by restriction of fluids and a high-calorie diet containing little or no protein will be required.

When anuria is diagnosed at its onset, conservative treatment should be all that is required to allow the kidneys to recover. This treatment, though properly called conservative, must not be thought of as meaning therapeutic inactivity; it is rational and demands attention to detail for which "doing nothing" is the least suitable epithet imaginable" (Black and Stanbury 1948).

We describe here in detail the successful management of a case of prolonged anuria (complete for 11 days, partial for a further 10 days) following septic abortion treated in a gynaecological ward of a general hospital. We believe that the methods adopted can easily be used by others who may encounter a similar case. The feature of the treatment to which we draw particular attention was continuous infusion through a catheter in the inferior vena cava for 17 consecutive days.

Case-record

A 3-para married woman, aged 31, was admitted in the early hours of April 1, 1953. She had last menstruated 17 weeks previously, and just over 2 months later she tried to procure abortion by taking 60 or more "corrective capsules" over a period of days. Violent purgation and vomiting followed but not abortion. So she syringed herself with a soap solution on the night of March 31 and was admitted to hospital some hours later.

On admission her general condition and physique were good, her temperature was 99.4°F, pulse-rate 100, and blood-pressure 110/75 mm. Hg. Her tongue was moist and clean, and her heart and lungs showed no fault. The size of her uterus, which was tender, was compatible with a 17-week pregnancy; the cervix admitted a finger-tip, and there was some fresh blood on the examining finger. The initial diagnosis was threatened abortion.

Later the same morning, coincident with the expulsion of the gestation sac, there was much vaginal bleeding, which was soon controlled by the injection of ergometrine 0.5 mg. The systolic blood-pressure fell to 90 mm. Hg, but after a transfusion, given without reaction, of one pint of whole citrated blood it rose again.

At operation at 12.45 P.M. the same day the cervix was found to be widely open, permitting the digital removal of several portions of offensive placental tissue. No curette was used, and bleeding was slight. At the operation a small quantity of bloodstained urine was obtained by catheter.

Immediate Postoperative Stage.—The patient soon regained consciousness and showed no signs of shock. Her pulse-rate was 100 and temperature 99.4°F. She had been started on a course of penicillin 600,000 units 12-hourly and sulphadimidine, but the latter was discontinued after 2 g. had been given, in view of the urinary findings at operation.

1st Postoperative Day.—The patient's general condition was unaltered, but suprapubically the abdomen was tender and slightly rigid; the temperature and pulse-rate were unchanged. During the first 24 hours 105 oz. of fluids was estimated to have been taken by mouth, and 16 oz. to have been lost in vomit; 17 oz. of bloodstained urine, most of which had been secreted early in the day, was passed.

2nd Postoperative Day.—During this day only 4 oz. of urine was secreted, confirming the suppression of urine; this was complete by 9 P.M., when catheterisation showed that the bladder was empty. During this day the fluid intake was restricted to 30 oz.

3rd Postoperative Day.—Cystoscopy and ureteric catheterisation revealed no mechanical obstruction; 5 drops of heavily bloodstained urine was obtained from the right ureter, and none from the left. The urine was sterile on culture and contained several hyaline casts. A Ryle's tube was passed through the nose into the stomach, and an emulsion of glucose 400 g., peanut oil 100 g., and acacia to emulsify in 1 litre of water as recommended by Bull et al. (1949) was dripped slowly day and night. Vomiting occurred once, but most of this was strained through gauze and returned to the intragastric drip.

4th Postoperative Day.—A gastric drip was continued although vomiting occurred on several occasions.

5th Postoperative Day.—Vomiting had by now assumed serious proportions and was causing the patient distress and

TABLE II—BIOCHEMISTRY OF BLOOD-SERUM

Postoperative day	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
Non-protein nitrogen (mg. per 100 ml.) ..	135	..	190	185	240	..	190	220	..	234	220	280	240	254	260	..	240	320	320	380	160	190	..	220	185	
Sodium (mg. per 100 ml.) ..	295	..	275	295	290	..	290	..	270	270	275	280	310	285	270	270	270	..	290	..	285	..		
Potassium (mg. per 100 ml.)	21	..	22	22	21	22	..	22	18	19	20	19	22	21	20	..	19	..	20	..
Chlorides as chlorine (mg. per 100 ml.)	330	323	330	..	220	220	240	300	255	17	..	280	290	315	280	..	280	
Alkali reserve (vol. %)	62	60	..	52	54	57	59	58	60	58	61	58	62	61

ourselves anxiety. In the previous 48 hours she had absorbed little more than 1 litre of the mixture and was noticeably more drowsy. A sensitisation rash, which we assumed was due to penicillin, made its appearance on the thighs, abdomen, and arms, but fortunately the irritation it caused was rendered less disturbing by the patient's continued desire to sleep. A litre of 5% dextrose in water was rapidly infused to restore the fluid balance, and in an attempt to stop vomiting the stomach was washed out with water, and a dilute glucose solution was substituted for the previous mixture. Since no improvement followed, we abandoned all further attempts at gastric feeding.

6th Postoperative Day.—The problem now was how to provide the patient with the necessary calorie value without exceeding a daily fluid intake of 1 litre. Obviously a very hypertonic 40% dextrose solution could not be introduced into a peripheral vein without producing thrombosis and localised oedema. The patient's temperature had been normal for 2 days, and we did not wish to make matters worse by adopting measures which were certain to lead soon to inflammation with its dangers of increased tissue breakdown (Borst 1948). We therefore introduced a cardiac catheter as far as the superior vena cava and dripped through it a 40% dextrose solution day and night, as recommended by de Keyser et al. (1949) and Bull (1952). This provided the patient with at least 1600 calories a day and a basic fluid allowance of 1 litre to offset the insensible loss. At the same time in each 24-hour period the volume of fluid lost by vomiting was accurately measured and balanced by addition to the intravenous infusion of an equal volume of 5% dextrose in water.

TABLE I—INTAKE AND OUTPUT

Postoperative day	Intake					Total Intake (ml.)	Chlorides as sodium chloride (g.)	Output		
	Oral fluids (ml.)	Dextrose 40% i.v. (ml.)	Dextrose 5% i.v. (ml.)	Physiological saline solution 2% i.v. (ml.)	Insulin (units)			Vomit (ml.)	Urine (ml.)	
1	2982	2982	..	454	483	
2	852	852	114	
3	1306	1306	
4	994	994	..	600	..	
5	994	1000	994	..	300	..	
6	..	800	200	1000	..	210	..	
7	..	800	200	1000	0.4	45	..	
8	..	800	200	940	0.6	185	..	
9	..	800	200	835	0.7	150	..	
10	..	800	200	800	3.0	270	..	
11	..	800	200	890	1.4	278	..	
12	..	800	200	886	1.3	225	..	
13	..	800	..	200	60	1000	1.3	145	..	
14	..	800	800	..	40	2000	3.2	265	700	
15	227	800	200	..	40	1227	0.9	65	250	
16	227	800	..	200	..	1227	0.8	..	220	
17	170	800	..	200	..	1170	1.4	71	239	
18	..	800	800	400	..	2000	4.1	310	590	
19	..	800	1800	400	..	3000	3.7	465	280	
20	..	800	1200	1000	70	2000	4.9	442	850	
21	..	800	1600	600	..	2000	4.8	..	960	
22	..	800	1200	1000	40	3000	7.9	125	1520	
23	..	800	1200	1000	..	3000	10.9	162	1950	
24	..	800	500	1200	..	2500	11.7	154	2520	
25	284	800	..	1200	..	2840	12.8	..	2560	
26	600	..	+ 1000	13.9	..	2790	..	
27	++	400	
	Intravenous therapy stopped									

During the first five days the recorded quantities of oral fluids and vomit are approximate.

Vitamins given from 23rd day onwards.

*On these occasions the bottles were changed before they were quite empty; hence the intake did not quite amount to 1000 ml.

10th Postoperative Day.—After 4 days' continuous intravenous therapy, during which the patient remained cheerful and surprisingly well in view of the continued vomiting of small quantities of fluid, thrombophlebitis was noticed along the left basilic vein, with pain, oedema, and reddening of the arm, but unaccompanied by febrile reaction. The catheter was therefore withdrawn on the 4th day of its use and with it a six-inch length of sloughing intima which we presumed had come from the basilic vein. Had the catheter not been withdrawn, the infection would probably have spread to the greater veins of the neck, with serious consequence to the patient (de Keyser et al. 1949). Since the right basilic vein had previously been marred by an unsuccessful attempt to introduce a cardiac catheter, an alternative route had to be considered. The inferior vena cava was chosen; so the right saphenous vein was exposed in the femoral triangle and a 'Polythene' catheter was introduced to a distance of 8 inches. For the next 17 days the patient received fluids and nutrition by this route without any complications arising; and, when the time came to discontinue this form of therapy, the infusion was working as perfectly as it did on the first day of its use. From this day until the 22nd postoperative day insulin was given by subcutaneous injection (table I).

14th Postoperative Day.—The patient passed 700 ml. of dark murky urine, sp. gr. 1.014, containing numerous red cells, pus, and squamous epithelial cells but no casts or crystals. Her general condition was remarkably good, as it had been throughout the anuric phase, but in the evening she became drowsy and had a febrile reaction with a mild rigor. Her skin was dry, and she complained that her tongue "tasted salty." Next day she was once again free from symptoms, but her temperature rose to 100°F during the succeeding two evenings. Vomiting persisted, and it was therefore necessary to persevere with intravenous therapy.

16th Postoperative Day.—Since the amount of haemoglobin had decreased to 48%, a pint of group-O rhesus-positive packed cells was transfused.

17th and 18th Postoperative Days.—Cautious attempts were made to introduce water and fruit juices by mouth, but this provoked increased vomiting, wherefore we postponed further attempts at giving nourishment orally.

22nd Postoperative Day.—The non-protein-nitrogen level reached its peak at 380 mg. per 100 ml. despite an increase in daily output of urine. About now the patient began to complain of generalised severe pain, principally in the right hypochondrium and in the lumbar regions, for which we could find no cause. Possibly these symptoms were related to renal recovery.

23rd Postoperative Day.—The daily output of urine had almost reached 2 litres, and from now onwards diminishing nitrogen levels in the blood were recorded. The extent of the fall in the level of non-protein nitrogen in the serum on this day (table II) is remarkable but coincides with a reawakening of intestinal function, which up till then had been in complete abeyance. The first motion passed resembled an ordinary constipated stool, but thereafter, and until oral nourishment was resumed, faecal material similar in appearance to meconium was passed in small quantities twice or three times a day. Once again a mild febrile reaction developed, although the patient continued to feel well.

26th Postoperative Day.—Since vomiting had ceased the day before, the patient was encouraged to take nourishment by mouth. At first we only allowed her to sip small amounts of water, soup, and fruit juices, but a more solid diet was gradually introduced over 2-3 weeks.

27th Postoperative Day.—Intravenous therapy was discontinued after 21 days.

The patient's return to health was rapid and uneventful, and 4 weeks later (7 weeks after admission to hospital) she was discharged home. Renal recovery was not yet complete,

for the specific gravity of the urine was low at 1.008-1.010, and the non-protein-nitrogen level in the blood was 72 mg. per 100 ml.

Discussion

The conservative management of anuria has been discussed by Bull (1952), Darmady (1952), and Vest and Kelley (1953), and considerable agreement has been reached on the principles of treatment. It is generally accepted that the anuric patient should be provided with at least 1600 calories a day, to reduce to a minimum the endogenous breakdown of tissues, together with water up to but not exceeding 1 litre, just sufficient to replace the insensible loss. Usually these provisions can be given in the form of an emulsion of glucose and peanut oil in 1 litre of water dripped through an intragastric tube, the technique advocated by Bull et al. (1949). In many cases this form of treatment, though unpleasant for the patient, is tolerated well and is successful, even though on occasion some of the emulsion may be vomited, when it has to be strained back into the intragastric drip. Repeated vomiting or diarrhoea is more serious, though urea and potassium are said to be lost by these routes. In the present case the continued vomiting may have helped towards recovery by getting rid of these substances.

Only when the vomiting becomes persistent will intragastric feeding have to be stopped and be superseded by intravenous therapy. Since only 1 litre of fluid in each 24 hours is permissible, and since this must provide 1600 calories, the concentration of sugar solution, if such a solution is to be chosen, must be at least 40%. Such a solution cannot, however, be run into a peripheral vein for more than a day or so without producing thrombosis; so one of the great veins must be chosen for the infusion if the drip is to be given for any great length of time. The infused hypertonic solution is apparently so quickly diluted by the blood-flow in the large vein that no thrombus is formed. From our limited experience and from discussing this matter with those of our colleagues who are accustomed to cardiac catheterisation we believed that this procedure need not be looked on as formidable or dangerous. Several technical details, however, require further consideration.

PREVENTION OF THROMBOPHLEBITIS

Unless thrombophlebitis is successfully prevented, it may not be possible to continue the only treatment likely to preserve the patient's life. The most scrupulous asepsis must be practised in putting up the drip; and this asepsis must be maintained all the time that the drip is in use. Heparin 15,000 units per 24 hours and penicillin should be added to the infused fluids. Two other factors may help to reduce the incidence of thrombo-

phlebitis: (1) the amount of movement permitted at the point of entry of the catheter and throughout its length should be reduced to a minimum; and (2) the length of vein of small calibre traversed by the catheter should be as short as possible. Infusion into the inferior vena cava has these two merits; therefore we recommend this route rather than the alternative route, into the superior vena cava. If signs of inflammation develop despite these precautions, the catheter must be withdrawn without delay.

INFUSION INTO INFERIOR VENA CAVA

To minimise the risk of infection masks, gowns, and gloves should be worn and full asepsis and antisepsis practised.

The apparatus required is the same as for cutting down on a vein; a transfusion bottle containing the appropriate solution; a polythene catheter 4 mm. in diameter and about 12 inches long; a short piece of thick-walled rubber tubing to fit tightly over the polythene tube; and all connecting pieces (see figure).

A 2-inch incision exposes the upper end of the saphenous vein, whose three or four main tributaries and distal end are carefully ligated. The vein is opened and the polythene catheter passed for 8-10 inches and secured firmly with a double ligature of fine catgut. The following arrangement exerted pressure on the wound not only while the catheter was in situ but also when the time came for it to be removed.

At the time of insertion of the catheter a stout nylon suture (size 8) was passed through the skin, under the saphenous vein $\frac{1}{4}$ inch proximal to the point of entry of the catheter, over the vein, and then under it once more, and brought out through the skin on the opposite side. This suture was securely tied over a small pad of sterile gauze, with its ends left long. When the time came to remove the catheter, the nylon knot over the gauze was loosened; as soon as the catheter was withdrawn, the suture was tightened over the gauze pad rather more firmly than before; this kinked the saphenous vein, thus preventing haemorrhage. The nylon suture was removed by firm traction 72 hours later.

Specimens of blood for biochemical analysis may readily be collected through the polythene tube by temporarily stopping and disconnecting the drip and aspirating blood with a syringe. When the drip is reconnected, as much as possible of the blood remaining in the tube should be flushed back into the circulation without delay by momentarily racing the drip; otherwise a thrombus may form in the tubing.

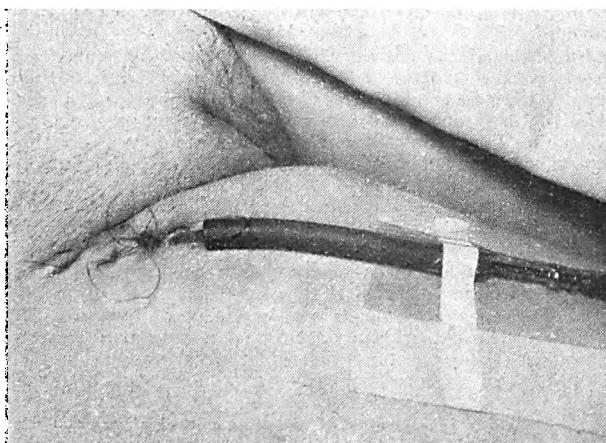
INFUSION INTO THE SUPERIOR VENA CAVA

For catheterisation of the superior vena cava certain additional points in technique must be observed. The catheter should be of the type normally used for cardiac catheterisation; the median antecubital vein, preferably the right, is exposed and the catheter inserted first into the basilic vein, thence into the subclavian vein, and onwards under the fluorescent screen into the superior vena cava. Sometimes the tip of the catheter enters the wrong vein, especially the internal jugular vein. When this happens, it should be partially withdrawn and the patient's arm abducted and rotated before the catheter is reinserted. The tip of the catheter should not remain in either the jugular or the subclavian vein, because the continued use of hypertonic solutions may cause them to thrombose (de Keyser et al. 1949).

CONTROL OF INTRAVENOUS THERAPY

In the present case 1 litre of 40% dextrose was infused daily together with such additions as were required to make up fluid lost in vomit or urine. For convenience, the additions consisted of 5% dextrose in water.

The correction of electrolyte deficiency during anuria is not normally practised (Bull et al. 1950) and therefore we were reluctant to give saline solution, but after a very careful day-to-day tally of the amounts of sodium chloride lost by vomiting it became clear on the 14th postoperative day that a real deficit amounting to nearly 9 g. existed. Moreover, at this time the sodium and chlorine levels in the serum were somewhat lower than they had been; therefore 4 g. of sodium chloride was added to the dextrose drip. Next day diuresis began, and thereafter we had no hesitation in adding to the



Distal end of polythene tube which was passed through right saphenous vein into inferior vena cava, and through which continuous infusion was maintained for seventeen days without producing any complication.

infusion amounts of saline equal to, but never in excess of, the chlorine and sodium deficit at the time.

Table II shows that the serum-potassium level during the anuria remained at fairly constant low values and never exceeded 22 mg. per 100 ml. Small amounts of potassium chloride were introduced into the drip on three occasions during the recovery period, during which the serum-potassium levels fluctuated from 17 to 22 mg. per 100 ml.

Ketosis and acidosis did not develop—a fact which is all the more remarkable when it is remembered that for 3 weeks the patient was given nothing by mouth and throughout this time vomiting continued without respite.

HANDLING OF BIOCHEMICAL DATA

Since the patient's life appeared to depend on the careful recording and assessment of biochemical results, and on a meticulous regard to detail in many small but important practical matters, the following programme of management was evolved.

Samples of blood with the 24-hour collections of either urine or vomit or both were dispatched for analysis each day at 9.30 A.M. The laboratory findings in these specimens were telephoned back to the ward by 2.30 each afternoon; and all results so notified were received and recorded immediately either by one of us (J. C. B.) or by the ward sister.

Biochemical and fluid deficits were calculated from the daily laboratory results, and from these the nature and amount of extra parenteral fluid therapy for the succeeding 24-hour period was estimated. For convenience this 24-hour period always began at 3.30 P.M.

Except for a few days, one of us (J. C. B.) accepted the responsibility for the close handling and scrutiny of the biochemical data, and for the control of the intravenous therapy. This arrangement was an important factor leading to our patient's recovery.

Summary

The principles to be adopted in the treatment of anuria are briefly considered.

The successful management of prolonged anuria (complete for 11 days, partial for a further 10 days), following septic abortion is described in detail.

The limitations of oral feeding for anuric patients with gastric intolerance are emphasised. In the present case excessive vomiting precluded the continuation of feeding by intragastric tube. The patient's nutritional requirements were effectively supplied for 21 days by the intravenous administration of dextrose 400 g. daily. Over-hydration was prevented by infusing a 40% solution of dextrose at first into the superior vena cava and later into the inferior vena cava.

The two techniques of infusion into the superior vena cava and into the inferior vena cava are neither difficult to perform nor particularly distressing to the patient. For reasons discussed here we prefer infusions into the inferior vena cava, and in the present case we maintained the infusion into this vein for 17 consecutive days without complication.

We believe that infusion of a 40% glucose solution into one of the great veins may have a wider application than hitherto in the treatment of patients who cannot obtain nourishment through the alimentary tract; but this method may not achieve what is hoped for it, unless the electrolyte and fluid balance is carefully assessed daily and close attention is given to the management of the infusions. If this can be done by one and the same person, so much the better.

We wish to thank Mr. F. J. P. O'Gorman, F.R.C.S., for his cystoscopic examination of our patient, Mr. B. W. Auchinachie, Ph.D., and his staff for the daily biochemical analyses, and Dr. F. W. Leigh, of the cardiovascular department of the Hospital, for his assistance with the intravenous infusions, and Sister Mitchell and the nurses for their invaluable help.

References at foot of next column

METHONIUM COMPOUNDS IN THE ANGINA OF HYPERTENSION

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THE careful administration of hexamethonium bromide (H.M.B.) and its homologues is probably the most effective treatment at present available for arterial hypertension, and with it a great measure of improvement may be obtained in almost all patients. Papilloedema, where present, disappears in almost all adequately treated cases, and reduction in heart size is common (Smirk 1953b and c). Improvement can be seen in the electrocardiograms in most cases (Doyle 1953). In most cases, congestive heart-failure or left ventricular failure can be relieved without the use of digitalis, mersalyl, or salt-free diet (Smirk 1953c).

Many hypertensive patients suffer from angina pectoris. In some series the proportion is as high as 20% (Schottstaedt and Sokolow 1953), while 13% of the 1264 hypertensive patients reviewed by Goldring and Chasis (1944) died of coronary thrombosis.

Hayward (1952) has suggested that the reduction of aortic diastolic blood-pressure produced by effective treatment with the methonium compounds may lead to a decrease in coronary blood-flow, and hence to myocardial ischaemia or to cardiac infarction. Morrison (1953) preferred not to use these compounds in treating hypertensive patients with angina. There is some evidence that myocardial ischaemia may sometimes follow reduction of the blood-pressure. Lindgren and Frisk (1948), for example, reported prolonged precordial pain in 3 anginal patients and coronary thrombosis in a 4th after the blood-pressure had been reduced by tetraethylammonium chloride. In an earlier publication from this department (Smirk and Alstad 1951) it was reported that methonium salts should be administered to anginal patients very cautiously, but that improvement was detectable in some patients.

Test injections of H.M.B. or similar substances have now been given here to over 450 patients, of whom 250 have been treated for long periods. Of the 450 patients who have had test injections, 50 had angina pectoris. 40 of these have been treated for three months or more with a methonium compound.

We report here the effects of test injections and prolonged treatment in these hypertensive patients with angina, with particular reference to spontaneous chest pain resulting from reduction of blood-pressure and the effects of treatment on the severity of the angina.

Case-numbers correspond with those in earlier publications (Smirk and Alstad 1951, Kilpatrick and Smirk 1952, Doyle 1953).

Methods

Selection of Patients

All patients with angina whose casual systolic blood-pressure was over 160 mm. Hg and who received test injections of H.M.B. or related compounds have been included in this series, and all such patients who were

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referred to the clinic have been tested to avoid errors of selection. Angina was diagnosed by one of us, and where there was doubt separate opinions by each have been obtained. Only patients in whom the pain was agreed to be undoubtedly anginal have been included in this series.

Method of Treatment

Patients were weighed at each attendance. No form of therapy was given until a methonium compound had been tried. Test injections were made subcutaneously and the blood-pressure was recorded in the standing and sitting positions at half-hourly intervals. Treatment in most patients has been by subcutaneous injection of H.M.B. Oral treatment was effective in 13 patients, and these were given hexamethonium bitartrate by mouth or 'M. & B. 2050A' by mouth. A few have been treated with M. & B. 2050A by subcutaneous injection (Smirk 1953a). The initial dose of H.M.B. used was 7.5 mg., while the initial subcutaneous dose of M. & B. 2050A in polyvinylpyrrolidone (P.V.P.) was 2 mg. The initial dose of M. & B. 2050A by mouth was 20-40 mg. Our methods of control of treatment with these substances have been described elsewhere (Smirk 1953b). In treating patients with angina we have taken additional precautions. Initial doses were half of those usually given to other hypertensive patients. The dose was then raised daily with close supervision until a dose was reached which reduced the systolic blood-pressure in the standing position to about 140 mm. Hg, provided that there had been no spontaneous chest pain before this point was reached. Careful watch was kept for such pain, and immediately it was felt the patient was made to lie down. This relieved the discomfort at once. Spontaneous chest pain associated with falls in blood-pressure was always regarded as indicating that the limit of safe dosage and of blood-pressure reduction had been exceeded. Occasional mild attacks of spontaneous chest pain were regarded as an indication, not for stopping treatment but rather for reducing the dose.

Results

SEVERITY OF ANGINA

Of 50 patients with definite angina, 10 refused, or were thought unsuitable for, prolonged treatment. The remaining 40 patients have been treated with one of the methonium compounds for three months or more. The longest period of treatment has been three and a half years. The average time of treatment for the 40 patients was ten and a half months.

In 11 of the 40 patients the pain has disappeared altogether, and all of these patients are much more active than before treatment was given.

In a further 22 patients the severity of the angina has been reduced, so that most are able to take more exercise with less frequent pain. Several have returned to work, and some have been able to lead almost normal lives.

The remaining 7 patients were unimproved by treatment.

The effort tolerance did not appear to be reduced in any of the patients treated. Those in whom spontaneous chest pain developed are referred to below.

Improvement in the angina is rare with less than about a week's treatment and may not take place for up to a month. Benefit is usually greatest by the end of the third or fourth month of treatment, and further improvement after this period is unusual. Relapses of pain do not seem to occur provided that doses producing adequate falls of blood-pressure continue to be taken.

Accuracy of dosage is most important, since doses which cause excessive falls of blood-pressure may produce spontaneous chest pain, while doses followed by ineffective falls of blood-pressure do not often improve the effort tolerance.

The following are some of the cases in which improvement took place.

Case 343.—A man, aged 66, was first seen in November, 1952. There had been severe angina of effort for three months, but no protracted attack of pain. For several years he had had headache and giddiness and there had been some dyspnoea on exertion. The blood-pressure was 200/120 mm. Hg; the fundi showed grade-II changes (Wagener and Keith 1939); the electrocardiogram showed grade-III (advanced hypertensive) changes (Doyle 1953); and radiography showed no cardiac enlargement.

Treatment was started in January, 1953. Within a week his effort tolerance was considerably improved, and the patient could walk very much further with less frequent pain. The improvement continued, and when seen in May he said that his activity had returned to normal and there had been no further pain. He was seen again in July, when he said that there had been some recurrence of pain after he had reduced the dose because of dryness of the mouth. On restoring the dose to its previous level the pain disappeared again. When last seen (in October) he was free of pain and was more active than before treatment.

Case 52.—A woman, aged 45, was first seen in June, 1948, with a blood-pressure of 248/140 mm. Hg. She complained of severe headaches of many years' duration, attacks of giddiness, and shortness of breath and anginal pain on effort for the past year. The heart was much enlarged; and there were many retinal haemorrhages, some exudate, retinal oedema, and an ill-defined edge to the disc. She was admitted to hospital in December, 1949, when the blood-pressure was 260/180 mm. Hg. There were frequent attacks of left ventricular failure and breathlessness at rest, and she was almost bedridden. There was advanced papilloedema. The angina had been severe for two and a half years.

Treatment with H.M.B. was started. Within two months headache, breathlessness, and the dizzy attacks had disappeared, and within six months the papilloedema had cleared. Until April, 1951, the patient lived a substantially normal life, apart from the injections, and had no chest pain or breathlessness with moderate activity. She died in April, 1951, of a cerebral haemorrhage. Post-mortem examination showed that the heart was much enlarged (weight 575 g.), the enlargement being almost entirely due to left ventricular hypertrophy. The coronary arteries were widely patent, and although there was some concentric intimal thickening there was no gross atherosclerosis. There was no evidence of myocardial infarction.

Case 704.—A woman, aged 66, was admitted to the Dunedin Hospital in April, 1953. She had had typical angina for fifteen years, and for the last year the attacks had come on with the slightest exertion and sometimes in bed. The electrocardiogram showed grade-III changes; the basal blood-pressure was 222/124 mm. Hg, and radiography showed considerable left ventricular enlargement.

Treatment was started with M. & B. 2050A in P.V.P. by subcutaneous injection. The patient was last seen in September, 1953. Since treatment had been begun there had been two long attacks of severe precordial pain starting in the early hours of the morning. These were associated with attacks of abnormal rhythm which the electrocardiogram showed to be ventricular tachycardia. Generally speaking, she was much improved. There had been no other attacks of pain at rest, and she could do considerably more with less frequent pain.

Case 708.—A woman, aged 46, was first seen in September, 1950, with a history of angina of effort for eighteen months. The pain came on with slow walking up a slight hill. The casual blood-pressure was 210/130 mm. Hg. The electrocardiogram was normal at rest but showed distinct depression of the s-t segment in the left-sided precordial leads after exertion.

The patient was treated with hexamethonium bitartrate by mouth, and doses of 1 g. reduced her blood-pressure to about 140/90 mm. Hg. She was last seen in October, 1953, when there was no pain on ordinary activity; she could walk up moderate hills and ride a cycle to work without pain. The electrocardiogram had not improved.

Case 712.—A man, aged 55, was first seen in the outpatient department in March, 1953. He had had angina of effort for six weeks. There had been no severe attack, but the electrocardiogram showed right branch bundle block with distinct s-t-segment depression over the left-sided precordial leads.

Treatment was started in June, 1953; and he was last seen in October. At this time he said that he still had pain on hills and on the level against a wind. He could ride some three-quarters of a mile on a bicycle before the pain came on, whereas before treatment he could not do more than two hundred yards. Although clinical improvement was considered to be doubtful and the electrocardiographic pattern of right branch bundle block was unchanged, the s-t-segment depression previously present had disappeared. Treatment was difficult in this patient because of spontaneous pain when the systolic blood-pressure fell below about 150 mm. Hg.

SPONTANEOUS CHEST PAIN

Of the 50 patients with angina who have had test injections or prolonged treatment, 13 had spontaneous chest pain during the period of blood-pressure reduction. In addition, a further 2 patients who had never previously noted angina had spontaneous anginal chest pain when the blood-pressure was reduced. We believe that the smallness of the proportion of patients who have had such spontaneous pain is largely due to careful supervision of treatment.

The blood-pressure level at which spontaneous pain develops varies from patient to patient. Most do not get spontaneous pain unless the systolic blood-pressure falls below about 120 mm. Hg; but in some patients (for example cases 712 and 143) spontaneous chest pain occurred at rather higher levels, case 143 complaining of pain when the systolic pressure fell to 180 mm. Hg. In 2 patients spontaneous chest pain has occurred in association with paroxysmal tachycardia—in one of ventricular type, in the other of auricular type. We have had the impression that spontaneous pain is more likely in the early stages of treatment, although it may occur at any stage if doses causing excessive falls of blood-pressure are given. In some patients the pain seems to be caused by the abrupt falls of blood-pressure, and this may occasionally be avoided by giving oral preparations or slowing agents to delay the fall of blood-pressure (Smirk 1952). In some patients, however, the effects of oral administration are too unpredictable for accurate control of treatment, since capricious alimentary absorption may lead to occasional excessive falls of blood-pressure.

Treatment had to be discontinued in 5 patients (cases 139, 143, 176, 197, and 719) because of spontaneous chest pain.

Case 139.—A woman, aged 67, was admitted to the Dunedin Hospital in February, 1951, with a history of dyspnoea on exertion for four years and angina of effort for three years. On clinical examination there was moderate cardiac enlargement. The casual blood-pressure was 190/130 mm. Hg. The electrocardiogram showed grade-III changes.

Treatment with oral hexamethonium bitartrate was begun, but this had to be discontinued after a month because of diarrhoea, and treatment by subcutaneous injection was substituted. There was slight improvement in the severity of the angina after two months' treatment, but at the end of this time the patient had a long attack of chest pain. It was thought that this attack probably followed an overdose of the drug since the patient had not understood the instructions for dosage. The treatment was discontinued because of the onset of presenile dementia.

Case 143.—A woman, aged 53, was admitted to the Dunedin Hospital in February, 1951. She had been treated for angina of effort for five years, and cardiac infarction had occurred four years previously. On admission there was clinical and radiographic evidence of gross cardiac enlargement. The casual blood-pressure was 268/130 mm. Hg, and the basal blood-pressure was 210/118. The electrocardiogram showed grade-III hypertensive changes.

A subcutaneous injection of 20 mg. of H.M.B. reduced the blood-pressure to 196/98, at which level the patient complained of pain in the chest. An injection of 0·9% saline the next day also produced an attack of pain with the blood-pressure at 218/106 mm. Hg. Treatment was discontinued because of the ease with which pain occurred and because the patient was particularly apprehensive and suggestible.

Case 176.—A man, aged 49, was first seen in 1946 with angina of effort following a myocardial infarction. The angina persisted, and he was seen again in July, 1951. The casual blood-pressure at this time was 210/120 mm. Hg. It was decided to assess the effects of H.M.B.

The blood-pressure could be reduced to 116/90 mm. Hg without the development of spontaneous chest pain. With administration of H.M.B. there seemed at first to be some subjective improvement, but at the end of two months the angina was substantially as severe as before. At about this time the patient had a severe attack of spontaneous chest pain, and, since improvement had been slight, treatment was discontinued. He continued to have angina until his death from another cardiac infarction fifteen months after stopping treatment. Necropsy revealed severe coronary sclerosis with a recent anterior myocardial infarction and an old posterior infarction.

Case 197.—A woman, aged 58, was first seen as an outpatient in May, 1951, with complaints of headache and giddiness. There was no angina at this time. The casual blood-pressure was 250/140 mm. Hg. There was no clinical evidence of cardiac enlargement, and the fundi showed grade-II changes. The basal blood-pressure was 162/114 mm. Hg. The electrocardiogram showed advanced hypertensive changes.

Treatment by subcutaneous injections of H.M.B. was started in August, 1951, but a month later the patient was readmitted after a long attack of chest pain which was due to coronary insufficiency; the pain had come on six hours after the last injection of H.M.B. Treatment was discontinued at this time, but the patient was readmitted in December, 1951, with congestive heart-failure. The casual blood-pressure at this time was 212/152 mm. Hg. The failure was rapidly overcome by administration of H.M.B., and this treatment was continued without further incident until May, 1952. At this time the patient was readmitted with severe bronchopneumonia. Treatment was again discontinued and was not subsequently recommenced. She died in September, 1952, of a cardiac infarction. There was no necropsy.

Case 719.—A woman, aged 42, was seen as an outpatient in January, 1953, with a history of angina of effort for three years and of cardiac asthma for three months. The casual blood-pressure was 175/110 mm. Hg. There was no clinical or radiographic evidence of cardiac enlargement, and the electrocardiogram at rest was normal, although there was depression of the s-t segment in the left-sided precordial leads after exercise.

Treatment with oral hexamethonium bitartrate was started. There appeared at first to be some improvement, but this was never very great. Three months after treatment was started severe diarrhoea developed, and treatment with subcutaneous H.M.B. was substituted. The patient proved extremely sensitive to the drug, and 7½ mg. subcutaneously reduced the blood-pressure to 110/70 mm. Hg and spontaneous chest pain occurred. In view of doubt about the improvement and the spontaneous chest pain, treatment was discontinued. The angina has since persisted.

CARDIAC INFARCTION

Of the whole series of 450 patients, 10 have had cardiac infarctions. Of these, 4 were under treatment at the time of the infarction and the remaining 6 were not being treated. In each of the untreated patients the infarction was fatal. 2 of the patients who were under treatment recovered from the infarction, but both died from subsequent cardiac infarction before treatment had been recommenced. In only 1 patient did cardiac infarction occur at a time when the blood-pressure was low as the result of administration of H.M.B. In the remaining patients the pain started when the blood-pressure would normally have risen after the previous injection. We have the impression that careful treatment with these substances, producing moderate falls of blood-pressure, does not lead to cardiac infarction even in patients with angina. We have ordinarily not treated patients with these substances if cardiac infarction has occurred in the preceding six weeks.

Discussion

The normal ratio of cardiac work to coronary blood-flow is disturbed in patients with angina (Wégrin 1951).

It is apparent that arterial hypertension increases the cardiac work. Blumgart et al. (1940) and Davis and Klainer (1940a, b, and c) demonstrated, in studies of the relation of the clinical manifestations of angina and myocardial infarction to the pathological findings, that some patients with clear-cut angina had normal coronary arteries, the heart being considerably hypertrophied because of hypertension or valvular disease. Harrison and Wood (1949) concluded from a study of hypertensive patients with angina that in many there was coronary dilatation rather than narrowing, so in these the main cause of the angina seemed to be increased cardiac work. In the present series some of the cases examined post mortem showed no evidence of coronary arterial narrowing.

There is little doubt that in the hypertensive patient reduction of the blood-pressure appreciably reduces cardiac work. In those patients with hypertension who obtain relief from angina after reduction of the blood-pressure, it seems probable that the reduction in cardiac work is greater than the reduction in coronary blood-flow when the aortic blood-pressure falls. In a few patients, however, with moderate falls in blood-pressure the reduction of the mean aortic diastolic blood-pressure, and hence of coronary blood-flow, may exceed the reduction of cardiac work so that spontaneous chest pain occurs. In our experience, such a sequence is unusual if the fall of blood-pressure is carefully controlled. We have had the impression, however, that if the blood-pressure is allowed to fall excessively spontaneous chest pain will occur in a larger proportion of patients. The level of blood-pressure at which such pain occurs can be determined in the individual patient only by the most circumspect increments after a small initial dose.

In practice, therefore, angina pectoris complicating hypertension need not be a contra-indication to the use of the methonium compounds. Indeed, the use of those compounds seems to be indicated, provided that they are administered very cautiously. For the ordinary hypertensive patient the fall of blood-pressure in the standing position should be such that recumbency will immediately restore the pressure to about the original level, and it is essential that this precaution be observed in treating the hypertensive patient with angina. This entails frequent observation of the patient in the preliminary period of stabilisation, and critical adjustment of dose; this can be achieved only by the use of syringes graduated to 0.01 ml. Furthermore, the standing systolic blood-pressure should not be reduced below 140 mm. Hg, at least in the preliminary period of treatment when attacks of coronary pain are commonest. We have the impression that spontaneous pain is less likely if the blood-pressure is reduced slowly by the use of delaying agents and sometimes by oral therapy. Oral H.M.B. is, however, not often successful (Kilpatrick and Smirk 1952) and even patients who can take adequate doses by mouth without prohibitive side-effects may have excessive falls of blood-pressure because of the irregular effect of administration by this route.

It has not been possible in the present series to assess the placebo action of these drugs in relieving angina. It is well known that angina can commonly be relieved by placebos. The improvement in other symptoms of hypertension after hypotensive therapy, with the induction of hypotensive symptoms, makes it difficult to substitute ineffective therapy without the patient's knowledge. The main object of treatment in our patients, however, has not been so much the relief of angina as the control of the hypertension in general; and in most cases the angina has been one of numerous symptoms. We have the impression that the striking improvement which occurs gradually over a period of several months can be more reasonably attributed to the reduction of blood-pressure than to a placebo action.

Summary and Conclusions

The methonium compounds may be safely administered to hypertensive patients with angina, with close supervision by experienced physicians and well-trained technical assistants.

The effects of reducing the blood-pressure by this means have been studied in 50 cases. About a quarter of the patients had occasional attacks of spontaneous chest pain and in 5 treatment had to be stopped because of such pain after modest falls of blood-pressure.

A third of the patients treated lost all angina after some months' treatment, while two thirds of the remainder were much improved in this respect.

Cardiac infarction was no commoner in treated patients than in similar untreated patients.

We are indebted to Prof. F. H. Smirk for much helpful advice and criticism. We wish to thank also Miss B. Hoare, Miss B. Stanton, and Miss O. Fraser without whose technical assistance at the hypertensive clinic these observations would not have been possible. We are indebted to Miss N. Richardson and Miss M. Poppelwell for secretarial help. The hexamethonium bromide and related compounds were supplied by Messrs. May & Baker Ltd., Dagenham, Essex.

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PORPHYRIA TREATED WITH NEOSTIGMINE

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WE have recently studied a case of porphyria combining clinical and biochemical features not hitherto described in this disease. The patient recovered after treatment with neostigmine. Successful therapy of porphyria with this drug has not previously been described.

The presenting clinical features were (1) severe colicky abdominal pain associated with nausea and vomiting; (2) dark urine; (3) progressive loss of weight producing emaciation (fig. 1); (4) progressive weakness of the limbs; (5) hoarseness; and (6) hirsuties (fig. 2).

Case-report

A woman, aged 37, was apparently perfectly well until January, 1951, when she was admitted to a general hospital in the West Country with severe generalised lower abdominal pain accompanied by nausea and vomiting. The diagnosis of acute appendicitis was not substantiated at operation, nothing abnormal being discovered. After this operation the patient lived in Jersey, and continued to have severe colicky abdominal pain, constipation, rectal discomfort, frontal headaches, and intermittent bouts of pyrexia. After returning home, and while she was working as a supervisor in a large café,

these symptoms became so severe that she was admitted to a large general hospital for investigation. In hospital she passed dark urine and her voice became husky. Nervous dysfunction of the bowel was diagnosed, and the patient was discharged. Late in September, 1951, she was readmitted to the West Country hospital. She became depressed and tried to commit suicide by taking gr. 18 of soluble phenobarbitone. She was transferred to a mental hospital and shortly after admission complained of numbness and weakness in the limbs. Electroconvulsion therapy was ordered, and immediately afterwards both legs became useless. After seven days the treatment was repeated, and next morning her arms as well as her legs were useless. Deterioration in her general condition continued, and on Feb. 9, 1952, she was taken home by her relations and within a few days was admitted to this hospital.

On examination gross emaciation of all the muscle-groups throughout the body was apparent, a thick growth of hair covered most of the body, especially the face, and there was slight exophthalmos (figs. 1 and 2). The blood-pressure was 120/90 mm. Hg. The heart-rate was increased, and the apex-beat was felt in the fifth intercostal space $3\frac{1}{2}$ in. from the midline. Nothing abnormal was detected in the respiratory system and abdomen. All the cranial nerves except the tenth were normal. Paralysis of the right recurrent laryngeal nerve caused complete inability to move the right vocal cord. The arms and legs could not be moved. The tendon-reflexes were all present, and the planter responses were flexor. There was no impairment of sensation.

Investigations.—A full biochemical, bacteriological, and cytological examination of the cerebrospinal fluid, including a Wassermann reaction and Lange curve, revealed no abnormalities. Examination of the blood gave a normal electrolyte pattern, calcium and phosphorus, glucose-tolerance test, urea, gonococcal fixation test, and blood-count; liver-function tests were also normal, as was the calcium in urine and faeces, and the basal metabolic rate. The blood-cholesterol level was raised on admission but dropped to normal on discharge.

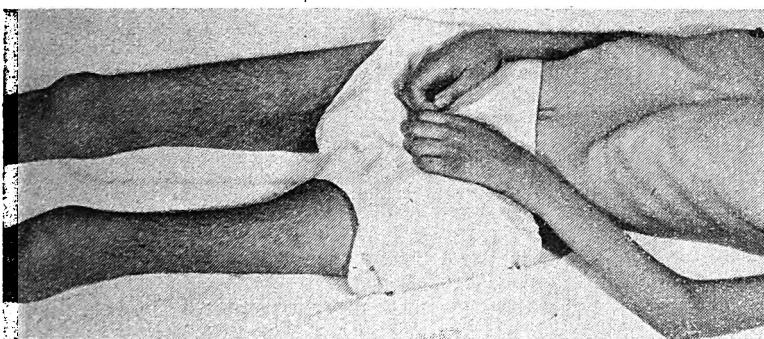


Fig. 1.—Emaciation and hirsuties of thighs on admission.

Urinary creatinine excretion was somewhat depressed, whereas creatine excretion was raised. Examination of bone-marrow revealed that the erythropoietic system was active, and many macronormoblasts were seen. None of the red-cell precursors were megaloblastic. The white-cell maturation was normal. Radiography of the chest and lumbar spine showed no abnormalities, whereas radiography of the hands showed osteoporosis of the carpus and metaphyses of the bones, suggesting osteoporosis due to disuse. The electrical reaction of the muscles was normal to faradism and galvanism, and no myasthenic reaction was present. A biopsy specimen showed an increase of nuclei and small collections of lymphocytes between the muscle-fibres, with atrophy of the muscle (this is the essential appearance of myasthenia gravis). An electrophoresis pattern of the serum-proteins showed a very slightly raised gamma-globulin level.

The urine became pinkish red on standing and on treatment with hydrochloric acid, and gave a pink fluorescence in ultraviolet light. Examination of the spectrum of a 25% solution of hydrochloric acid in the urine showed bands at 5956 and 5520 Å, the spectrophotometric absorption pattern being characteristic of an acid porphyrin solution. Ehrlich's reagent gave with the fresh untreated urine a pink colour which could

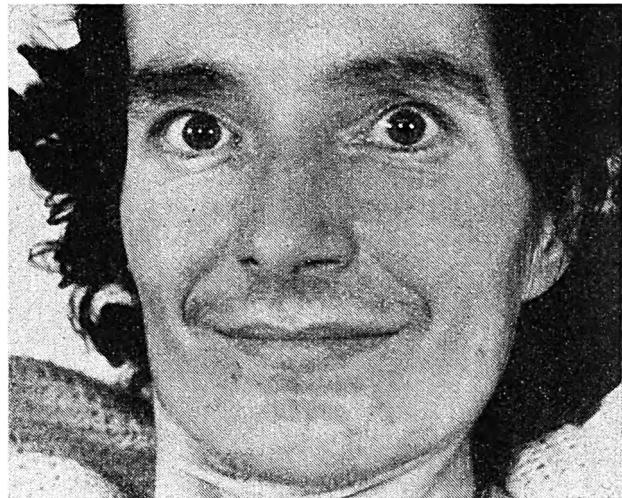


Fig. 2.—Exophthalmos and facial hirsuties on admission.

not be extracted with amyl alcohol. Porphyria was therefore established. The urine-uroporphyrin levels were quantitatively estimated during four phases of the patient's stay in hospital. Levels of up to 10 mg. a day were found during the first fortnight, although accurate estimates were made difficult because of the patient's bed-wetting. After two, eight, and ten months the average daily level during a week's excretion was 1.41, 2.85, and 2.11 mg. a day respectively. The peak excretion was noted during menstruation. From its behaviour in ethyl acetate solution, the uroporphyrin appeared to be type I. The urine-coproporphyrin levels were also estimated and varied between 0.1 and 1.0 mg. a day. Column chromatography of an extract from a six-day collection of faeces showed the presence of coproporphyrin plus a decarboxylic porphyrin.

Treatment of Porphyria.—The treatment of porphyria is empirical; but, since the histological picture of the muscle was similar to that associated with myasthenia gravis, neostigmine 1 mg. was injected subcutaneously three times a day, with a remarkable response. Within half an hour of the first injection the patient moved her arms and legs easily, and her voice, hitherto very hoarse and faint, became stronger and clearer. She sat up without assistance for the first time since the electroconvulsion therapy in November, 1951. This improvement gradually declined until the next dose was given. Ashby (1924), Gray (1924), Schmidt-Labaume (1926), and Mackay and Garrod (1926) reported that a megaloblastic picture is sometimes present in porphyria and that injections of liver extract proved helpful. The presence of macro-normoblasts in the marrow may have been due to subnormal amounts of the liver factor; so 'Anahæmin' 2 ml. weekly was given. After a few weeks of this treatment the marrow became normoblastic. The patient's general condition improved steadily, and after a month she could sit comfortably without support on the edge of the bed and could move her right arm across the body and touch the tip of her left shoulder. As her strength increased, her ability to turn in bed returned. After seven weeks distilled water was substituted for the neostigmine, and within a few hours the muscles became stiff, and control of the arms and legs was lost. When neostigmine was given again the symptoms rapidly disappeared. After a few more weeks' therapy the voice became clear and strong, and crossing and recrossing of the legs became possible. Small

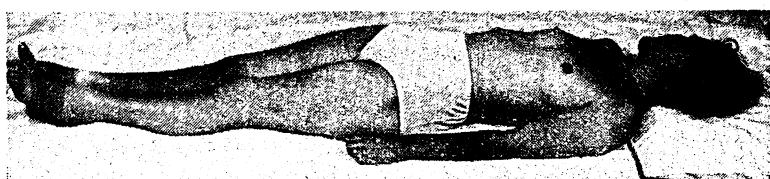


Fig. 3.—Patient after full recovery.

objects could be placed in the mouth, and the patient ate without assistance. After pronation of the wrists returned, ability to write and to turn the pages of a book soon followed. Steady improvement continued, and walking with mechanical devices on the limbs began after ten months, enabling the patient to be discharged from hospital.

Follow-up.—A rehabilitation course was arranged, and tuition as a telephone operator (one of her former occupations) was given. Recently she omitted the neostigmine for four days and listlessness, acute abdominal pain, and nausea returned but quickly disappeared when neostigmine was taken again. The patient has now fully recovered (fig. 3).

Discussion

Treatment with neostigmine was tried because the histological appearance of the muscle resembled that of myasthenia gravis. The favourable result cannot be doubted, because there was an immediate improvement in the muscle power and well-being, with a relapse when distilled water was substituted for the neostigmine. Further, a relapse occurred when the patient omitted neostigmine after discharge. This favourable response might be explained by a coexistence of a constitutional defect leading to porphyria and of myasthenia gravis, the improvement being due to the influence of the neostigmine on the myasthenia. This hypothesis is supported by the fact that the patient continues to excrete as much porphyrins in her urine and faeces as before the start of therapy; but the absence of other signs and symptoms of myasthenia gravis makes this argument unlikely.

The finding of porphobilinogen in the urine leads to the diagnosis of acute porphyria, although the presence of uroporphyrin I is more in keeping with congenital or mixed porphyria.

Hirson (1953) reports two patients with acute porphyria who recovered spontaneously. Therefore the start of neostigmine therapy in the present case may have coincided with a natural remission of the porphyria, but the return of the symptoms after the withdrawal of neostigmine on two occasions is against this argument.

We therefore think that there was a response to neostigmine and urge that this drug be tried when porphyria has been diagnosed.

As in previous cases, barbiturates had been taken before acute porphyria was detected.

Physiotherapy and rehabilitation considerably helped the patient's recovery.

Summary

A patient with acute porphyria exhibited unusual clinical features, including paralysis of the left recurrent laryngeal nerve, deterioration in the clinical condition following electroconvulsion therapy, hirsuties, lymphocytic infiltration of the muscles, and the presence of uroporphyrin I and porphobilinogen in the urine.

The patient recovered when treated with 1 mg. of neostigmine given subcutaneously three times a day and later by mouth in 10 mg. doses.

We thank Dr. W. Whitelaw, director of pathology, and Miss H. Trought, chief biochemist, to the Dudley Road Group of Hospitals for advice and suggestions; Prof. C. Rimington, F.R.S., of University College Hospital, London, for kindly sending us a solution of coproporphyrin; Mr. H. G. Sammons, Ph.D., of Queen Elizabeth Hospital, Birmingham, for permission to use the Beckmann spectrophotometer; and the staff of the Dudley Road Hospital photography department for their co-operation.

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NEW LIVER-FUNCTION TEST

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THE number of so-called liver-function tests has greatly increased, and the older mercuric-chloride tests (Takata-Ara, Gros, &c.) have been superseded by more sensitive and more convenient means of discovering damage to the liver parenchyma. All these tests reveal abnormalities of the serum-proteins—e.g., in parenchymatous liver disease the γ and β globulins are usually increased and are precipitated more easily, and the albumins exert less protective action than is usual—and all have one feature in common: they give precipitations (produce turbidity or flocculation) in pathological sera but none in normal sera.

When chloranilic acid (2 : 5-dihydroxy-3 : 6-dichloroquinone), which precipitates protein, was tried in sera from different cases, including some of liver damage, it did just the opposite: it formed a precipitate in all normal sera and in all sera that gave a negative Takata-Ara test. In the sera where the Takata-Ara reaction was positive the more strongly positive the Takata-Ara reaction the less protein was precipitated by

TABLE I—INFLUENCE OF pH ON CHLORANILIC-ACID REACTION

Reagent no.*	pH of reagent	Serum no.	pH of mixture	Chloranilic-acid test
1	2.50	1	3.19	++
		2	3.18	-
		3	..	-
		4	..	-
2	2.53	5	..	-
		1	3.36	(+)
3	2.75	1	3.88	-
4	2.44	2	3.83	-
		1	2.86	+++
		2	..	+++
		3	..	+++
		4	..	+++

* 1, Usual reagent. 2, Reagent without acetic acid. 3, Reagent with 5 drops of 10% sodium-carbonate solution instead of 0.2 ml. of glacial acetic acid. 4, Reagent with 1.0 ml. of glacial acetic acid.

chloranilic acid, there being no precipitation at all in the most strongly positive sera.

The new reaction was investigated in the Central Laboratory, Aker Hospital, for over a year and then taken into use as our routine method. The results obtained with this method compare very favourably with those given by the Takata-Ara test. Since the new test offers several advantages in simplicity and rapidity, I describe it here.

Method

Reagent	Parts
Chloranilic-acid solution 0.1% (w/v)	.. 70.0
Sodium-chloride solution 0.85% (w/v)	.. 5.0
Glacial acetic acid 0.2	
Distilled water ad 100.0	

The pH of this mixture is about 2.50. The reagent keeps almost indefinitely if stored in the ice-chest but deteriorates slowly at room-temperature and when exposed to light.

Procedure

To 2 ml. of the reagent in a small test-tube 0.1 ml. of serum is added, and the whole is mixed well. Precipitation usually takes place in a few minutes and is practically complete within 15–30 minutes. Readings can therefore be made after half an hour, but the precipitates must then be thrown down by centrifugation. Alternatively the samples may be left to stand overnight for sedimentation. Both these methods have been used and usually

give identical results. The following grading of the readings was used:

Precipitate	Supernatant fluid	Grading
Heavy ..	Clear ..	-
Heavy ..	Opalescent ..	(-)
Less heavy ..	Turbid ..	(+)
Small ..	Very turbid ..	+
Trace ..	Very turbid ..	++
None ..	Translucent ..	+++

Usually there is no difficulty in assessing the results, but occasionally it is not easy to decide whether a test is positive or not. In some very rare cases the reading after 30 minutes differs from that obtained after 24 hours. These cases include both normal sera which do not precipitate at once and pathological sera which give "false" precipitations on standing.

Since part of the chloranilic acid is precipitated with the protein, a more quantitative assessment may possibly be made by determining the amount of chloranilic acid (which is a dye) colorimetrically in the precipitate and/or in the centrifugate after treatment with trichloro-acetic acid.

Results and Discussion

For the selectivity of the test the pH of the reagent seems to be important. The influence of the pH (table I) was studied in the following way:

In 5 serum samples the test was made with the usual reagent (reagent 1). 3 of the tests were negative, 1 was read as +, and 1 as ++.

When a reagent was used which contained 1.0 ml. of glacial acetic acid instead of 0.2 ml. (reagent 4) ++ reactions were obtained in all the sera tested. The pH of this reagent was 2.44, and a pH of 2.86 was found in the mixture in the case of serum 1.

The substitution of 5 drops of 10% sodium carbonate for the glacial acetic acid (reagent 3) increased the pH of the reagent to 2.75, and of the mixtures of serum and reagent to 3.88 and 3.83; and the test, which had been positive in both sera, became negative. If the glacial acetic acid was omitted from the reagent (reagent 2), the change of pH in the reagent was only slight; it was larger in the mixture, and the test became decidedly less positive with serum 1.

As can be seen from table I, a relatively slight increase in pH of the reagent caused all the positive tests to become negative, whereas a decrease in pH had the opposite effect.

The possibility that the difference observed between normal and pathological sera was due to a difference in the final pH of the mixture was ruled out by measuring the pH in the centrifugates from tests made on 17 samples (table II). For comparison, in 13 of these cases readings with the Takata-Ara test are listed.

The pH in the 9 negative samples ranges from 2.93 to 3.19 (av. 3.07) and in the 8 positive ones from 2.96 to 3.09 (av. 3.04). The difference (if any) between the

TABLE II—pH OF CENTRIFUGATES

Sample no.	Chloranilic-acid test		Takata-Ara test
	Reading	pH	
1	+	3.03	..
2	+	3.12	..
3	(+)	2.96	..
4	(-)	3.19	..
5	-	2.93	-
6	++	3.05	++(++)
7	++	3.01	++(++)
8	(-)	3.01	-
9	-	2.94	-
10	-	3.08	-
11	-	3.09	-
12	-	3.16	-
13	-	3.11	-
14	-	3.12	-
15	++	3.06	++
16	++	3.00	++
17	+	3.09	+

TABLE III—CORRELATION BETWEEN CHLORANILIC-ACID AND TAKATA-ARA TESTS IN 120 BLOOD SAMPLES FROM 25* PATIENTS

Choranilic-acid tests	Takata-Ara tests								
	Negative (56)			Positive (64)					
	-	(-)	±	(+)	+	+ (++)	++	++ (++)	+++
Negative (56)	-	31	3	2	7	7	1	4	..
	(-)	1	3	1	1	1	1
	±	..	1	1	1	..
Positive (64)	(+)	4	2	2	3	8	1	3	1
	+	..	2	2	..	1	3	1	2
	+ (++)	1	3	5
	++	3	1	1
	++ (++)
	+++	1	2

Agreement was found in 86(83) samples (71.7(69.2)%).

Agreement was complete in 49 samples, good in 27(24) samples, and fairly good in 10 samples.

Discrepancy was found in 34(37) samples (28.3(30.8)%).

Positive Takata-Ara and negative chloranilic-acid test in 23(24).

Negative Takata-Ara and positive chloranilic-acid test in 11(13).

- Diagnoses: acute hepatitis (6 cases); hepatitis (2); hepatic cirrhosis (6 cases + 1 doubtful case of alcoholic cirrhosis); cholelithiasis (1); cholangitis or cholecystitis (?) (1); hepatic cyst (1); cancer of pancreas with metastases (1); heart-disease and arteritis (1); leukaemia (1); sarcomatosis (1); mammary cancer (Op.); carcinomatosis (1); pulmonary tuberculosis (1); and proteinuria (1).

two series is clearly too small to be of any significance for the outcome of the reaction.

That the present test may be as useful as the Takata-Ara test in the diagnosis of severe liver damage is clearly shown by the excellent agreement between the results obtained by the two tests.

From Oct. 15, 1951, to Oct. 15, 1952, 650 blood samples were tested by both the chloranilic-acid and the Takata-Ara methods. In only 37 samples (5.8%) were dissimilar results obtained—i.e., the chloranilic-acid test gave 15 "false" positives and was negative in 21 samples which gave a positive Takata-Ara reaction.

All the 120 results recorded in the 25 patients from which the 37 samples mentioned were derived are shown in table III. They show that the two methods agree well on the whole but occasionally give discordant results, in some cases rather striking.

Since Jan. 15, 1953, the new method has been used as our routine method at the Aker Hospital, 1064 samples of blood being tested thereby up to Jan. 15, 1954. In 26 cases a Takata-Ara test was also made; in 3 of these cases a positive Takata-Ara was associated with a negative chloranilic-acid test.

The Takata-Ara test was usually made in cases where the clinicians threw doubt on the result of the chloranilic-acid test, especially where they thought that a negative result did not harmonise with the clinical picture. This may explain the higher degree of discrepancy (11.5%) between the two methods in this small series.

It may be inferred that the chloranilic-acid and Takata-Ara tests seem to be related in so far as they both reveal grosser changes in the proteins and thus may be regarded as approximate measures of the severity of the liver damage.

The test described here has, however, the advantage that it is much easier to make, because only a single tube is needed for each sample of blood, and the result can be obtained within half an hour if the mixture is centrifuged.

Summary

A new liver-function test (with chloranilic acid) is described.

The chloranilic-acid reagent gives voluminous precipitates in normal sera, whereas the precipitate formed in sera from cases of parenchymatous liver disease decreases with increasing severity of the liver damage. In the worst cases no precipitate is formed.

Like the Takata-Ara test the chloranilic-acid test detects grosser changes in the serum-proteins accompanying the more severe degrees of liver damage.

The test is easier and less laborious to make than the Takata-Ara test, and the result may be obtained within half an hour, provided the readings are made after centrifugation.

Preliminary Communication

SIGNIFICANCE OF ASCORBIC ACID IN THE ADRENAL CORTEX

THE significance of the high concentration of ascorbic acid in the adrenal glands, anterior pituitary, and corpus luteum is still obscure. Its rapid disappearance from the adrenals of animals exposed to various kinds of stress has not been satisfactorily explained, although the degree of depletion has been used for quantitative biological assay of adrenocorticotrophic activity.¹ The simultaneous reduction in the cholesterol content of the gland has led to the belief that both these substances are concerned with the production of the cortical hormones.² A second suggestion was that ascorbic acid might in some way be incorporated to render the steroid hormones water-soluble.³ Vogt⁴ and Oesterling and Long,⁵ however, found no evidence to support either view. Recently, Dugal and Therien⁶ have stated that though ascorbic acid fails to replace corticotrophin (A.C.T.H.) in maintaining adrenal weight in hypophysectomised rats, the two substances seem to act synergistically in this respect when given together.

Hypophysectomy in the rat results within a few days in pronounced reduction of the adrenal weight.⁷ Histological sections of such glands show atrophy of the zonea fasciulata and reticulosa, owing to a great reduction in their cell volume. The consequent crowding of the nuclei in these layers becomes very conspicuous. Such atrophic glands also lose their high degree of sensitivity to corticotrophin as judged by Sayer's ascorbic-acid-depletion method. The administration of corticotrophin as replacement therapy can prevent this atrophy, and has in fact been used as an alternative method of assaying adrenocorticopic activity (adrenal maintenance test).

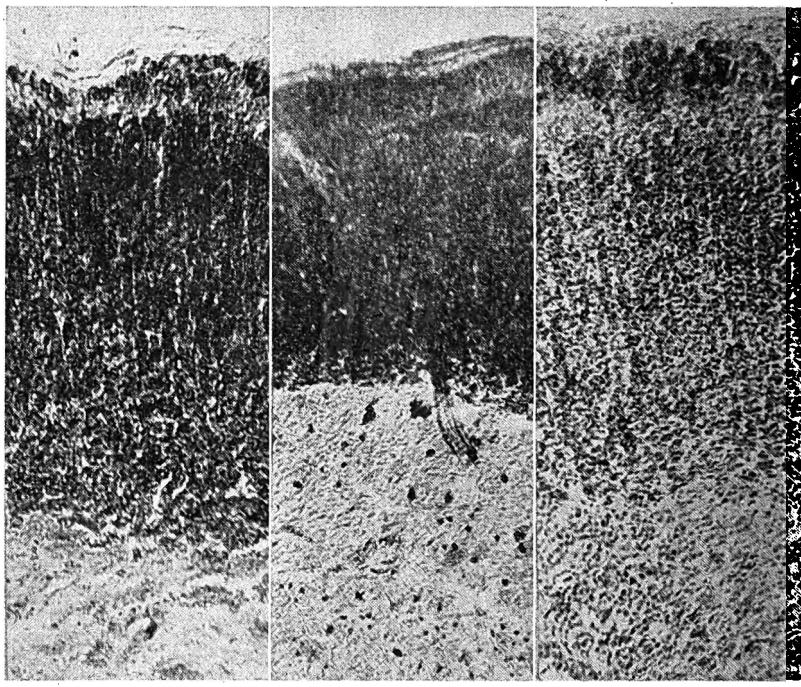
The possibility that the high concentration of ascorbic acid in the adrenal glands might have a rôle in maintaining the adrenal weight was investigated in the following experiment. Twenty male albino rats, each weighing

about 100 g., were hypophysectomised and were divided into two equal groups. Each animal in the first group was given a daily intravenous injection of 100 mg. sodium ascorbate (Roche) in saline. Each animal in the second group was given the same volume of saline by intravenous injection. After a week all the animals were killed and their adrenals weighed immediately. A third group of ten intact animals of the same weight were also killed and their adrenals similarly weighed. The average weights of the glands in each of the three groups are shown in the accompanying table.

WEIGHTS OF FRESH ADRENAL GLANDS (MG. PER 100 G. BODY-WEIGHT)

Control rats	Hypophysectomised rats	
	Saline	Ascorbate
25.0 ± 1.2	12.2 ± 0.2	21.8 ± 1.3

These figures indicate that following hypophysectomy the reduction in adrenal weight, which would otherwise take place, can be almost averted by means of ascorbic acid only. The observed difference between the saline-treated group and the two others is statistically



Sections through adrenal cortex, fixed in formol saline and stained with Sudan III. (a) Intact control. (b) Hypophysectomised treated with saline. (c) Hypophysectomised treated with sodium ascorbate. ($\times 110$)

significant; that between the control and ascorbate groups is barely significant ($P = 0.05$).

Frozen sections of such glands are shown in the accompanying figure. It appears that the adrenals of hypophysectomised rats treated with ascorbic acid contain much less cholesterol than the adrenals of the other two groups. Further work is in progress to find out whether ascorbic acid has any potentiating effect on the adrenal weight-increase or adrenal weight-maintenance produced by corticotrophin in hypophysectomised rats.

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Effects of Antibiotics

The section of comparative medicine met on April 21, with Prof. T. J. BOSWORTH, the president, in the chair, to discuss the Effects of Antibiotics on the Host.

Prof. L. P. GARROD said that the ideal antibiotic would not harm the host at all; but of the many antibiotics which had been discovered only a very few had stood the test of time, because in one way or another they could be more harmful than beneficial to the host.

Five types of effect on the host could be recognised: toxicity, sensitisation, vitamin deprivation, super-infection, and growth promotion.

Toxicity.—Of all the antibiotics penicillin was by far the least toxic—astonishingly high concentrations of penicillin (even up to more than a thousand units per ml.) could be achieved in the blood without ill effect. One of the great dangers with streptomycin was the production of deafness, which might be permanent. The toxic effects of chloramphenicol on the bone-marrow had caused much discussion, and excessive doses of aureomycin and oxytetracycline (terramycin) were known to harm the liver. Polymyxin and bacitracin, particularly the latter, were apt to attack the kidney. Professor Garrod pointed out that his experience of these toxic effects was mainly in man. The effects in animals might be different; some effects in animals might also be more difficult to detect—for example, deafness in a cow.

Several antibiotics had been found to cause *sensitisation*. Some 20 cases of sudden death following administration of penicillin had been reported. These cases were thought to be anaphylactic; they apparently occurred always in persons who had had a previous injection, especially when procaine penicillin had been used. Penicillin and streptomycin were both commonly the cause of skin rashes, especially in nurses who were frequently handling the drugs, or when these antibiotics were applied repeatedly to the skin. Here again it was not so easy to say what happened in animals, in which some types of hypersensitivity reaction would be much more difficult to detect than in man.

Vitamin Deprivation after prolonged use of antibiotics had been described. This could be the result of suppressing the kinds of bacteria in the gut which contributed to the vitamin requirements of the host. Cases of this kind could not arise if vitamins were given with the antibiotic.

Super-infection was a serious problem and could take many forms. For example, a pneumococcal infection might respond to an antibiotic such as penicillin only to be replaced by a *haemophilus* infection which failed to respond. The use of the "broad spectrum" antibiotics was sometimes followed by staphylococcal or candida infections of the air-passages or bowel: staphylococcal enteritis might be fatal. The mechanism of this type of catastrophe was at present obscure.

Growth Promotion.—This was one of the most interesting effects of antibiotics on the host. Professor Garrod would leave it to other speakers who were actively working in this fascinating field to say more about it.

Prof. ALAN KEKWICK discussed certain aspects of the pharmacology of penicillin, streptomycin, chloramphenicol, aureomycin, and oxytetracycline. Despite the very great volume of work that had been done, there were still enormous gaps in our knowledge of the optimum dosage of these drugs, in relation to route and frequency of administration, ease of absorption, excretion, toxicity,

and so on. Often an adequate clinical response might be obtained with doses far lower than those customarily used; these usual doses sometimes approached the maximum which could be tolerated, though the tolerance might vary greatly between different species of animal.

Mr. W. S. GORDON, PH.D., after describing briefly the discovery of the growth-promoting effects of antibiotics, gave an account of the work which he and his colleagues have been doing in recent years in an attempt to find the mechanism responsible for this feature. Its occurrence was well established in many species of animals—including young children—and even in young plants as well. Increases in growth-rate of the order of 10–15% in treated over controls had been recorded, together with an improvement in food conversion, which resulted in more rapid fattening of pigs and poultry for human food with consequent increase in profit to the producer. Of equal, if not greater, importance, however, was the apparent reduction in clinical and subclinical infections which retarded growth.

Certain experiments gave a clue to the probable explanation. For example, the addition of antibiotics to the "germ-free" chick embryo did not stimulate growth, whereas after hatching a growth response could be elicited. The fundamental study of "germ-free" life by Professor Reyniers at the Lobund Institute of Notre Dame University clearly showed that "germ-free" animals derived no benefit from an antibiotic supplement, but would grow as fast as conventional, or bacteriologically contaminated, animals receiving such a supplement. The growth stimulation appeared to occur only in conditions where the environment had been contaminated by previous populations of the same species, and if the antibacterial properties of an antibiotic were removed it no longer appeared to possess the ability to stimulate growth. Even with concentrations of penicillin or aureomycin as low as 4 parts per million in the diet (approximately 0.13 mg. per kg. body-weight) antibiotic was detectable in the small intestine, stomach, and urine in the case of penicillin, and throughout the digestive tract with aureomycin. With concentrations of 128 parts per million in the diet (approximately 4.2 mg. per kg. body-weight), detectable levels in the serum were obtained with both antibiotics.

Mr. S. K. KON, D.Sc., described experiments indicating that the effect of antibiotics on growth is related to environmental conditions. When a few years ago tests with antibiotics were begun at the National Institute for Research in Dairying, where chicks had been kept for a long time, positive results were consistently obtained; but workers at the Glaxo Laboratories found at the same time no response. Joint work showed that under otherwise identical conditions antibiotics were ineffective where chicks had not been kept before but improved growth in long-used premises. In these the antibiotics acted not so much by promoting growth as by removing a growth-depressing effect attributed to an inapparent "infection" in birds otherwise quite healthy by conventional standards. Further studies at the N.I.R.D. in isolation boxes showed that the "infection" could be transmitted by addition to the food of raw gut contents, but not of autoclaved ones of "infected" chicks or of those raw from "uninfected" birds. The gut weight of chicks responding to antibiotics was less than in the lighter controls. There was good indication that this effect on the gut was not direct but mediated by the microbial population since the gut-weight of "uninfected" chicks was not reduced by antibiotics. The nature of the "infection" was still obscure, and we had still much to learn both about the normal population of the gut of chicks and other animals and the effects on it of antibiotics.

Tonsils and Adenoids

The section of general practice met on April 21, with Dr. A. TALBOT ROGERS, the president, in the chair, to discuss the problem of Tonsils and Adenoids.

Dr. OLIVER PLOWRIGHT said that in children over 12–15 years old there was no problem : "If in doubt, take them out." The discussion was centred on younger children, and the two structures had to be considered independently. Sometimes the adenoids alone required operation, though not every surgeon could be persuaded of this. The indications for adenoideectomy were fairly straightforward ; in the majority of cases there was either nasal obstruction, evinced by mouth-breathing with snoring in the absence of coryza, or recurrent otitis media or deafness. The mother's story, the child's breathing, and an indrawn fixed ear-drum on auriscopy usually led to the diagnosis. The indications for tonsillectomy were less universally agreed. Before the present century it was a rare operation ; but recent surveys showed that at least a quarter of all children in England and Wales had been subjected to what the Medical Research Council termed "a routine prophylactic ritual" by the age of 14, and the proportion was higher in the United States. More than three-quarters of boys starting at Eton had had their tonsils out. Dr. Plowright thought that today repeated upper respiratory infections were commoner ; in consequence tonsils were larger. Size was no index for operation, nor was persistent enlargement of the tonsillar lymph-gland ; while chronic infection of the tonsil was difficult if not impossible to detect. He regarded the theory of focal sepsis as completely dead. Recurrent frequent tonsillitis with persistent lymph-glands, or one or two quinsies, pointed to the need for operation ; but tonsillitis had to be distinguished from a plain sore throat, and recurrent colds suggested rather focusing attention on the adenoids, or better still on the conditions of overcrowding the child probably suffered at school and at home whence he drew his infections. The tonsils, after all, were there to protect the child, and should be preserved if possible. But it was often difficult to convince parents of this : unfortunately tonsillectomy had prestige in their eyes. Tonsillectomy was very rarely necessary for respiratory obstruction, or for treating the diphtheria carrier (when other methods had failed). A few children who had their tonsils and adenoids removed for no very good reason did proceed to grow and enjoy better health afterwards. But it was wise to be conservative : there were 85 deaths per annum from the operation ; there were the psychological risks of night terrors and enuresis, to say nothing of sudden haemorrhage or of the enhanced risk of bulbar paralysis in poliomyelitis.

Dr. WILFRID SHELDON agreed that tonsils and adenoids must be considered apart, and to Dr. Plowright's indications for adenoideectomy he added three diagnostic points. The first was that chronic sinus infection was commonly linked with enlarged adenoids. The second was that a child who was sick in the early mornings before breakfast, with a slimy vomit, had probably been swallowing mucopus all night, and needed attention to the adenoids ; but neither of these associations was invariable and absolute. The third was a diagnostic warning. The child brought with a history of frequent absence from school because of colds, of much early morning sneezing, and of vigorous nose-blowing with very little result, was suffering from allergic rhinitis, for which operation on tonsils and adenoids was useless. Dr. Sheldon also advised caution in recommending tonsillectomy. Acute tonsillitis was a sign that the tonsil was functioning effectively as a trap for infection. Three attacks in a year meant nothing if the tonsils were healthy between them, and a source of infection in the household should rather be sought and treated. A tonsil was probably unhealthy, no matter its size, if there were congested vessels in the anterior faucial pillar, and if there were a granular pharynx and

persistent firm lymphatic glands at the angle of the jaw and in the anterior triangle of the neck. A child who failed to thrive, or lost its appetite, might benefit from tonsillectomy, while some cases of vomiting and of bad breath were cured by this operation. He also believed that focal sepsis was still a valid idea ; and tonsillectomy might relieve, for instance, recurrent nephritic haematuria. This operation was valuable in the treatment of tuberculous glands in the neck, because the tonsil was usually the portal of entry of the tuberculosis. Tonsillectomy should be done whenever tonsillar disease impaired the child's health, no matter what his age.

Mr. R. J. CANN explained that while the tonsil could be removed completely by dissection or by the guillotine (much more difficult—a dying art) because it had a capsule and was visible, the adenoids had no capsule, were more concealed, and had to be scraped away ; so it was physically impossible to remove them completely. When the tonsils were completely removed, particularly in the first five years of life, lymphoid tissue around the pharynx tended to hypertrophy as a substitute for regeneration. Thus rounded mounds swelled up on each side of the tongue base (lingual tonsils) ; the pharyngeal wall became speckled with plaques of lymphoid tissue ; and a thick band of it developed behind the soft palate, particularly around and in the eustachian openings, where it tended to cause persistent middle-ear obstruction and deafness. Further removal was extremely difficult, but radium or deep X-ray therapy could be used. This tendency to hypertrophy or regeneration was a further reason for conservation rather than operation. In the nasopharynx the size of the lymphoid tissue created the trouble ; whereas in the fauces it was infection which called for the operation, though the number of attacks per annum was not the guide. He thought continuing deafness was commoner than recurrent otitis, and eustachian obstruction commoner than nasal obstruction, in bringing the patient to operation. Tonsillectomy was avoided during epidemics of poliomyelitis, not because it increased the risk of catching the infection, but because it enhanced the likelihood of the disease taking the fatal bulbar form.

The subsequent discussion showed general agreement on the necessity for operating on tonsils and adenoids independently, and for avoiding operation altogether whenever possible.

MANCHESTER MEDICAL SOCIETY

Asthma Treated by Oral Cortisone

At a meeting of the section of medicine on April 7, Dr. WILLIAM BROCKBANK, with Dr. R. S. SAVIDGE, discussed the Treatment of Asthma with Oral Cortisone, on the basis of a blind trial on 24 patients severely incapacitated by asthma of long standing ; their ages ranged from 17 to 70 years. 13 received regular maintenance doses of cortisone and 14 an indistinguishable control substance. 3 who were failures on the control were given cortisone. Of the 13 cortisone cases, 6 improved sufficiently to make a great difference in the ability to work and play ; 4 more improved, but mostly subjectively ; 1 was no better (this patient, who had severe emphysema, died eight months after the cortisone was discontinued) ; and 2 died while taking the drug. These results are very much better than in the control group ; in 57% of this group there was no improvement, and 1 patient died. Side-effects of cortisone were few, increasing weight being the most important. The longest remission after withdrawal of the drug was eleven weeks. Most cases tended to relapse within a few days.

Cortisone cannot cure asthma, but some cases of long-standing chronic asthma can be effectively controlled by moderate doses of cortisone by mouth. But cortisone treatment is dangerous to life in some undefined types of asthma.

Reviews of Books

Peptic Ulcer

C. F. W. ILLINGWORTH, C.B.E., M.D., CH.M., F.R.C.S.E., F.R.F.P.S., regius professor of surgery, University of Glasgow. Edinburgh : E. & S. Livingstone. 1953. Pp. 287. 42s.

So much clinical and experimental research has been done on peptic ulcers that it is important from time to time to take stock of the facts and discard untenable hypotheses. Professor Illingworth does this with lucidity, simplicity, and elegance of language.

His own work on the incidence of ulcer in Glasgow enables him to condense the evidence as well as to indicate the fallacies in similar studies elsewhere and to emphasise the unexplained differences between peoples and places. In the section on gastric physiology he draws a clear distinction between speculation and fact that will be a great help to those who try to keep abreast of new work. The chapters on symptoms and treatment are outstanding, for here he writes with the intimate knowledge that only personal experience can give. The description and analysis of pain in peptic ulcer gives the reader a new comprehension of the experiences and reactions of an ulcer patient. Professor Illingworth's estimation of the value of the various methods of treatment, ranging from psychotherapy to surgery, is penetrating and practical.

The book is of modest size with well-selected graphs and illustrations and an extensive bibliography. It should be in the possession of everyone who deals with ulcer patients.

General Virology

S. E. LURIA, professor of bacteriology, University of Illinois. New York : John Wiley. London : Chapman & Hall. 1953. Pp. 427. 68s.

TEN years ago there were only one or two textbooks on viruses, but today nearly all self-respecting virologists have written or are writing one. Professor Luria's book is the first to treat virology as a separate branch of biology in its own right. His aim is to study plant, bacterial, and animal viruses as a group, despite uncertainty as to the extent of taxonomic kinship among what we call viruses.

He does not attempt to describe individual virus diseases or viruses ; instead he deals with the facts and methods of virology as a whole. He first describes the techniques of virology and then the physical and chemical properties of virus particles in the resting state, and next considers virus-host interaction. Understandably, he gives most space to the bacterial viruses, since here the greatest advances have been made, many by himself and his colleagues. His experience with bacteriophages enables him to throw light on many important biological problems of animal and plant viruses, including variation, virus ecology, the relationship between viruses and tumours, and the origin and nature of viruses.

This book began as a course on viruses which Professor Luria gave to graduate and advanced undergraduate students at the University of Illinois. It has emerged as a collection of essays written with enthusiasm, imagination, and clarity, and it should appeal to mature as well as embryo virologists. Our respect for Professor Luria is only equalled by our respect for the intelligence of the students of the University of Illinois.

Medical and Scientific Investigations in the Christie Case

F. E. CAMPS, M.D., lecturer in forensic medicine, London Hospital Medical College. London : Medical Publications. 1953. Pp. 244. 30s.

Few criminal cases have enough medical and scientific interest to justify the compilation of a book of this part of the evidence ; but like R. v. Ruxton and R. v. Dobkin, the case of R. v. Christie was full of problems : it was a job for a team—the forensic pathologist, the microscopist, the toxicologist, the mycologist, the anatomist, and the dental histologist, with ancillary radiology, plan and diagram drawing, and photography, not to speak of the C.I.D., and counsel and psychiatrist for each side.

Notable contributions to this book come from Professor Miles on the dental identity studies and from Richard Harrison on the ageing, sexing, and stature estimations (for assigning skeletal remains to missing victims). The former give further encouragement to the use of Gustafson's method of "points-value" ageing of individual teeth. But the dental experts do not seem to have read Thomas Bell's *Anatomy, Physiology, and Disease of the Teeth* (1829) which described pink teeth accurately—nor Tomes's later copying of this account. Had they done so their "considerable speculation" would have been averted.

The anatomical work provides strong support for the recent American stature estimation tables of Trotter and Gleser—undoubtedly less inclined to overestimate than Karl Pearson's famous regression figures—and there are good colour diagrams for reconstruction data by Peter Cull which must have made the jury's problem much easier. American criminal courts are taking more readily to the artist than ours in England, and the Attorney-General's authoritative use of these colour plans is welcome.

Just as we despair of accuracy in estimating the lapse of time since death (and these studies provided no help in this respect) so we are beginning to learn more of the longevity, after death, of the sperm in the vagina, and of the consequent insecurity of opinion on the date of intercourse. Contrary to general belief HbCO and myo HbCO are also long-lived : more bench-work on this problem would have improved Smith's chapter on CO absorption.

This is a painstaking account of the enormous amount of work that forged the medical and scientific links in the chain of evidence against Christie. A vast amount of useful observation and well-informed reasoning has been piled into the text, which is well illustrated and produced.

Resection-Reconstruction of the Hip

Arthroplasty with an Acrylic Prosthesis. JEAN JUDET, ROBERT JUDET, JEAN LAGRANGE, JEAN DUNOYER. Editor : K. I. NISSEN. Edinburgh : E. & S. Livingstone. 1954. Pp. 151. 30s.

THE Judet arthroplasty, as it is usually called over here, achieved immediate popularity because of the simplicity and directness of its conception, the relative ease of its execution, and the excellence of its early results as compared with any previous form of hip arthroplasty. Large numbers of patients were subjected to the operation even though no-one knew what the late results would prove to be. Though the gloomier prognostications of early critics have not proved correct, complications have nevertheless been sufficiently numerous to provoke a smart reaction ; and now some maintain that the operation should be reserved for elderly lightweights who are never going to put any great strain on the new joint.

The Judet brothers and their co-authors have done 850 of these operations, and they claim some 80% of excellent or good results in their more recent cases, in which they have used their new prosthesis ; but they are at pains to emphasise that patients have to be selected with great care. The appearance of an English edition of their book will be welcome to all orthopaedic surgeons in this country, and Mr. Nissen is to be congratulated on his editorship. The book is modestly written, and the difficulties and complications are described with an engaging frankness. Naturally, as the originators of the method, the Judets and their team have tried it in various conditions where there appeared reasonable hope of getting improvement—sometimes with disappointing results. Each type of disorder is discussed, and the chapter on late cases of congenital dislocation of the hip is particularly helpful, giving a clear picture of the limitations. The Judets use Hueter's approach as a routine, and believe that the exposure should be as limited as possible, so as to reduce interference with the blood-supply of the femoral neck. They obtained no better results with an extensive capsulectomy. In discussing the rationale of the operation in osteoarthritis they say : "the femoral head is the principal site of pathological change, and hence the main source of pain"—a conclusion with which not all would agree. They now do an acetabuloplasty more often than not.

Their results, good and bad, are given with obvious fairness, and they do not attempt to put the method

forward as a panacea. They have been responsible for a great step forward in the surgery of the hip-joint, and much honour is due to them. This well-illustrated book gives a worthy account of their stewardship.

Man's Ancestry

A Primer of Human Phylogeny. W. C. OSMAN HILL, M.D., F.R.S.E., prosecutor, Zoological Society of London. London : Heinemann Medical Books. 1954. Pp. 194. 21s.

Dr. Osman Hill has converted a short course of lectures to Edinburgh students of social anthropology into an excellent account of the probable path of evolution from the lowest forms of life to man. Naturally, he gives considerable space to the emergence of the primates, the rise of the anthropoids (the Australopithecinae are regarded as "essentially apes"), and the emergence of man. The various forms of fossil man and the chief prehistoric cultures, from palaeolithic to iron-age, are briefly described. He concludes that man is not descended from an anthropoid ape but from some more primitive animal :

"The hominid line, after emerging from the common Eocene pool of tarsioids, must have been represented by an unspecialised quadrupedal monkey-like Primate, possibly represented by *Parapithecus*. The line leading to the apes separated from that which gave rise to Man probably in the Oligocene."

The illustrations are good and an abundant bibliography, a glossary, and an index round off a useful work.

French's Index of Differential Diagnosis

(7th ed.) Editor : ARTHUR H. DOUTHWAITE, M.D., F.R.C.P., senior physician, Guy's Hospital, London. Bristol : John Wright & Sons. 1954. Pp. 1058. 5 guineas.

THIS edition appears after a ten-year interval under the new editorship of Dr. A. H. Douthwaite, who has collected a strong team of contributors, mainly from the teaching staff of Guy's Hospital and the Westminster Hospital. He has had the help particularly of Sir Adolphe Abrahams, whose many articles are models for publications such as this.

Dr. Douthwaite would be the first to acknowledge the magnitude of the task he has set himself—to cover medicine, surgery, and obstetrics and gynaecology in one diagnostic volume.

Many of the articles are admirable—clear, brief, and to the point. Some others are less effective, perhaps because for some symptoms—notably the neurological—there must be long lists of causes and classifications, and differential diagnosis cannot be set out in a short article.

It must have taken much hard work and great determination to complete this book without excessive repetition or overlapping. The index alone, on which a main purpose of this book must depend, covers nearly 150 pages and is a comprehensive and successful achievement. There are over 700 illustrations, many in colour, and high praise must go to the publishers for the printing and production.

Doctors will find the new "French" a practical help in their daily work, and they should be grateful to Dr. Douthwaite and his colleagues for their careful, thorough, and skilled revision of an old friend.

Medical Terms

Their Origin and Construction. FFRANGCOON ROBERTS, M.A., M.D., F.F.R. London : Heinemann Medical Books. 1954. Pp. 88. 6s.

THE curtailment of a liberal education through too early specialisation, which is the usual lot of the modern medical student, has prompted Dr. Roberts to explain to those who lack knowledge of Greek and Latin how medical terms have been constructed and how new ones should be formed. As our correspondence columns have lately shown, this is a subject in which many would like enlightenment, and Dr. Roberts is always a lucid and lively expositor. But his book is designed on an elementary level, and it unfortunately contains a good many small errors which will alienate the kind of reader who already has any considerable knowledge of words and may be correspondingly sensitive to inaccuracy in their employment. Thus, though the word "eponyms" is used correctly, the word "eponymous" is used

incorrectly to qualify the words instead of the persons who lend their names; "ballottement" is spelt wrongly ; and the derivation of "anaphylaxis" is faulty, because Richet (who coined this word) preferred the meaningless "ana" as being more euphonious than the correct "a," meaning "without." Similar slips may be found every week in our own columns ; but in a philological work they warn the reader that he is being addressed by a fellow doctor rather than a professional philologist.

Maxillo-Facial Laboratory Technique and Facial Prostheses

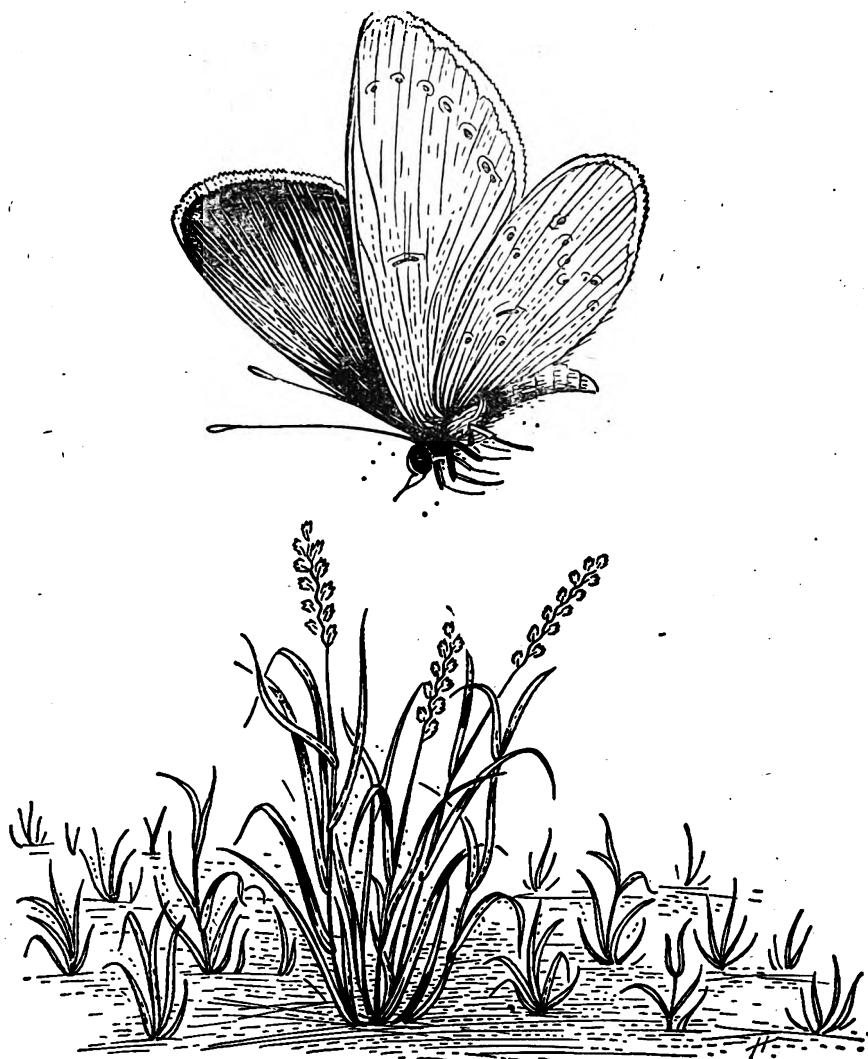
STANLEY BRASIER, chief technician, prosthetic laboratory, plastic surgery, burns, and jaw injury centre, St. Lawrence Hospital, Chepstow, Mon. London : Henry Kimpton. 1954. Pp. 230. 31s. 6d.

THIS is a good practical textbook for the trained dental technician who has no knowledge of the special procedures involved in making dental splints and non-dental prostheses. Plastic surgeons, too, may find it useful, for though in general they have not had enough technical training to be able to carry out the various laboratory techniques described, even if they wished to do so, they like to have a fair idea of what can be achieved with prostheses, as well as the limitations imposed by the materials available. There are a few statements with which both surgeons and dental surgeons may well disagree—e.g., "the edges of the ideal splint should extend into and beyond the gingival margin to a depth of about 2 mm." With all normal gingiva this will rupture the periodontal ligament. Again, if connecting bars between sections of a splint are situated only 1 mm. from the mucosa, as suggested, the maintenance of good oral hygiene will be much more difficult than if these bars have a clearance of 5-6 mm. Minor criticisms such as these do not really detract from the value of this book, which should certainly be in the possession of all technicians undertaking maxillofacial laboratory work.

Peripheral Nerve Injuries (2nd ed. Philadelphia and London : W. B. Saunders. 1953. Pp. 333. 35s.).—Dr. Webb Haymaker and Prof. Barnes Woodhall note in the preface to this edition that in the Korean conflict peripheral nerve injuries have presented many diagnostic problems to medical officers not familiar with them ; and it is to such officers, as well as to medical students and civilian doctors, that their book is directed. The first edition lacked an account of the pathological changes in injured nerves, but this omission has now been made good in a new chapter ; and there have been many other changes and additions in response to suggestions and criticisms. The numerous illustrations, too, have been augmented by a further 47, and greater emphasis has been given to pain, trick movements, contracture, and electromyographic studies. It is a useful work.

Medical Register (London : General Medical Council. 1954. Two volumes. 65s.).—This year the Register contains 83,090 names of doctors (a decrease of 824 since 1953). The new registrations in 1953 totalled 507 (2390 below the average for the last ten years). These figures are at first sight astounding, but they are explained by the fact that provisional registration has come into force and accounts for another 1813 persons who have passed all their qualifying examinations. The Commonwealth list of new registrations, which jumped from 471 in 1951 to 1452 in 1952, fell back to normal at 436 (plus another 50 on the provisional register) ; and the list of new registrations of foreigners shrank to 7 (average for the past ten years 205).

Simple Craft Jewellery (2nd ed. London : Faber & Faber. 1954. Pp. 69. 8s. 6d.).—Under the auspices of the Worshipful Company of Goldsmiths of London, Mr. Claude Geoffroy-Dechaume has been responsible for the introduction of jewellery-making into hospitals, as a form of occupational therapy. Since the first edition of this book appeared he has arranged special courses of training for occupational therapists all over the country, and many hospitals have introduced this enjoyable little craft to their patients. One London hospital has even established a small anodising plant to serve its own makers of jewellery and those in other hospitals. A film has been made showing how the work is done, which serves as a supplement to this pleasant and well-illustrated book.



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THE LANCET

LONDON : SATURDAY, MAY 1, 1954

Management of Coronary Thrombosis

In recent years preoccupation with the use of anti-coagulants has perhaps tended to obscure other issues in the treatment of coronary thrombosis. WRIGHT et al.¹ and TULLOCH and GILCHRIST² have stated dogmatically that anticoagulants should be administered in all cases of cardiac infarction, and nearly all clinicians would agree that they should be given in cases of severe infarction accompanied by hypotension, circulatory insufficiency, prolonged pain, arrhythmia, or uræmia. Furthermore, anticoagulants may avert impending infarction in patients with progressively severe attacks of anginal pain occurring at rest as well as on effort.³ On the other hand, there is a growing weight of opinion in favour of withholding anticoagulants from patients who have had a clinically mild infarction without prolonged pain, circulatory failure, arrhythmia, or much fever. RUSSEK and ZOHMAN⁴ divided a group of cases untreated with anticoagulants into "good risks" and "bad risks," according to criteria similar to those already mentioned. The mortality was 60% in the "bad risk" group but only 1% in the "good risk" cases, while the incidence of thrombo-embolism was 10·6% in the former and only 0·8% in the latter group, although no anticoagulants had been given to either. LITTMANN⁵ reported 112 "good risk" cases, not treated with anticoagulants, in which there were 5 deaths, none of which was found at necropsy to be due to thrombo-embolism. Pulmonary embolism occurred in 6 additional patients, of whom 4 were having anticoagulants and 2 were not. FELDMAN⁶ found no difference in the mortality (30%) between 76 patients with myocardial infarction who had been treated with anticoagulants and 76 who had not. Although the difficulty of predicting which "good risk" cases will become "bad risks" within a few hours does suggest that anticoagulants should always be given, the risks and problems of anticoagulant therapy and the excellent immediate prognosis in most mild cases may persuade some physicians to restrict anticoagulant therapy to cases of severe infarction and to those with coronary insufficiency and threatened infarction.

The treatment of myocardial infarction does not begin and end with anticoagulants. Much remains to be learnt about the haemodynamics and management of the acute phase in severe cases. CONNER and HOLT⁷ and PARKINSON and BEDFORD⁸ pointed out that in patients with shock and severe and continuing pain the immediate prognosis was grave, and sustained hypotension is clearly a source of danger. SELZER⁹ found this complication in 69 of 528 unselected cases of myocardial infarction, and noted that the mortality-rate was more than double that of patients without shock. He divided hypoten-

sion in his cases into four categories: immediate and brief; immediate and irreversible; coinciding with, and apparently due to, cardiac arrhythmias; and delayed, associated with congestive failure, which was always fatal. Apparently two mechanisms are at work—peripheral vasoconstriction, and acute left ventricular failure—but whatever the contribution of each there can be little doubt that persistent hypotension, with resulting inadequacy of the coronary circulation, materially lessens the chances of recovery. Detailed haemodynamic data in the acute stage would be of great value, but are very difficult to obtain. The physician, moreover, is in some difficulty in choosing therapy, being poised between the Scylla of overloading the heart by treating the peripheral failure with intravenous fluids, and the Charybdis of losing his patient as a result of prolonged hypotension. Accordingly the treatment in this stage has hitherto been based on the well-tried combination of morphine, oxygen, and intravenous aminophylline if signs of pulmonary congestion are present. Adrenaline is contra-indicated in view of its action in increasing cardiac irritability, and the danger of inducing ventricular fibrillation. More active treatment has been advocated. SCHWARTZ¹⁰ and SAMPSON and SINGER¹¹ gave blood and plasma transfusions, without striking results. The use of pressor amines was suggested by BROFFMAN et al.¹²; and *l*-noradrenaline, which does not increase cardiac output, and is said to increase coronary-artery flow,¹³ has been given to relieve hypotension¹⁴⁻¹⁶: 4 mg. of *l*-noradrenaline bitartrate monohydrate ('Levophed') is dissolved in 1 litre of 5% glucose, and administered by slow intravenous drip at a rate that maintains the systolic blood-pressure at about 100 mm. Hg. SHIRLEY SMITH and GUZ¹⁸ commented favourably on this method, while SAMPSON and ZIPSER¹⁴ reported recovery of 20 out of 30 cases with severe hypotension in which *l*-noradrenaline was given. Although the value of this form of therapy has still to be proved, it seems well worth trying in cases with persistent hypotension, in which the prognosis is known to be very bad, despite the risk that it may cause serious arrhythmia. Digitalis, especially by the intravenous route, is held to be dangerous in view of the liability to ventricular fibrillation¹⁷; but if rapid auricular flutter or fibrillation develops, digitalis is essential to slow the ventricular rate.

When the patient is past the acute stage, further treatment consists in continuation of anticoagulants, bed rest, sedation, and a light, salt-free diet. The action of anticoagulants in preventing thrombosis in the calf and pelvic veins should be assisted by leg exercises, supervised if possible by a physiotherapist or nurse. Straining at stool should be avoided, and the bowels kept well open. The physical and mental stress associated with struggling upon a bedpan is more hazardous to the patient than the use of a bedside commode or transport to the lavatory on a portable

1. Wright, I. S., Beck, D. F., Marples, C. D. *Lancet*, Jan. 9, 1954, p. 92. See *Ibid*, 1953, ii, 171.
2. Tulloch, J. A., Gilchrist, A. R. *Brit. med. J.* 1950, ii, 965.
3. Wood, P. *Diseases of the Heart and Circulation*. London, 1950; p. 384.
4. Russek, H. I., Zohman, B. L. *Amer. Heart. J.* 1952, 43, 871.
5. Littmann, D. *New Engl. J. Med.* 1952, 247, 205.
6. Feldman, L. *Amer. Heart. J.* 1952, 44, 112.
7. Conner, L. A., Holt, E. *Ibid*, 1930, 5, 705.
8. Parkinson, J., Bedford, D. E. *Lancet*, 1928, i, 4.
9. Selzer, A. *Amer. Heart J.* 1952, 44, 1.

10. Schwartz, W. B. *Ibid*, 1947, 33, 169.
11. Sampson, J. J., Singer, I. M. *Ibid*, 1949, 38, 54.
12. Broffman, B. L., Hellerstein, H. K., Caskey, W. H. *J. Lab. clin. Med.* 1950, 36, 802.
13. Goldenberg, M., Angar, V., Deterling, R., Pines, K. L. *J. Amer. med. Ass.* 1949, 140, 776.
14. Sampson, J. J., Zipser, A. *Circulation*, 1954, 9, 38.
15. Miller, A. J., Baker, L. A. *Arch. intern. Med.* 1952, 89, 591.
16. Smith, K. S., Guz, A. *Brit. med. J.* 1953, ii, 1341.
17. Travell, J., Gold, H., Modell, W. *Arch. intern. Med.* 1938, 61, 184.

seat. Adequate sedation is important. LEVINE¹⁸ has suggested that, once the acute phase is over, patients often do better if allowed to sit in a chair rather than lie in bed; he remarks on the reduction in bowel and bladder troubles, and the improvement in morale. Some support for this view comes from COE,¹⁹ who measured the cardiac work in bed and in a chair, in 6 patients—3 without cardiac disease and 3 with degenerative heart-disease. In all 6 patients the cardiac work was appreciably less in the chair than in bed. The same is not necessarily true for patients who have recently sustained a severe infarction; and the "chair treatment," although widely used in America, has not become popular in this country. Complications such as congestive cardiac failure and arrhythmias will require treatment as they arise. Elderly patients tend to develop hypostatic infection at the bases of the lungs, and the signs of infection may be obscured by basal rales due to left ventricular failure and by the fever associated with the infarction; appropriate chemotherapy is thus of great importance. Many patients develop frequent ectopic beats, and these may be the precursor of auricular fibrillation, or, far more serious, of ventricular tachycardia. The incidence of these sequelæ may be reduced by the administration of prophylactic doses of quinidine (0·5–1 g. daily) or of procaine amide ("Pronestyl") (0·25 g. two to four times daily). In such doses these drugs have no hypotensive action, but in large dosage they may cause an undesirable fall in blood-pressure. After a major infarction patients should remain in bed for six weeks, after which six weeks' to three months' convalescence is usually needed. Every effort should be made to encourage the patient to return to as normal a life as is consistent with his cardiac condition, while avoiding undue sudden mental or physical stress.

The further prognosis is that of the ischaemic heart-disease, and is necessarily uncertain in the light of our present knowledge. That the outlook is not necessarily gloomy is shown by an analysis of 412 patients with myocardial infarction by MASTER and JAFFE,²⁰ who found that 40% recovered completely, and of these 83% returned to employment; only 3% died in under three years, while 40% survived for more than five years and 25% for more than ten years. COLE et al.²¹ studied 285 patients who had their first infarction between 1932 and 1942 and who survived the first two months: 60% survived for more than five years, 40% for more than ten years, and 10% for more than fifteen years. These workers emphasise that the prognosis worsens with each succeeding infarct, and also that the longer a patient survives after one infarct the better is the immediate prognosis after subsequent infarcts, presumably because of the development of collateral vessels. Recent work points to disordered lipid metabolism as the cause of atherosclerosis^{22 23}; but there is still no incontrovertible evidence that any form of low-fat diet is of value in preventing further attacks of coronary thrombosis, despite the observations of Fullerton et al.²⁴ that fat

ingestion influences coagulation. Moreover, Professor DUGUID, in his paper at the front of this issue, is somewhat sceptical of the relationship of coronary atherosclerosis (as opposed to simple fatty changes in the arteries) to disordered fat metabolism. Obesity, however, is known to exert a harmful influence in persons with degenerative cardiovascular disease,²⁵ and patients who are overweight should certainly be encouraged to reduce their weight.

While the uncertainties of prognosis must be made clear to the relatives, an attitude of optimism should be maintained towards the patient, who should be encouraged to regard himself, not as a hopeless invalid in fear of his life, but as a useful member of the community who, though obliged to live within the limits of his disability, can still earn his living.

Malaria and Milk

In the last two years several scattered observations on different aspects of malaria have been explained in the light of the discovery that a milk diet has an antimalarial effect. The story begins with work by MAEGRAITH et al.,^{26 27} who were investigating what happened to *Plasmodium berghei* in rats if its supply of haemoglobin were handicapped by feeding the animals on a diet poor in iron. For this purpose a milk diet was given, and it was found that the malaria parasite failed to develop. It was then found that the suppression of the malaria parasite had nothing to do with iron, but depended on some characteristic of milk. (Fresh cow's milk, dried cow's milk, and human milk were all effective.) This remarkable suppressive action of milk was confirmed in many different parts of the world and was shown to apply to other malaria parasites, such as *P. cynomolgi* and *P. knowlesi* in monkeys. The action was exerted only on the blood forms of the parasite and did not affect the pre-erythrocytic stages in the liver.²⁸

The story entered a new stage when HAWKING^{29 30} discovered that the suppressive action of milk was due to its deficiency in *p*-aminobenzoic acid, which was known to be a growth factor for many malaria parasites—especially *P. berghei* in rats and *P. knowlesi* in monkeys.³¹ *p*-Aminobenzoic acid is well known as the bacterial growth factor which is antagonised by sulphonamides. The body-fluids of animals and man usually contain very little of this substance (otherwise sulphonamides would not cure streptococcal and other infections); but it is present in many diets, and when ingested in the food the blood-level rises sufficiently for malaria parasites to grow; it is rapidly excreted or destroyed, so constant renewal is necessary. Cow's or human milk usually contains extremely little *p*-aminobenzoic acid (only about 1 part in 200 million), which is insufficient for the growth of malaria parasites in either rats or monkeys; but if even 1 mg. is added daily to the milk diet of a rhesus monkey, infection with *P. knowlesi* can follow its usual acute and fatal course.

- 25. Master, A. M., Jaffe, H. L., Chesky, K. *J. Amer. med. Ass.* 1953, 153, 1499.
- 26. Maegraith, B. G., Deegan, T., Jones, E. S. *Brit. med. J.* 1952, ii, 1382.
- 27. Liverpool School of Tropical Medicine, Annual Report 1952–53; p. 23.
- 28. Bray, R. S., Garnham, P. C. C. *Brit. med. J.* 1953, i, 1200.
- 29. Hawking, F. *Ibid.* p. 1201.
- 30. Hawking, F. *Ibid.* Feb. 20, 1954, p. 425.
- 31. Anfinson, C. B., Gelman, Q. M., McKee, R. W., Ormsbee, R. A., Ball, E. G. *J. exp. Med.* 1946, 84, 607.

18. Levine, S. A., Lown, B. *Trans. Ass. Amer. Phys.* 1951, 64, 316.
 19. Coe, W. S. *Ann. intern. med.* 1954, 40, 42.
 20. Master, A. M., Jaffe, H. L. *J. Amer. med. Ass.* 1951, 147, 1721.
 21. Cole, D. R., Singlan, E. B., Katz, L. N. *Circulation.* 1954, 9, 321.
 22. Allen, E. V., Katz, L. N., Keys, A., Gofman, J. W. *Ibid.* 1952, 5, 98.
 23. Oliver, M. F., Boyd, G. S. *Brit. Heart J.* 1953, 15, 387.
 24. Fullerton, H. W., Davie, W. J., Anastasopoulos, G. *Brit. med. J.* 1953, ii, 250.

Although a milk diet usually prevents infection of rats by *P. berghei* in a very striking manner, in certain animals this action is not manifested. Probably such rats contain in their intestine bacteria which can synthesise *p*-aminobenzoic acid and so maintain an appreciable level in the blood. Intestinal bacteria which synthesise many components of the vitamin-B complex are well known; but it is difficult to prove their presence except by procedures which themselves exert an antimalarial action. These exceptions to the antimalarial effect of a milk diet, although common in rats, have not been encountered in monkeys. The malaria parasite requires besides *p*-aminobenzoic acid many substances for growth—e.g., methionine and ascorbic acid. *p*-Aminobenzoic acid is outstanding because the parasite needs it but the host can flourish without it.

The recognition of *p*-aminobenzoic acid as a growth factor for malaria parasites explains many diverse observations. Thus it elucidates the antimalarial action of sulphonamides (since these antagonise *p*-aminobenzoic acid), and of proguanil and pyrimethamine which are known to be antagonists of folic acid (a complex derivative of *p*-aminobenzoic acid) and which resemble sulphonamides in many other ways. Secondly this observation links up with the extensive work of microbiologists in elucidating the rôle of *p*-aminobenzoic acid in cell metabolism. Briefly, in bacteria *p*-aminobenzoic acid is largely built up into folic acid or similar compounds; then these compounds (or perhaps the original acid) act as catalysts for various important synthetic reactions, including the formation of methionine from homocysteine and the synthesis of purine and pyrimidine rings. These substances are essential for the formation of nucleoprotein and so for the growth and multiplication of nuclei and cells. In the case of the malaria parasite there is morphological evidence for a relation between the supply of *p*-aminobenzoic acid and the division of the nucleus. By histochemical methods (e.g., Feulgen staining) it can be shown that the division of the parasite's nucleus to produce sixteen or more merozoites necessitates the formation of a great deal of new desoxyribonucleic acid. And it is just at this stage of the parasite's development that it succumbs and disintegrates under the antimalarial action of sulphonamides, proguanil, or pyrimethamine (each of which interferes with the use of *p*-aminobenzoic acid or folic acid).

Finally, these findings may have an important application to malaria in man. Although men and women rarely subsist on a milk diet, there is one important class of human beings who do—namely, babies. It has long been recognised that babies in regions of hyperendemic malaria do not contract the infection as early or as intensely as would be expected from the degree of their exposure to infected mosquitoes.³² Hitherto it has usually been supposed that this insusceptibility was due to immunity transmitted in utero from the mother; but it now seems quite possible that the insusceptibility may rather be due to the milk diet. Suckling rats whose mothers have been placed on a diet free of *p*-aminobenzoate have proved relatively insusceptible to infection by *P. berghei*, but become highly susceptible if this compound is administered to them or to their mothers (thus increasing the concentration in the milk).⁵ Similarly baby monkeys maintained on milk from the breast or from a bottle are insusceptible to infection

by *P. cynomolgi*, but they readily become infected if they or their mothers are given *p*-aminobenzoate. The human parasites, *P. vivax* and *P. falciparum*, are sensitive to sulphonamides, so they presumably require *p*-aminobenzoate for their growth. It would be easy to jump to the conclusion that babies in West Africa are protected against malaria during the early months of life because they are fed exclusively on breast-milk, and that they become susceptible only when their diet is supplemented by foods containing *p*-aminobenzoate, or if the bacteria in their own or their mother's intestine synthesise this substance. But careful observation will be needed to prove such a hypothesis.

Epidemiology in Population Control

"GENERALLY, it is to be foreseen, that the Population of a Kingdome (especially if it be not mown down by wars) doe not exceed, the Stocke of the Kingdome, which should maintaine them." Thus, FRANCIS BACON anticipated the gloomy predictions of THOMAS MALTHUS. Ever since the publication of his essay, that English clergyman has been a centre of vituperative controversy.¹ Yet his basic postulates were indubitable: "First, that food is necessary to the existence of man. Secondly, that the passion between the sexes is necessary and will remain nearly in its present state." He then stated: "Population, when unchecked, increases in a geometrical ratio. Subsistence increases only in an arithmetical ratio. A slight acquaintance with numbers will show the immensity of the first power in comparison with the second." The happiness and welfare of a country depends on a balance between needs and material resources; with unchecked increases in population, "sickly seasons, epidemics, pestilence, and plague, advance in terrific array, and sweep off their thousands and ten thousands;" while "gigantic inevitable famine stalks in the rear, and with one mighty blow, levels the population with the food of the world." This "Malthusian scarecrow" has been dismissed by optimistic nutritionists, but ORDWAY² classifies such optimists as Cornucopians who believe that earth, sea, and atmosphere can deliver to the ingenuity of man an unending, inexhaustible supply of raw materials. Certainly the intensive development of agricultural methods in the past hundred and fifty years, which has allowed our planet to support a population of 2400 million, gives solid basis for that optimism. But as ORDWAY points out, in the United States in the past fifty years the population has doubled, while the consumption of minerals has increased eightfold and of fuel thirteenfold. There can be no comforting guarantee that the development of new material resources will keep pace with the pressure of needs. Conservation, he believes, is now the proper course; and in their recent discussion of public health as a demographic influence, Prof. JOHN GORDON and his colleagues³ share this cautious approach. Stung, no doubt, by VOGT's acid comment that physicians have "set the stage for disaster, and like PILATE, wash their hands of the consequences"

1. Smith, K. The Malthusian Controversy. London, 1951.

2. Ordway, S. H. Resources and the American Dream: a Theory of the Limit of Growth. New York, 1953.

3. Gordon, J. E., Wyon, J. B., Ingalls, T. H. Amer. J. Med. Sci. 1954, 227, 326.

(a thought which EVANG,⁴ as a doctor, has expressed in less astringent terms), they review the repercussions of public-health practice in furthering population increase and suggest ways and means for harmonising population size and food-supply.

Realistic appraisal is the first task of epidemiology—the diagnostic science of public health. If population pressure be regarded as a disease of a society, an epidemiological survey of present circumstances will show its geographical distribution. In fact, the Asian peoples present the most serious economic and public-health problem. Western curative and preventive medicine has increased the population potential by cutting death-rates in circumstances of high fertility. In India, for example, between 1921 and 1941, declining mortality allowed a population increase of 83 million. As long as present birth-rates continue, population increases will tend to outstrip food production, leaving a precarious balance between needs and resources. Emigration and colonisation of undeveloped territory has long been the result of such pressure; but we are now approaching the limits of territorial expansion and overcrowding. Where that alternative is not available, the results of population increase can be disastrous. In British Guiana, for example, an effective antimalarial campaign between 1945 and 1948 reduced the infant-mortality rate from 250 per 1000 to 67 per 1000, with the result that by 1948 only 1500 calories per head were available to the people of the country. In India the caloric intake per head fell from 1976 to 1570 between 1934 and 1951. Where, as in Japan, an island community has no outlet for expansion, the problem is particularly acute. Ireland, Puerto Rico, and Sicily exemplify the drive towards emigration fostered by failure to achieve a satisfactory ecological balance between food and mouths. Only the Western nations of the U.S.A., United Kingdom, Scandinavia, and France have attained a reasonable stability in population numbers. The reasons for these disparities between countries in their demographic trends may suggest useful courses of action. The success of measures to control mortality depends on the whole population acquiescing in their application. The control of fertility must likewise depend more on general measures than on the unconcerted action of individuals. Such measures must take into account the historical and cultural background of a nation. A long period of high mortality demands a compensatory high level of fertility; and even when the death-rate falls, national procreative habits persist. Religious scruples determine both the drive towards family limitation and the methods used. Again, methods designed for adoption throughout a country must be both practicable and widely acceptable. While drugs such as phosphorylated hesperidine may prevent the sperm entering the ovum, it is unlikely that many men or women could be persuaded to achieve continual sterility by taking a tablet three times a day every day of life. GORDON and his colleagues believe that the traditional methods of epidemiology must be applied. The first essential is to recognise impending ecological disequilibrium from a simultaneous rise in population numbers, fall in the

average available number of calories per person, rise in unemployment, and increase in political ferment. Measurement of severity is the second essential for intelligent control; this calls for a detailed analysis of fecundity and fertility and their relation to marital habits and population age structure. Finally a carefully planned and controlled field trial will be needed to assess the efficacy of any measure of population control designed for universal use in an overcrowded community. Only thus, GORDON believes, can we fulfil COBBETT's recipe for rural content—that "the labourer must have his belly full and be free from fear."

In all this GORDON and his associates betray a caution which is hardly typical of their country. "Americans," said Mr. ADLAI STEVENSON, "have always assumed subconsciously that *all* problems can be solved, that every story has a happy ending"; and a report from the Rockefeller Foundation and the Twentieth Century Fund⁵ certainly suggests that there is a technical answer to every problem of human population needs. Yet CROMWELL would have approved of GORDON's tempering blind faith with an informed caution in order to maintain man's control over his own ecological balance.

Annotations

SPREAD OF MYXOMATOSIS

LAST October myxomatosis appeared in Kent, and since then it has been recognised in some eighteen areas, mostly on the South Coast but extending north to East Suffolk. We still do not know how the disease reached us from France, and there is no apparent connection between the various epidemic foci here. Official attempts to limit the area of infection by rabbit-proof wire fencing were, as we said,⁶ almost certain to fail; and the report⁷ of an advisory committee of the Ministry of Agriculture shows that this policy was rapidly abandoned. Faced with the probability of widespread myxomatosis in which 90% of the country's 100 million wild rabbits may perish in the next two years the committee has tried to forecast the economic consequences of such an epizootic. The total income from the wild-rabbit meat and fur trades is about £15 million. This is roughly the same as the damage caused by rabbits to cereal crops alone; and when we add to this the damage to pasture, vegetable crops, and young trees and the cost of pest protection, then the loss caused by the depredations of rabbits is likely to be three or four times as much. Nine rabbits are said to eat as much as two sheep; and in South-East Australia, where four-fifths of the rabbits were killed by the disease, the increase in rural production was estimated at £50 million. There is already evidence, however, that in some areas of Australia the mortality-rate from myxomatosis has fallen considerably; and if, as seems likely, this continues the gains may be short-lived.

While nothing can usefully be done to arrest the natural spread of myxomatosis in wild rabbits in this country, the protection of tame-rabbits is important—among other reasons, because some 40,000 are used every year for diagnostic and research work. The only known prophylactic is a preparation of the living virus of Shope's fibroma, and this is now being studied at Weybridge. Some workers in France claim that this

5. Woytinsky, W. S., Woytinsky, E. S. *World Population and Production: Trends and Outlook*. New York, 1953.

6. *Lancet*, 1953, ii, 1031.

7. Report of the Advisory Committee on Myxomatosis, Ministry of Agriculture and Fisheries. H.M. Stationery Office, 1954. 9d.

4. Evang, G. *Eugen. Rev.* 1953, 45, 247. See *Lancet*, March 13, 1954, p. 558.

vaccine has not come up to expectations, and clearly we need much more information. Meanwhile breeders should take all possible precautions against the introduction of infection, and mosquito-proof screening and insecticides must be used until we know how the disease is spread. At present we rely on the excellent Australian work to guide us about the epidemiology of the disease, but this may have little relevance to conditions here. The introduction of myxomatosis into this country provides the epidemiologist and ecologist with a unique opportunity not only to provide practical information but to study what may be, in effect, a field experiment on an enormous scale.

A YEAR'S WORK IN THE TROPICS

THE report for 1952 of the Institute for Medical Research at Kuala Lumpur¹ describes an impressive amount of work.

'Daraprim' (pyrimethamine) gave a disappointing cure-rate in the treatment of malaria caused by *Plasmodium falciparum*. There were 13 failures in 97 cases of acute infection; increasing the total dose to 0.3 g. in five days did not improve the rate and produced leucocytopenia. Proguanil in doses of 400 mg. daily for a week failed to cure most attacks due to *P. falciparum*. Laboratory workers are glad to hear that the small Malayan *Macacus irus* monkey can act as a reservoir of *P. knowlesi*. Some of these monkeys have been imported to European laboratories to restock with fresh strains the dwindling strains maintained in rhesus monkeys.

American workers based on Kuala Lumpur have completed their stay and have now described interesting observations on rickettsial immunology. Clinical scrub-typhus has a latent period of about ten days and burns itself out naturally within two weeks of infection. Smadel and his colleagues² have isolated *Rickettsia tsutsugamushi* from an axillary lymph-node fifteen months after a natural infection. Using chloramphenicol to control the disease, they inoculated volunteers intradermally with known doses of the Karp strain, and demonstrated that immunity to a homologous strain lasts several years but infection with a heterologous strain is possible within a few weeks of the initial infection.³ By starting to administer chloramphenicol on the seventh day after inoculation they produced in volunteers both a demonstrable rickettsæmia and a long-lasting immunity (shown by subsequent challenge doses) with little or no overt clinical typhus.⁴ This production of immunity by chemoprophylactic control of a pathogenic vaccine *in vivo* is of some theoretical interest; but as Smadel et al. point out, it is of limited practical value because of the difficulty of exact dosage and timing of vaccine and prophylaxis. In 1941 a similar procedure⁵ was tried in South Africa, when sulphonamide was given to subdue infections in cattle with the rickettsia of heartwater disease.

Filariologists in Malaya add some interesting findings on treatment of *Wuchereria malayi* with diethylcarbamazine ('Hetrazan'). Some physicians have stopped using this drug on account of the sharp febrile reaction and allergic skin manifestations to which it quickly gives rise. The reaction is thought to be due to the release of parasite protein after the death of the microfilaria, and anti-histamine drugs do not entirely eliminate it. The severity of the reaction does not necessarily depend on the number of circulating microfilariae, and the workers

in Malaya now report that it seems to be independent of the size of the initial dose. They also point out that once this reaction has subsided the dose can be increased up to fourfold without ill effect. They have given one dose daily, which they find adequate. Reappearance of the microfilaria in the blood is slow, taking place over a year or so. (It is commonly believed that hetrazan kills the microfilaria and damages the production of it without actually killing the adult worm.) Nevertheless the decimated microfilaræmia has the effect of controlling transmission through mosquitoes. When the 1st Battalion Fijian Regiment left Fiji all those whose blood showed *W. bancrofti* were treated with hetrazan: on arrival in Malaya only 43 out of 725 had microfilaræmia, and in these the numbers were very low. A similar epidemiological situation arises with the arrival of East African troops infected with *Shistosoma haematobium*, and the entomologists are busy finding out whether this can be transmitted by any local fauna.

RENAL FAILURE COMPLICATING PEPTIC ULCER THERAPY

ALKALOSIS and renal dysfunction due to excessive intake of milk and absorbable alkali in the treatment of peptic ulcer was first described by Hardt and Rivers¹ over thirty years ago. Cope² reviewed the condition in 1936 and emphasised the importance of hypercalcæmia from high calcium intake. A patient who has had this treatment for many years begins to complain of weakness and lethargy with impaired mental efficiency and powers of concentration. This may progress to stupor or even to terminal uræmic coma. The urine, often increased in volume to three litres or more daily, is alkaline in reaction and usually contains small quantities of albumin and hyaline or granular casts. The levels of blood-urea and of bicarbonate, pH, and calcium in the serum are all increased.

The disorder was further defined by Burnett et al.³ in 1949, and Dufault and Tobias⁴ have now described four further cases. The patients in order to alleviate ulcer pain often insist on taking vast amounts of milk—in some cases a gallon daily. (In a striking example recorded by McQueen⁵ this almost amounted to an addiction, the patient continuing to take milk despite the warnings of his physician.) This amount of milk contains 5.6 g. of calcium, which is many times the calcium content of an ordinary diet. Some patients take considerable quantities of calcium carbonate as well. If renal function is normal, excess dietary calcium is excreted in the urine and significant hypercalcæmia does not develop.⁶ This hypercalciuria in a constantly alkaline urine leads to the progressive deposition of calcium phosphate in the distal and collecting tubules and eventually to renal failure and uremia. At this stage the calcium output cannot be maintained and there is increase of serum calcium and phosphate, often leading to widespread metastatic calcification. Corneal calcification is of especial diagnostic importance; it is readily recognised in early cases by use of the slit-lamp and later by naked-eye examination.

It has been shown that the intake over short periods of large quantities of alkali and milk does not impair renal function.⁷ In most of the reported cases a high intake has been continued for many years before renal failure developed. This may develop more rapidly if there is unrelated renal disease, or after temporary acute

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 2. Smadel, J. E., Ley, H. L. jun., Diercks, F. H., Cameron, J. A. P. *Amer. J. Hyg.* 1952, 56, 294.
 3. Smadel, J. E., Ley, H. L. jun., Diercks, F. H., Paterson, P. Y., Wissemann, C. L. jun., Traub, R. *Amer. J. trop. Med. Hyg.* 1952, 1, 87.
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 5. Neitz, W. O., Alexander, R. A. *J. S. Afr. vet. med. Ass.* 1941, 12, 103.

1. Hardt, L., Rivers, A. *Arch. intern. Med.* 1923, 31, 171.
 2. Cope, C. L. *Clin. Sci.* 1936, 2, 287.
 3. Burnett, C., Commons, R. R., Albright, F., Howard, J. E. *New Engl. J. Med.* 1949, 240, 787.
 4. Dufault, F., Tobias, G. J. *Amer. J. Med.* 1954, 16, 231.
 5. McQueen, E. G. *Lancet*, 1952, ii, 67.
 6. Knapp, E. L. *J. clin. Invest.* 1947, 26, 182.
 7. Van Goldsenhoven, G. M. T., Gray, O. V., Price, A. V., Sanderson, P. H. Communication to Medical Research Society, December, 1953.

renal failure associated with severe haematemesis or pyloric stenosis. Rapidly developing uræmia secondary to hypercalcæmia is known to occur in many other conditions, particularly hyperparathyroidism,⁸ multiple myelomatosis,⁹ calciferol intoxication,¹⁰ and sarcoidosis.¹¹

The early diagnosis of uræmia associated with hypercalcæmia is of paramount importance since the renal failure is potentially reversible. Determination of the serum-calcium is essential since reliance on the Sulkowitch reaction for hypercalcuria may be misleading when excess calcium is no longer being excreted. The avoidance of alkalis together with a low calcium diet may be all that is required in treatment, but in severe cases the use of calcium-chelating agents, particularly ethylene diamine tetra-acetic acid, may be of great value initially.¹² This compound does not reduce the serum-calcium level but converts a portion to a biologically inactive complex which is excreted more rapidly. Differential diagnosis may be difficult in a comatose patient incapable of giving a history. The hypercalcæmia of excessive milk intake and of calciferol intoxication will respond to conservative methods alone; that associated with some cases of myelomatosis and sarcoidosis has been shown to be corrected by corticotrophin or cortisone.^{13 14} Hyperparathyroidism will prove resistant to all measures other than surgical removal of the causative adenoma.

GRADUATE WIVES

EDUCATION is an expensive but enduring possession, and in their latest broadsheet¹⁵ P.E.P. consider whether we are making the best possible use of married women graduates. Each year 4000 women graduate from our universities, and in due course about three-quarters of them marry. What happens to them? During the years when they are bringing up their family their education—as distinct from any vocational training—is certainly being well used. But are we giving them the opportunity to use it in middle age by returning to work suitable to their qualifications? P.E.P. have looked at these questions against the background of facts supplied by a survey of married women graduates made by Mrs. Judith Hubback, M.A.

Mrs. Hubback's findings are based on the answers to a questionnaire sent out, in 1953, to 2000 married women who had taken their degree in and after 1930 at Oxford, Cambridge, London, Birmingham, Durham, Reading, Nottingham, the University College of Hull, the University of Wales, St. Andrews, and Aberdeen; and 1165 (58%) of them replied. An almost identical set of questions was answered by 420 married women of the same age-group, none of whom had been to a university: they were drawn from the sisters, relatives, and friends of those who filled in the first set of questions.

Of the graduates, only 1% said they would not, if they had their lives over again, go to a university at all; and almost three-quarters said that they would study the same subject or subjects over again. Of the non-graduates, only 52% were satisfied with the education they had received, and would do the same again. Just under two-thirds of the graduates, and a comparable proportion of the non-graduates, had planned a career for themselves (other than marriage), though the careers aimed at by the two groups were slightly different. In both groups, however, teaching was a common choice: 34% of the graduates and 14% of the non-graduates had planned to teach.

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12. Spencer, H., Vankinscot, V., Lewin, I., Laszlo, D. *J. clin. Invest.* 1952, 31, 1023.
13. Thorn, G. W., Forshaw, P. H., Frawley, T. F., Hill, S. R., Roche, M., Stachellin, D., Wilson, D. L. *New Engl. J. Med.* 1950, 242, 824.
14. Phillips, R. W. *Ibid.* 1953, 248, 934.
15. Planning, 20, no. 361, April 5, 1954. Obtainable from P.E.P. (Political and Economic Planning), 16, Queen Anne's Gate, London, S.W.1.

Marriage ended the planned career more often among non-graduates than graduates; and a larger proportion of non-graduates (79%, as against 64% of graduates) found housework to be a full-time occupation. The size of the families was much the same in the two groups, and both experienced much the same difficulty in getting domestic help. About half the women in each group enjoyed domesticity, and the rest either tolerated it or regarded it with mixed feelings. About 19% of the graduates and 9% of the non-graduates were doing paid full-time jobs, and 34% of the graduates and 11% of the non-graduates were doing part-time paid work. Many women seek work when their children are old enough to spare them. Of the 1165 women graduates questioned, nearly 500 plan to work at some chosen job in the future and a further 88 intend to do some work but have not yet decided what sort.

In summarising these findings the broadsheet does less than justice to the contribution made to the community by women graduates—"it is probably fair to say that the majority of the graduate wives covered by this sample were making no direct use of their academic qualifications"—for in fact more than half of them were doing full-time or part-time paid work likely to draw on their education. But the return we expect from education in this country cannot be assessed entirely in terms of paid work, and, as the broadsheet points out, "the indirect contribution which a trained mind and cultured outlook can make to family life and to the life of the nation generally is very great indeed." Education is never wasted, and least of all on those who have the task of civilising the next generation.

BRACKEN POISONING

BRACKEN poisoning occurs in horses and cattle, and it can be produced experimentally in sheep and rats. In horses the condition is known as "bracken staggers," since incoördination is a prominent sign. "Bracken staggers" is a manifestation of thiamine deficiency, caused by a thiaminase contained in bracken, and the condition can be cured by administration of thiamine.¹ In ruminant animals the signs of bracken poisoning are different.² Sheep or cattle receiving a diet that contains more than 40% of bracken may continue to thrive for some weeks. Then the animals lose appetite, have a raised body-temperature, pass blood with the faeces, which become soft and contain much mucus, and die within a few days. The disorder is not improved by thiamine injected or given by mouth; and it seems that bracken poisoning in such animals, unlike that in horses or rats, is not associated with thiamine deficiency. The level of pyruvate in the blood of affected animals increases little, and the level of thiamine in the tissues is only slightly reduced.³

Naftalin and Cushnie⁴ have described their haematological and necropsy findings in adult cattle and young calves that had died after being given bracken. The essential lesion is extensive bone-marrow damage, affecting the megakaryocytes, the primitive white cells, and the primitive red cells; thrombocytopenia and leucopenia result. Subsequently there are multiple haemorrhages, and bacterial invasion of the blood-stream leads to a generalised non-specific bacteraemia. After the onset of bacteraemia haemorrhage becomes more severe and leads to death. Though erythropoiesis is affected, the number of circulating red blood-cells is little reduced until the onset of severe haemorrhage. Moon and McKeand⁵ have reported the haematological changes in sheep given bracken. Poisoning is indicated by a progressive fall in red cells and haemoglobin, though leucopenia and thrombocytopenia are also found. The

1. See *Lancet*, 1952, i, 140.
2. Stockman, S. *J. comp. Path.* 1917, 30, 311. Moon, F. E., Raafat, M. A. *Ibid.* 1951, 61, 88.
3. Moon, F. E., Raafat, M. A. *J. Sci. Fd. Agric.* 1951, 2, 223.
4. Naftalin, J. M., Cushnie, G. H. *J. comp. Path.* 1954, 64, 54, 75.
5. Moon, F. E., McKeand, J. M. *Brit. vet. J.* 1953, 109, 321.

difference from the blood picture in bracken-fed cattle may be due to the ability of sheep to tolerate bracken feeding for much longer periods. Red cells have an appreciably longer life than white cells, and probably cattle do not survive long enough for the changes in the bone-marrow to affect the red-cell count. Several groups of earlier workers⁶ reported similar haematological changes in cattle with bracken poisoning, but the cause of the bone-marrow lesions in ruminants is not yet known.

The ruminant differs from simple-stomached animals in that it depends for its nutrition largely on the metabolic activity of the micro-organisms in its rumen. These micro-organisms break down cellulosic material, assimilate nitrogen from the feed, and synthesise vitamins of the B complex and vitamin K. When the mixture of food particles and micro-organisms passes from the rumen into the abomasum, or true stomach, the bacterial cells are broken down and their contents become available for absorption through the normal digestive processes. Bracken poisoning in the ruminant may result from disturbance of normal microbial activity in the rumen leading to a deficiency in the animal of some nutrient necessary for the maintenance of normal bone-marrow function. Several groups of workers³⁻⁵ have excluded the possibility of this nutrient being one of the known vitamins of the B complex, vitamin K, or vitamin C; but, as Naftalin and Cushnie point out, the dysfunction may be caused by lack of some essential amino-acid or of some still unidentified vitamin. An alternative hypothesis is that bracken contains a factor (or causes the rumen organisms to produce one) with a toxic action on the bone-marrow. But so far the only noxious principle discovered in bracken is thiaminase, which probably plays no important part in the production of bracken poisoning in ruminants.

VECTORCARDIOGRAPHY

THE diagnostic reliability of the electrocardiogram is now so soundly established that it is easy to forget that the absolute limits of normal—particularly of the P-R interval, and of the width of the QRS and the QRS-T complexes—are still not exactly agreed. Variations due to age, posture, and perhaps race, in addition to those caused by instrumental distortion, faulty technique, and inaccurate measurement, constitute the chief difficulties in the way of establishing statistically acceptable criteria.⁷ The use of newer leads, although invaluable in diagnosis, has increased the problem. There are other theoretical objections to the present electrocardiogram: the standard and unipolar limb leads and the chest leads record electrical activity only in the frontal plane of the body, although the heart, being a three-dimensional structure in a volume conductor, has electrical forces in other planes. The study of these forces as spatial vectors was first undertaken by Mann in 1920 but made little progress because their determination from successive measurements of the electrocardiogram was tedious even when aided by optical devices, such as that of Shillingford and Brigden.⁸

The conception, put forward by Wilson and his colleagues,⁹ of the ventricular gradient has helped both in understanding the electrocardiogram and in distinguishing changes in the T wave due to abnormalities of QRS from those due to local abnormalities of the myocardium. The gradient is a vectorial expression of the combined electrical forces producing the QRS and T waves. Its magnitude is calculated by planimetry from the

algebraic sum of the areas bounded by the QRS and T deflections and its direction determined by plotting measurements in any two standard leads on Einthoven's triangle or Bayley's triaxial reference system. Fundamentally it is a measure of the duration and magnitude of the electrical forces produced by lack of uniformity in the processes of excitation and repolarisation of the heart muscle. Ashman and his associates¹⁰ have worked out normal values for the ventricular gradient and have found them to vary within wide limits; but they have been able to establish constant spatial relationships between the direction of the gradient, the QRS vector, and the long anatomical axis of the heart, and have shown that the gradient lies posteriorly to the long axis and the QRS vector still farther behind. Unfortunately measurement of the ventricular gradient is difficult and too cumbersome to be really useful in practice.

The adaptation of the cathode-ray oscilloscope by Shellong and others in Germany, and by Wilson and Johnston,¹¹ has made it possible to record automatically the time-course of the cardiac vectors. In some ways the direct vectorcardiograph is a more sensitive instrument for studying the myocardium than the electrocardiograph, but it has considerable limitations—for example, in the study of temporal relationships such as the P-R, Q-T, and T-P intervals—while normal standards are hard to define. In addition, a standard reference frame has still to be agreed on. Some favour Wilson's equilateral tetrahedron with the Einthoven leads and Wilson's central terminal, recording in the frontal plane, supplemented in the sagittal plane by an electrode on the back; whereas others prefer more complicated frames, such as those proposed by Duchosal and other Continental workers. The Wilson frame is at least simple in practice and has the theoretical advantage of being based on the Einthoven triangle. The presentation of frontal and sagittal loops so that they can be viewed as a single spatial vectorcardiogram is not easy. Stereovectorcardiograms have been attempted in several ways, including double photography of model loops and the use of additional electrodes to define other planes, but they are unsatisfactory in practice. A special circuit with unequal resistances producing oblique-plane vectorcardiograms which can be viewed simultaneously on adjacent oscilloscopes has been devised by Burch et al.,¹² and seems more promising. In an attempt to overcome the spatial limitations of frontal-plane leads, Trethewie¹³ has proposed an interesting simplified electrocardiography. By placing an electrode on the manubriosternal junction and another at the xiphisternum, with two others at the same horizontal level in the left midaxillary line and at the back of the right chest near the midline of the back, he has been able to record three leads at right-angles to each other. These should detect electrical abnormalities of the heart in both horizontal and vertical directions of the frontal plane as well as in the sagittal plane. Satisfactory electrocardiograms have been obtained from cases of known heart-disease, but confirmation from larger numbers is needed. Variations in the normal values of the leads, especially of the T wave in the horizontal lead, require statistical study if the method is to be of more than theoretical interest.

It is unlikely that either vectorcardiography, which is still chiefly a research method, or Trethewie's simplified system will replace electrocardiography. In doubtful cases clinicians, probably rightly, rely on the case-history and on other methods of examination rather than on statistical criteria.

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7. Kossman, C. E. *Circulation*, 1953, 8, 920.
8. Shillingford, J., Brigden, W. *Brit. Heart J.* 1951, 13, 233.
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10. Ashman, R., Goldberg, M., Byrd, E. *Amer. Heart J.* 1943, 26, 473.
11. Wilson, F. N., Johnston, F. D. *Ibid.* 1938, 16, 14.
12. Burch, G. E., Abitsovskiy, J. A., Cronovich, M. S. *Spatial Vectorcardiography*. New Orleans, 1953.
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Special Articles

TREATMENT OF THE CHRONIC MENTAL PATIENT

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If a layman were to visit the nearest mental hospital he would see patients who had been admitted ten, twenty, fifty years ago ; and he would wonder at the poverty of the resources at the command of psychiatry, that these fellow citizens should have existed for so many years in such a state and yet be as far from being cured as they were on the day of their admission.

In the De la Pole Hospital there are some 450 men other than those in the admission ward and the convalescent ward, and 67 of these have been in the hospital for less than one year. The remainder have been in for periods shown below :

<i>Duration of Stay (in years) of 384 Patients</i>							
2-4	5-9	10-14	15-19	20-24	25-29	30-39	over 40
Number ..	63	87	46	63	37	38	29

Psychiatrists are no less intelligent than general physicians ; and mental nurses are probably more efficient, and certainly much more humane, than nurses in other kinds of hospitals. Mental hospitals are ugly and uncomfortable, but so are many other general hospitals. Why should results be so bad ?

There are many points to be considered. Each doctor in a mental hospital will have under his care hundreds instead of tens of patients. The total cost of a mental patient is not likely to be more than £5 a week, whereas the cost of a general patient will be usually more than £10, and of a sanitorium patient, or a patient in a maternity hospital, it will be nearer £12-15 a week. Out of this money, the sum set aside for medical care for each patient will be some £2 in a general hospital ; in a mental hospital it is about 4s.

The patient who develops a mental illness would be shocked if he knew how little the community is prepared to spend on him. If he asked about it, he might be told that he would be fed and sheltered and all his physical needs would be looked after ; but that once his nursing was paid for there would be hardly any money left to pay for medical attention. There is in fact a general if unspoken belief that the patient in a mental hospital has no need of a doctor, and that he must be glad to be kept alive. Even the procedure of being kept alive is not perfect ; perhaps for tens of years he will go without touching solid food after 5 P.M. He will usually be clad in shapeless tweeds, sometimes many years older than himself. Often he will be unable to go out of doors because he will have no shoes. As he eats, so will he sleep and live—without any privacy, and often in the company of 50-100 others. Such fresh air as he gets will be in a courtyard about twice the size of a tennis-court, surrounded by high railings. He may well feel that he matters little to his fellows.

The psychiatrist who works in a mental hospital has to contend with all these conditions ; yet it can be truly said that he fails to make the most of his opportunities. The sickness from which psychiatry suffers is fundamentally that of the whole community : things are always divided into opposites, the good and the bad, the quick and the dead, the sheep and the goats ; and to these categories doctors (and psychiatrists in particular) add the acute and the chronic, the curable and the incurable.

All psychiatrists agree that no effort must be spared to cure the patient when he first falls sick. So he is admitted to a modern, well-furnished, and comfortable

ward ; he is treated sympathetically and energetically, and conferences are held by the medical staff to ensure that he is treated by the most effective means available. If he fails to recover within some three to six months, his treatment changes ; he is still treated with kindness and sympathy, but skill and energy are tacitly withdrawn. He becomes a chronic patient ; and as the tempo of his illness changes so does that of his treatment. He is moved from the admission ward to the main building where he is kept physically healthy. Spontaneous remissions of his mental illness are often observed (though the mode of his care discourages their occurrence) ; yet when they do occur they are not always acted upon. The statutory documents are accurately and regularly completed during the tens of years which remain. Where will he live, and how will he live ?

There will be no privacy, no curtains or carpets, no pictures on the walls—save possibly framed illustrations from the Christmas magazines of the last century. Some two or three times a year he will see his doctor ; if he particularly requests it he will get special interviews, but they will all be short : he is very lucky if he has any form of medical care directly from his doctor for more than half an hour in each year. His doctor cannot help this : he has many other patients. If the doctor works in both the admission wards and the chronic wards he will spend half his time in the one, seeing some 30 patients, and the remaining half in the other looking after some 200 patients. Or he may spend his whole time looking after the 30 patients in the admission ward, while his unfortunate colleague will spend his whole time looking after 400-500 patients in the chronic wards.

Clearly the psychiatrist feels that the acute patient needs more of his very limited time than does the chronic patient. Is this contention true ? I suggest that it is absolutely untrue. In the admission wards patients with acute illnesses treated by physical methods get better or fail to improve almost independently of any psychotherapy they are given. Those psychiatrists who work in the admission wards are those who dictate the policy of the hospital, and the admission wards are well favoured with doctors—to such an extent, indeed, that the patients are overburdened with medical attention. The psychiatrist no less than the patient appreciates the pleasant furniture and surroundings of the admission ward ; it is agreeable to talk to patients who are well dressed and who can talk sensibly. The senior psychiatrist will not willingly surrender these pleasant things to work in the aesthetically unpleasing and culturally barren atmosphere of the chronic wards. In the admission wards he is always surrounded by a relatively large proportion of patients who are improving—patients who remit spontaneously, and patients who cannot help but get better on physical treatments. But between the admission wards and the chronic wards there is a gulf bridged only by the chronic patient.

The Chronic Patient

The facile distinction into "curable" and "incurable" patients is not confined to the administrative buildings of a hospital but is spread far around. Sometimes the hospital has a block of buildings for acute, recent, and eminently recoverable patients some miles away from the buildings used for the chronic patients. Sometimes a city will have a hospital or two for acute cases ; patients who do not respond rapidly to treatment in these hospitals are discharged, and have to seek admission to another hospital which rarely admits cases of good prognosis. In it are usually found cases of organic intellectual deterioration, epilepsy, recurrent and chronic psychosis, and mental defect. Everywhere there are more doctors in the small hospitals than in the large overcrowded hospitals for chronic patients.

The rational treatment of psychotic illnesses is impossible unless their natural history is known; but very few psychiatrists have any conception of the natural course of these diseases. Schizophrenia will eventually remit: perhaps not for ten, perhaps not for fifty, years; but remit it will. The parole wards of mental hospitals are full of patients who have reached their remissions. They may still have some odd ideas, but they have learnt to live normally, and to avoid talking about their strange experiences or reacting to them. The possession of delusions is no reason why any patient should remain in hospital: what counts is the effect of the delusions on his behaviour. Patients with paranoid illnesses can be taught to live with their delusions unchanged but with their attitude so much modified that they need not be in hospital. Pathologically quarrelsome and difficult epileptics are often admitted to mental hospitals; but if they are handled with tact, kindly discipline, and encouragement they can be made fit to go home and live with their relations. The restless and violent senile patient rarely remains in this state for more than a week or two; after that he can easily be looked after, and the first step is to arrange for his admission to a geriatric unit.

Incarceration for the sake of incarceration is, of course, unknown; but spontaneous remission and adaptation are only rarely given an opportunity to develop. Yet praiseworthy efforts are made to make life in hospital pleasant for the chronic patient: occupational therapy classes, social clubs, frequent entertainments, games to watch and play, outside excursions in the summer, and instruction in painting and sculpture are all encouraged to some extent. These activities sound very impressive, and are ennobled by the name of "therapy"; but a visit to any occupational class will show this description to be false. The pattern is always the same: patients do, and continue to do, what they have some gift for doing. Patients make rugs who have done nothing else for years; women knit who would knit wherever they were: they would knit if the heavens were falling and the world crashing down around them. Painting is done by patients who have a gift for painting. There is nothing therapeutic in the overwhelming majority of occupational classes up and down the country. Occupational therapy has become an end in itself, the teachers and the taught indulge in activity which from the point of view of treatment is quite meaningless and absolutely useless.

Fitting Patients for Discharge

Psychiatrists who deal with chronic cases forget that the urgent need is to get patients out of hospital fit to work while they still have relations who are willing and able to look after them. The adolescent who develops an acute schizophrenic illness may remit in his late fifties; but by then he is unlikely to have fit and active parents, or even siblings, with a strong enough affection to look after him.

It should be made clear to patients when they enter hospital that they will not be allowed to stay indefinitely. The patient who leaves the admission ward for the chronic wards must be made to understand that his treatment has not finished, but rather that it has taken on the more obviously purposeful form of getting him fit to return to his home and work. A patient's relations will probably remain loyal to him and be prepared to look after him, even if he is not completely well, provided he is discharged within a year of his admission to hospital. If ten years have elapsed he may be completely well and yet be unable to leave hospital because he has no-one to befriend him.

The wards of a chronic hospital often contain 80-100 patients, and it is instructive to see how these patients pass their day. In the report book it may be stated that all but ten of them are working, either in or out of

the ward. In fact, some dozen patients will be out of the ward from 10 A.M. to NOON, and from 2 to 4 P.M.; 8 will go to occupational therapy classes, leaving 60-100 patients to clean and maintain the ward: and how they can all be usefully employed defeats reason. There are, in each ward, as many beds and chairs as there are patients; there are sufficient tables and a few leather sofas; there are lavatories, washbasins, and 4 baths; and there is the ward crockery. Surely it cannot take 60 or more patients all day to keep these objects tidy and clean—even though the curious importance attached to a well-polished floor consumes uselessly a considerable amount of time and labour. A patient is counted as "doing ward-work" if he carries a chair from one place to another at the direction of a nurse. No ward of this size could possibly take up the time and labour of more than a dozen patients, even if they took things very easily.

How then goes the rest of the day for the 60 patients who remain in the ward? They sit, or walk aimlessly about the airing-court or the ward; and do nothing else. Sometimes they are seen sitting tightly on benches against which a table has been pushed, because there seemed to be no other way of preventing them from fighting one another.

The annual reports of mental hospitals rightly stress the good work that is done, the new methods of treatment employed, the increasing number of cures, the provision of better recreational facilities and so on. Encouraging as it is to read these reports it would be even more encouraging if the hospital were to state the problems which have still to be solved and state them unmistakably in figures: reporting, for instance, how many patients have been kept in bed for disciplinary reasons; how many times disablement resettlement officers of the Ministry of Labour have failed to find work for patients who were fit for discharge; how many patients could not be discharged because there was no home for them to go to; how many were incontinent habitually; how many times the procedure for the follow-up of discharged patients has been inadequate, and how often this has led to the death of ex-patients.

An Experiment

In this hospital we are happy in that there has been for many years a liberal régime. Villas and open wards are available for about a third of the male patients; every day there is some form of entertainment; and parole outside the hospital grounds, as well as within, is readily granted. Despite these and many other good points the problem of the so-called dilapidated chronic patient has not been touched.

A patients' sports and social club did some good: an elderly man with an active delusional system, a most difficult patient, was transformed by this opportunity, and his good work for the club became well-known and widely appreciated throughout the hospital. He was willingly granted outside parole, and remains in hospital for no other reason than the lack of a home outside. An epileptic of poor intelligence, who for many years had been rightly regarded as one of the most dangerously aggressive patients responded to the same opportunities so well that he was granted first inside, then outside, parole and at last became a voluntary patient. When he left hospital he attended an industrial rehabilitation unit and was selected for a job.

Despite these measures the wards and their airing-courts were as full as ever of dilapidated patients, many of them regarded as actively homicidal and suicidal, many known to be incorrigible escapers for whom no control seemed effective except the one so readily adopted—confinement to the ward and all too often to bed.

The male side of the hospital was chosen for an experiment. The aim, it was agreed, should be to discharge all these apparently helpless patients in such a state that they would be fit to take and hold a job,

and live satisfactorily in lodgings or with their relations. Before a patient could be considered fit to do these things he must have proved himself fit to live in the hospital in a parole ward and to work in the hospital free from supervision.

The chronic wards were told to choose 6-12 patients for their hour-to-hour maintenance. Patients who worked usefully about the hospital or its grounds continued to do so. Every other patient was to be out of the ward in the morning and the afternoon. Apart from its dozen essential workers, then, each ward was emptied every morning and afternoon, and the patients were divided into groups, according to their age and physical fitness, and in these groups they worked or played. The fact that a patient was regarded as a persistent escaper, a homicidal or suicidal risk was taken as an absolute indication that he should be kept out of the wards and included in one or other of the groups.

Patients who were young and fit did what was essentially physical training, combined with games requiring thought. (Football, which tends to be purely mechanical pursuit, was forbidden except as a weekly game.) These patients trained together as a large group until they had learnt to do things as a well-coordinated unit; then they were divided into smaller groups wearing distinctive sports gear, so that each rank in the large unit was made up of different small groups. After a further period, each group worked on its own, always under the same nurse. Patients had to do things smartly and do them as a group. They were given things to do which they would enjoy doing, and which would provide them with thought as well as physical exercise, and everything they did had to have their active and their willing support. As they were seen to improve, individuals were put on a gardening squad, first under the care of a nurse and later under a gardener, and eventually they were given other jobs about the hospital or its grounds with the least possible supervision.

Older patients would sit about in the grounds, throw a light medicine-ball to one another, gather cut grass, or play cricket with a soft ball, never taking any strenuous exercise, or doing anything for so long that they became bored or physically overtired. They were encouraged to play bowls. Blind and infirm patients also left the wards and sat about or walked according to their physical abilities or their wishes.

There were some 20 patients who had all been in the hospital for many years and for whom no activity had ever been thought possible. Their behaviour was constantly violent and uncooperative, and they suffered almost continuously from distressing hallucinations.

They were placed under the care of one nurse and given a large plot of rough ground. It was explained to the nurse that this ground belonged to the patients, and that it was his responsibility to turn it into a couple of tennis-courts, a bowling-green, and an ornamental garden. He was told that he could take as many years to do this as he found necessary, and that he would never be given any patients who were likely to be helpful or cooperative. The ground was rough, the grass stood high, and it was rank with stinging nettles and docks. His men were given forks and spades but no other equipment. The details of the work were left to him, and he was told he would be given no assistance or advice by the hospital gardeners. The work has gone well, the grass was burnt or torn up, the turf has been cut and stacked, the ground is being prepared. The Hospital Management Committee allow the patients to buy seed potatoes from them, and they buy back the crop; the patients will have the profits to buy fresh equipment.

The patients on this project, specially picked because they were difficult and uncooperative, work very well and enjoy it. They resent wet days when they cannot go to their tasks. Once classed as "impossible" and "untrustworthy," they never make any attempt to run away, and they require only minimal supervision.

Nor is all this extravagant of nursing staff. No patients have been left in the wards except those whose

behaviour was very good; and their numbers were few so that ward nurses could readily be spared. Complete disuse of the airing-courts also released nurses; and in fact it was found that 180 patients could be well looked after by 8-10 nurses.

The whole of these activities were placed under the care of the hospital's good occupational therapy department. It was held that no patient should go to the occupational therapy department just because he was no trouble and worked well there. Patients can deteriorate as rapidly making rugs as they can while working with the hospital porters or just sitting in the wards doing nothing. We decided there must be a positive reason why they should indulge in any form of activity. The advantage of having the occupational therapist in charge of all these activities was that each separate activity remained a part of the whole and there were no separate kingdoms claiming allegiance from patients or demanding the allocation of additional nurses. A patient could easily be transferred from one unit to another as his progress dictated, still remaining under the same set of nurses.

On wet days, patients might give a ward an unusually good cleaning; and the recreational hall was used for some of the same sorts of activities as were carried on out of doors. With the coming of winter there had to be a change, though the improvement in the patients rather than the difference in the weather made it necessary. Other treatments were introduced. Young and active patients still continued to take physical exercise when possible, but in bad weather they were divided into groups of 12 who, with a nurse in charge, would sit and discuss the news of the day, read to one another, discuss their previous careers, or the places they had visited, read or write plays, listen to school broadcasts and discuss them, and so on. A group of deteriorated schizophrenics gave a very creditable concert. In the morning and afternoon the old men used one of the dayrooms in a villa as clubroom. Patients with gross organic brain damage, or a severe degree of mental deficiency, were given the job of constructing a cinder-path round the grounds, which will be useful to everybody because it is free from traffic. The emphasis, in this as in all other labouring activities, was on the therapeutic value to the patient of being employed usefully, and seeing that his work will benefit him and his fellows. No patient is kept at one job all the time; other ways of occupying him are introduced. The important thing is that the patient should see what he is doing and enjoy it; and no attempt is made to get the job finished in a given time.

Every effort is made to get patients home for the day, or the weekend, as soon as they show any sign of improvement. If there are no willing relatives, a nurse will take two or three patients into the city for an afternoon, and when a patient—who may not have been out of the hospital for twenty years—has improved enough, and gained enough confidence, he is encouraged to go on his own. If relatives are willing to have him home but are not convinced that he is well enough, a nurse will accompany him on the first occasion.

We accept that view that all psychoses have an organic cause; and the usual physical methods are used where they are indicated. A doctor who looks after 400-500 patients can give psychotherapy only at a superficial level, but it is an essential adjunct to other methods of treatment. It is important for the patient to be able to accept his false beliefs and his disabilities, and yet to be able to refrain from acting upon them: for the habit of acting on them usually makes it impossible for him to live out in the community.

Every request a patient makes for a change of ward or for leave is carefully considered, and the fact that he has behaved badly in the past is not allowed to weigh

too heavily against him—indeed the historical approach to a patient is discouraged. The patient who was dangerous twenty years ago is only too apt to be still classified as a desperate homicidal risk.

When a patient is transferred to the main building from the admission ward, the reason for this is explained to him. He is told that the plan is to get him discharged soon, and every effort is made to win his co-operation. I have said that a patient does not have to be free from delusions to be fit to leave hospital; nor need his conduct necessarily be perfect under all circumstances: whose is? A patient whose behaviour is impossible in one ward may behave perfectly in a parole ward, and be fit in every way to visit the city on his own, to seek work, obtain it and keep his situation.

Results

That this régime is successful needs no elaboration: the testimony of surprised and delighted relations and the great decrease in the amount of sedative drugs dispensed confirm this fact.

In the sick ward for older deteriorated patients, whose strength has declined with the years, many beds may be occupied by people who could, if they were encouraged, get up to go to the toilet, to eat, and to go out of doors when the weather permits. These patients tend to lie in bed, taking no interest in anything, constantly incontinent, and running a risk of developing contractures. In this hospital these patients are up and dressed and given simple occupational therapy—making paper bags for the canteen, sorting wool, and making rugs. Some who were formerly thought to be completely demented, and a permanent burden on the nurse, have become cheerful, more alert, and able in small ways to look after themselves and to get some enjoyment out of life and out of their families' visits. Within six months of starting this experiment there was not a male patient who was not receiving some form of active treatment every weekday.

Our revolution has been achieved without any increase in staff, without any patient being deprived of treatment which he needed because nurses were engaged with other tasks, and without the purchase of expensive equipment. Indeed it has been carried out without a penny's cost to the hospital. Confinement to bed is unnecessary, seclusion should never be employed, and it is rarely necessary to lock wards. Locked wards on the male side of this hospital are decreasing in number, and soon two-thirds of the male chronic patients will be in open wards. It is my belief that locked wards will eventually be dispensed with in all hospitals.

When the patient leaves hospital he will have to work; and he is therefore encouraged to work while he is in it. Meaningless tasks, such as hospital portering, are discouraged, and patients should never be allowed to continue doing them for more than a few weeks at a time without some pleasant and therapeutic activity being introduced as a break. A recoverable schizophrenic is not uncommonly discovered on the swill gang or on some other similar job where he will hardly ever see a doctor. Patients must have it explained to them time after time that they will one day leave hospital, and that they must prove themselves fit to start work and to lead a normal life by the time that day arrives.

Some Future Possibilities

If the opportunities were provided for patients to receive some pay for work when their stay was likely to be more than a few weeks, there are few who would not be fit to work and glad to do so. The problem of providing work for discharged patients could easily be solved, if industry would co-operate. Epileptics and chronic psychotics would be employed in a separate workshop, where they would not distress others by fits or strange behaviour.

Many patients require somewhere to live on first leaving hospital: a hostel run by nurses and supervised by the hospital would be of great service to them. Moreover, patients who have been in hospital for a long time often find it impossible to get work. Their relations might be willing to have them at home if they were occupied; but the prospect of having them about the house all day and every day makes many refuse to have them at all. We arrange that discharged patients can attend at the hospital on all weekdays for occupational therapy, and have their midday meal there. They are allowed one day off, to attend at the labour exchange to look for work themselves. The same device is used for treating those not needing inpatient care, but requiring supervision and help.

For the success of such a plan as ours one thing is necessary: the willing co-operation of the nursing staff. Once this is gained much becomes possible.

Conclusion

Though psychiatrists and nurses are kind and humane people, treatment for any but recent admissions is generally almost non-existent in mental hospitals. Psychotics have an almost irresistible tendency to recover; but the process is checked because most psychiatrists are unaware of the natural course of psychotic illnesses. Moreover, the community is united in refusing to accept the psychotic when he has recovered from his illness even if he is an efficient and willing worker.

The psychiatrist can always be sure of the help of his nurses if he proposes to put into action a plan such as that described here. There are nurses everywhere—just as there are here—who will volunteer to look after a group of apparently irredeemable and degraded patients, and will eventually help these fellow citizens to regain a life which is pleasant and useful not only to themselves, but to their relations and to the community.

CANCER RESEARCH

THE 51st annual report of the Imperial Cancer Research Fund shows that its policy has not yet succumbed to the view¹ that cancer research should devote itself to chemotherapy and that the cancer problem can be solved only by retreating to basic sciences like genetics and biochemistry.

At the Fund's laboratories, L. M. Franks and P. C. Williams have studied the relation of oestrogens to prostatic cancer, using the hamster and guineapig for their experiments. It is now well known that a considerable proportion of old men show histological evidence of symptomless prostatic cancer and benign enlargement of the gland. Changes resembling human nodular hyperplasia or adenocarcinoma have only recently been reproduced in experimental animals: firstly, adenocarcinomas have been obtained by subcutaneous transplants of mouse prostate, together with hydrocarbon-carcinogens; and, secondly, local application of "the carcinogen" (presumably oestrogen) to ageing oestrogen-treated hamsters has induced acinar carcinoma of the prostate resembling that seen in man.

Williams has observed the effect of cross-breeding a strain (RIII) of mouse liable to mammary cancer with the C₅₇ strain which has shown no tumours during six years' observation at the Funds' laboratories. The C₅₇ line shows a high vaginal responsiveness to oestrogen and there appears to be an inverse relation between oestrogen sensitivity and incidence of mammary cancer. The hybrids (C₅₇ x RIII) show a higher incidence of mammary cancer than even the C₃H line, and their vaginal oestrogenic sensitivity is nearly as great as that

1. Committee on Growth of the National Research Council: 6th Annual Report to American Cancer Society. July, 1950, to June, 1951. 1953.

of the C₅₇ mice. The comment of the report is a little hard to understand: "The assumption of a causal significance is not supported by tests carried out on the Foulds hybrids (C₅₇ x RIII)." (It may be that the theorists cannot bear to have their generalisations upset.)

The theme of the day in cancer research—the lung-cancer/smoking relation—is being pursued by A. M. Begg. A single intranasal inoculation of benzpyrene in arachis oil induces oat-cell carcinoma in Simpson mice after 200 days. The report mysteriously adds that "Dr. Begg has also been carrying out tests in rats, mice and rabbits of substances which, because of their nature and use, must necessarily be subjected to adequate tests for absence of carcinogenic activity."

C. Le Q. Darcel and G. Negroni are investigating fowl leucosis by tests on the transmissibility of lymphomatosis and erythroblastosis, the viral transmission factors, and the cytology of the tumours. Because one type of tumour is transmitted by cell-free extracts, and therefore by a viral-type agent, while the other is not, analogy between the two diseases suggests that a viral factor cannot be excluded in the second case, but that it could be too labile or liberated in too small amount to be demonstrated by the techniques so far developed.

Claims have been made by other workers to have demonstrated that cell-free extracts produce these tumours after a long latent period, but they also found that extracts of normal chick embryos have a similar activity. The active agents in these extracts therefore cannot be analogous to the erythroblastosis virus of the fowl since the virus can only be obtained from homologous tumours and not from normal tissues of apparently normal fowls."

James Craigie's technique of preserving tumour tissue has had some remarkable results: primary benzpyrene sarcomas, induced in C₅₇ mice, could still be grafted successfully after five years' storage at -70°C.

B. D. Pullinger has continued her work on mammary cancer in RIII mice which develops without the operation of the milk factor. Ovariectomy in ageing mice did not increase the incidence or total number of benign or malignant growths, but "ovariectomy in breeders at 9 to 10 months old produced a 14-fold reduction in the numbers bearing benign growths." Of special interest is Pullinger's conclusion, derived from "the part played by oestrogenic stimulation in the evolution of spontaneous growths in the mouse breast," that "in the strain used the action of oestrogen was analogous to the action of a *promoting* factor on experimentally induced papillomata of the skin."

Experiments on surface X-radiation of the nipple area of the mouse have yielded 7 mammary carcinomas in 29 mice which lived longer than 11½ months. The report says:

"It is highly improbable that any of these tumours were spontaneous, and none was associated with primary ovarian tumours. One striking change in the directly irradiated mammae was complete involution with atrophy and failure to respond to endogenous oestrogen. This appeared before there was any evidence that malignant tumour formation had started."

H. G. Crabtree has carried out experiments to test his suggestion that *p*-aminobenzoic acid may play a specific rôle in the induction of liver tumours in rats by certain azo dyestuffs. This suggestion sprang from his discovery that a series of non-carcinogenic azo compounds, all of which yielded *p*-aminobenzoic acid on metabolic breakdown, could significantly retard the rate of induction of liver tumours in rats by butter yellow or *o*-aminoazotoluene. An alternative interpretation assumes that the presence of additional azo compounds might retard the rate of metabolic rupture of the carcinogenic molecule by competing for the enzyme systems involved in this process. Crabtree has now prepared a similar series of

azo compounds which, on metabolic breakdown, yield the corresponding sulphonic acid—sulphanilamide—instead of *p*-aminobenzoic acid. Four out of five members of this series of sulphur-containing azo compounds, when fed to rats together with butter yellow, delayed the time of appearance of liver tumours, compared with that in animals receiving butter yellow alone, by about 6 to 7 weeks. Sulphanilamide itself also had a similar retarding action on the development of tumours by butter yellow. The one sulphur-containing azo compound which failed to protect was found to be itself a weak carcinogen.

EUROPEAN LEAGUE FOR MENTAL HYGIENE

At a conference of this body held in Rome from April 7 to 11 the main theme was the relation of mental health to public health—a subject that will also be discussed at the conference of the World Federation for Mental Health at Toronto in August.

In her presidential address, Dr. DORIS ODLUM (London) said that an important step towards mental health had been taken by establishing in many countries national associations for mental hygiene which could bring together representatives of every aspect of the life of the community. Yet in nearly every country a large proportion of the medical profession was among the opponents of the mental-health approach. Investigations (admittedly on a limited scale) suggested that, in England at any rate, some two-thirds of general practitioners either fail to recognise the neuroses and psychosomatic conditions or are so opposed to psychiatry that they never seek psychiatric help. There was great need for the better education of the public in the principles of mental health and in the great help that psychiatry can give to those who are mentally sick. A growing appreciation of the psychosomatic disorders was making it more obvious that mental and physical health cannot be separated; and "there is," said Dr. Odlum, "a tremendous demand on the part of the public for help and guidance in their personal problems."

Dr. J. R. REES (whose address was given in summary by his wife, Dr. Hemingway Rees) spoke of the need for partnership between mental health and public health. The World Federation for Mental Health (of which he is director) was composed of 50% professional associations and 50% mental-health societies coming from many countries. Part of its job was to encourage further research and better treatment; but we should never be able to provide treatment for all who need it, and the more important task was that of prophylaxis. The chief considerations included the upbringing of small children, the effects on small children of separation from their parents, and the effects of stress and anxiety leading to the development of psychosomatic illness. In all health education it was necessary to co-operate with colleagues whose primary concern had been with the prevention of physical disorders.

Dr. DONALD BUCKLE (regional officer for mental health of the European region of the World Health Organisation) said that the first task of education in this field was to bring the concepts of mental hygiene into the open. Without this change of outlook nothing could be effective. It was only because in some countries this educational change had already come about that we had seen the legislative changes which had created improvements in the treatment of the mentally sick.

Dr. ANDRÉ REPOND in his paper pointed out that it is very difficult for the principles of mental health to make headway against the deeply ingrained tendency of human beings to rely on magic, especially in relation to health. Those working in this field must not underestimate the unconscious emotional influences working against their efforts to develop human beings with well-integrated and harmoniously balanced personalities prepared to face and to accept reality.

Dr. P. SIVADON (France) said that after a long period of opposition and apathy in France there had recently been a considerable improvement in the official attitude towards mental-health concepts. Many of the ministries

now had psychiatric advisers who were called in for consultation and some even had psychiatrists permanently attached to them—e.g., the permanent commissions for health, for education, and even for housing. Prof. DE SANCTIS (Italy) described proposals by himself and Dr. Carlo Vetere, who was a public-health doctor, for furthering mental-health work in Italy. Dr. E. STENGEL (London) described investigations into the social significance of suicide and attempted suicide.

In the discussion, Prof. H. C. RÜMKE (Holland), president of the World Federation for Mental Health, said that we must beware of adopting the attitude of dictators in mental health and laying down the law. At present our knowledge of normal man was very limited, and had been obtained largely through the study of the abnormal. The time had now come when we could go out into the world and try to study, in company with our fellow men in every field, the workings of the mind and personalities of normal people. Thus we should hope to arrive at some real understanding of the factors concerned in producing mental health. Prof. HANS HOFF (Austria) replied that although it was true that there was much we did not know, we did in fact know a certain amount and could put it into action in certain fields. For example, we could advise mothers on the upbringing of their children, we could help young people with their emotional problems, and we could also give help and advice in relation to employment.

Medicine and the Law

Loss of an Eye

A CLAIM for £3000 damages against a former house-surgeon at Dundee Royal Infirmary was dismissed in the Court of Session by Lord Strachan,¹ although he found the doctor guilty of professional negligence.

The plaintiff was a girl who in March, 1951, at the age of 15 months, had fallen face downwards on a broken cup and injured her left eye. At hospital the house-surgeon found a laceration of the eyelid but failed to observe any injury of the eye itself and allowed the child to be taken home. When she was seen some weeks later by the family doctor the eye was found to be blind and it was afterwards removed lest sympathetic ophthalmia should affect its fellow.

The judge said that the expert evidence of seven eminent ophthalmologists had agreed that the defendant should have reported the case to a specialist. As to whether his neglect to do this had caused loss or injury to the child, his lordship held that, on the evidence, the doctor had established his defence that the condition of the eye was irreparable from the outset, and that no treatment could have made any difference.

Accidental Overdose of Insulin

At a recent inquest² at Sedgefield, co. Durham, the coroner recorded a verdict of accidental death on a woman who died after being given an injection of 5 ml. of insulin. The patient, who was under treatment for mental confusion, was being given 5 units of insulin daily. The sister in charge of the ward, who had been looking after the patient since her admission to hospital on Feb. 28, said she had instructed a nurse, who came on to the ward the previous day but who had had training in insulin treatment, to give the patient her usual 5 units of insulin on the morning of April 12. The nurse queried the dosage verbally and the sister, in evidence, said she thought "units" had been mentioned. The nurse stated in evidence that she had said "5 c.c.s.?" in an inquiring tone of voice, and the sister had replied "Yes." The patient was later found to be in coma and died despite attempts at resuscitation. The coroner said that he thought the sister stated the correct dose but that the nurse misheard her.

¹ Scotsman, April 10, 1954; Glasgow Herald, April 10.
² Darlington Times, April 17, 1954.

The Widdicombe File

XI. THE SAD TALE OF MRS. SMITH

The County Medical Officer of Health

DEAR DR. COBBLEIGH,

EVER since I settled in partnership here I have been meaning to ask if I might come to your office and introduce myself. Sir Daniel Whiddon showed me your letter about his farm and I was sorry I'd been so dilatory.

Since I qualified I've retained the impression that the public-health doctors are to be spoken to only in emergency or in protest, and district nurses and midwives are the only representatives of the service that I've actually met. But I'm beginning to realise that you and others provide my patients with services of which I'm still ignorant. And I'm wondering whether you can help me with my problem families.

I have about a dozen of them on my list, and they give me more trouble than all the rest put together.

This afternoon I've been visiting the Smiths, of no. 13 Downtown, who are in constant trouble with the diseases of dirt and ignorance. As a young and inexperienced doctor, with all my illusions still about me, I've tried to approach the family in the crusading spirit, as a challenge to preventive medicine and health education. But I've so far failed miserably and have for the moment retired, frustrated and fleabitten.

* * *

The central figure in the Smith drama is Mrs. Smith, known to her friends as Our Rita. She is 38 and has five children, a sixth on the way, and a seventh in the graveyard. She herself was one of a large family of kind and feckless parents, was fairly well fed but seldom washed, and grew up with little training or discipline other than the exasperated slap. She was educated at vast expense by the State, but her low intelligence and frequent absences from school prevented her from learning anything more advanced than to read the comics. After leaving school she drifted through various jobs in laundries and shops and eventually settled into quiet and unexacting employment sweeping out a large store. Here she learned from the other girls, who were kindly and rather brighter; following their ways she came under the magic spell of Hollywood and went to the Odeon twice a week, where she could enjoy luxurious surroundings and Romance in Glorious Technicolor for 1s. 3d. Following the example of the Stars, she took up Glamour in a big way, smartened herself up, used make-up, and was more or less clean. With some decent clothes, uplift, and a perm she fancied she might become a star herself if a talent scout happened to come her way, but somehow one never did. For the most part Hollywood was quite a good influence on Our Rita, although as she came to spend more time and money on her appearance than on food, she became poorly nourished and underweight.

At the age of 18, it seems, she met Bill Smith, a steady-going chap who worked for the council, digging holes in the road; as a result of some rather disappointing physiological experiments in a hayfield it became expedient for her to become Mrs. Smith, which was not so romantic as she had been led to expect. However, the baby which arrived six months after they were married left her little time to worry about that. After living with her in-laws for a while they were lucky enough to get a council house on a new estate. To begin with, Mrs. Smith was proud of her new house and tried to keep it nice, but as she had never learnt much about housekeeping and cooking she found this difficult. The baby was a great worry to her, and the unaccustomed responsibility and disturbed nights made her tired and irritable. She had ceased to care about her personal appearance soon after marrying Mr. Smith. When the second baby arrived, eighteen months after the first,

she had far too much to do and things got on top of her ; the house became dirty and the cooking neglected. By a slow but unrelenting process of decay, accelerated by each childbirth, the Smith family became slum-dwellers.

It is easy for the stranger to pick out the Smith house. Most of the council houses in Downtown are well kept, with cheerful curtains in the windows and productive gardens. The garden of no. 13 contains a wilderness of weeds and a derelict perambulator ; the gate is loose on its hinges, there are no curtains in the windows, and the washing on the line is dirty. On entering the door the visitor is assailed by a strong smell ; there is a general appearance of dilapidation, and the floor and walls are dirty. What furniture there is, is falling apart, and the rooms are cluttered with dirty clothes and rubbish.

Mrs. Smith wears some ancient garments, which I can't describe and hope not to have to take off some day to examine her. She is anaemic, her teeth are bad, and she looks about 50, though she is only 38. She suffers from menorrhagia and abdominal pain, largely the result of coitus interruptus, and her varicose veins get worse with each pregnancy. She is by nature kindly, feckless, and uncomplaining. There are five children—Alf, Ern, Linda, Georgie, and Doreen—a sixth died of diarrhoea in infancy. They have runny noses and one or other of them is usually on my visiting-list for discharging ears, impetigo, or diarrhoea. They are dirty and their clothes are ragged, though adequate to keep out the cold. They are usually shod in rubber boots or canvas shoes ; they become noticeably cleaner when they go to school and find themselves laughed at by the other children for being dirty.

They look surprisingly robust, though their diet is predominantly carbohydrate, with potatoes, cream buns, ice-creams, and chocolate high on the list ; protein is supplied by school meals, the fish-and-chip shop, and a few eggs which the chickens in the back-yard sometimes produce. Mr. Smith provides £7 a week, is affectionate to the children, and believes in keeping out of the way as much as possible. About £4 a week and the children's allowance go to the house-keeping, the rest to beer, cigarettes, and the television set on the hire purchase.

* * *

That is the Smith family, resigned, dirty, but struggling along as best they can. They are good-humoured, generous, and in spite of everything likeable. The sordid state they live in is not due primarily to poverty, nor to housing difficulties, nor to lack of schooling, but to the unalterable fact that Mrs. Smith is of very limited intelligence and unteachable by ordinary methods. She is, in fact, a high-grade mental defective ; and it's on her inability to learn that all efforts at preventive medicine come to grief. With considerable persistence she can be shown how to keep the house clean and the children cared for, but in a few weeks the family is back again in squalor, the new baby and the toddlers being fed milk out of an old beer-bottle with a rubber teat stuck on the top of it.

The health visitor, the district midwife, and the general practitioner share the task of trying to keep the Smiths out of trouble. I think the health visitor plays the biggest part ; she has the special training in nursing and social work and can help Mrs. Smith over the shopping and the children's clothes. She understands the Smiths and is liked by them, so that she can keep up the pressure of benevolent nagging without offending them. I have met the health visitor in Widdicombe and discussed the problem families of the practice, to my great advantage. The district midwife is also on good terms with the family and helps them spring-clean the house before each new baby arrives. As the G.P. I have tried to show Mrs. Smith how to kill the flies with a D.D.T. spray and have given her ferrous sulphate tablets which she does not take. The most pressing need is to stop Mrs. Smith having any more babies, which would

give her a chance to look after those she has already. I have fitted her with a dutch cap and spermicidal cream, but these she will not use and her husband considers his own methods of contraception good enough.

So far I feel that I have only scratched the surface of the problem, treating the various diseases of squalor as they appear. Probably the only measure which would alter the situation materially is to sterilise Mrs. Smith, to which I do not suppose either the Smiths or a gynaecologist would agree, and which I cannot persuade myself is really right ; it carries with it a great danger of encouraging promiscuity and breaking up the home.

I am anxious to take Mrs. S. into the local G.R. maternity home for her next confinement, her seventh. She has reached a dangerous degree of multiparity and I don't want to find myself dealing with a postpartum haemorrhage or prolapsed arm in no. 13 Downtown. If the children can be looked after for a while I would like to keep her in hospital for a good rest, proper food, and a course of iron and vitamins, and have her teeth seen to. At the same time we can enlist the help of Mr. Smith to clean up the house. Would your department be able to help with the children ? A month's holiday at a children's home would do them the world of good.

But what can we do for the future ? I suppose we should be thinking about the schooling of Mrs. Smith's daughters. They are no brighter than she is, and are not likely to derive any greater benefit from a formal State education. What they need is a simple training in the elements of house-keeping and mothercraft in a special school for the handicapped, if they are not to follow in their mother's footsteps.

I look forward very much to discussing all these problems with you, for I badly need a conducted tour of the Welfare State, which is confusing to the untutored traveller.

Yours sincerely,
W. BREWER.

Public Health

Infantile Gastro-enteritis in Exeter

DURING the eight months from July, 1953, to February, 1954, there were 21 cases of gastro-enteritis in babies under 1 year who were being treated in, or had recently been discharged from, the Royal Devon and Exeter Hospital. 6 of the babies were in the maternity nursery, and the remaining 15 were patients in the children's ward ; but in only 4 of these 15 did the infection show itself in hospital. In the other 11, symptoms did not develop for periods ranging from a few hours to ten days after discharge ; 7 of the 11 fell ill within two days. It may be that a few of these cases were infected after discharge. There were 3 deaths in the hospital, and 2 more babies died in an isolation hospital. In every fatal case there was some other substantial contributory factor which aggravated the infection : thus, 2 of the babies were grossly premature (3 lb. 4 oz. or less at birth). *Escherichia coli* 0-55 was recovered from 8 cases, and no other pathogen was discovered. Gastro-enteritis was prevalent in the area during the period and *Esch. coli* 0-55 was isolated from some of these outside cases. During the same period, apart from 4 children readmitted because of gastro-enteritis occurring after discharge, 4 cases of gastro-enteritis were admitted to the hospital, 3 of them in December (12 of the infections in infants occurred during December and January). These admissions may have kept the infection "alive."

The whole outbreak is an example of a creeping epidemic with a number of apparently disconnected episodes and, therefore, not readily recognisable at the time. Crowding of the maternity ward and nursery has caused anxiety for some time, and, on the advice of the paediatrician and the hospital's standing committee on cross-infection, a small isolation unit for children and a small premature-baby unit are being provided by the conversion of certain rooms. The committee is also reviewing the whole outbreak, and a report is being prepared for the regional hospital board and the Ministry of Health.

In England Now

A Running Commentary by Peripatetic Correspondents

As a passive amateur of the arts I always envy the active amateurs who open the piano, ring up the curtain, or seize the paintbrush with their own hands. To this courageous body belong, of course, the members of the Medical Art Society, and judging by their exhibition (at Walker's Galleries, 118, New Bond Street, London, W.1, till May 8) they have all had an enjoyable year, with a good deal more to show for it than I have.

To begin at the beginning, Sir Philip Manson-Bahr, appropriately maintaining the equine tradition of another president, contributes a study of his black hunter *Merrymack*; and I also liked the feathered flurry of his *Ducks and Drakes*. The landscapes were varied and accomplished. I recall with pleasure Sir Harold Gillies's brown and white study of *Beech Trees in Snow*; the rust and grey roofs on T. M. Ling's *Beedingwood Farm, Sussex*; the flat placid pattern of church and water in R. Ogier Ward's *Friston Church*; the space and the snow of A. M. Rackow's *Cumbrian Farm*; the purple shadows of E. M. Whetnall's *Santa Barbara Mission*; the inviting turn of the street in Henry Wilson's *Stand-on Village*; the black figures of three Negroes walking down a near-black road in M. G. Corco's *Near Oji River*; the effectively scrawled red-ink roofs and roads of Isabel Wilson's wide countryside in *Flight over Europe*; and the path through a dark wood in Ian Robin's *The Glen*. Clearly there are some seafaring folk among the society; A. S. Till saw *The Blackwater at Malden* as a pleasing study in blues and yellow, and T. Holmes Sellors shows us furled rust sails at *Ipswich Docks*.

Among the portraits W. Hartston's studies of Africans stand out, especially the profile *Ahmed*. In Lady Whitby's *Freda* the red, white, and green of the figure is supported by a background of dull blue and pink. Denis Cronin has contributed several small sensitive bronze heads.

The still lifes ranged from N. Newman's pleasing but restrained vegetarian arrangement of two spring onions, two Spanish onions, two carrots, and three pea-pods, to the eerie assortment of fungi in J. F. Stokes's *Conference*. Norman Ashton suggests a satisfactory *Design for Living*: his simple bread and cheese and boiled egg stand beside a brilliant microscope, graceful glass flasks, and the ophthalmologist's bottle of atropine, and behind it all a beautiful decorated plate. Lady Whitby's bottle, mug, red book, and knitting-needles backed by grey ruga suggests a simpler but also attractive way of life.

The implicit social criticisms of these pictures is explicit in B. N. Brooke's *The Choice* (a woman faced with three hellish hats); and in M. Partridge's *Evening—North London* which shows Mrs. Battle of Golders Green at the bridge table. Nor has the new wirework trend been neglected, and in the *Unknown Political Stunt* S. Hale offers his views on the National Health Service. Cecil Ruben's *Bar at the B.M.A.* looks inviting, but I think the one at the Folies Bergère still has it.

* * *

My 2½-year-old was drawing long lines all down her page. "This is a Zebwa Cwossing . . . but all the other animals can use it too."

* * *

I am still vaguely worried about Easter Monday. It was a beautiful sunny day and we all went to Plumpton Races. We got a good place for the car on the hill, just in time to watch the first race. Then I explained the horrors of betting to the boys, but said it was all right to put a small amount on a horse, if you could afford to lose that much, to give you an interest in the race. I had never backed a winner, I did not know the name of a single horse there, but I was going to put something on one for the second race, to have a horse to watch.

I had a newspaper which recommended Rowley Boy. Waiting my turn at the tote, I saw that one of the other horses was The Editor, and being an editor (of a small specialist journal) I put my money on him, and a very nice race he ran, winning the two-mile steeplechase by two lengths. After

collecting 17s. 10d. I explained to the children that if one betted, which of course one shouldn't really, and was lucky enough to win, one must not let it go to one's head, and double up. I then departed to place a small amount—that I could afford on Glim and Dim, the paper's selection for the next race. With ten seconds to spare I discovered the horse was not running, and glancing like lightning down the card, I saw that Athelney, very near my mother's old home in Somerset, had that lucky number 13. This fortunate coincidence brought me 16s. 2d., although I had been watching the wrong horse as Athelney's jockey's colours looked sea-green instead of turquoise. I explained to the children that it was wrong to be carried away by betting, that two was a coincidence, but it took three to make a syndrome, which I hoped they would think was a particularly wicked sort of sin.

I had to leave rather hurriedly to place my bet on the next race, the Abergavenny Challenge Cup, but I saw that there were only six runners and reasoned that each of them had a chance of a place. I selected Nome, as for years I wanted to go to Alaska. He turned out to be a lovely dark slim creature, frisky and heartening. He had the inside place, got the lead, and kept it. The favourite challenged him in the last half-mile but fell. Refreshed by this little coup (£2 0s. 8d.), I determined to lose next time by backing the outsider, Distani, but found my wife had the same idea and so gave the newspaper expert another chance—Diego Rubio was his choice. Distani, a little horse, led to start with, but of course Diego Rubio won.

I started to tell the children about betting, &c., but caught a cynical look in the eye of the eldest, and shut up. He said that he was going to bet this time, on Never Again (by Boozer's Gloom out of Officers' Mess). I declared for either Western Slipper or Windsor Light, but as I approached the tote window I thought everyone who wasn't on either of them was on Le Serpent, so I simply backed the favourite, Retlaw, and went to watch the race. The issue was at no time in doubt. Never Again was second.

The real tragedy is that I didn't double up, but what worries me is that although I don't know enough to work out whether picking five winners in a row is statistically significant, it looks it. And if it is, there is something queer about statistics, considering my methods of choosing winners. Perhaps the real solution is that there is something queer about racing. The only conclusion I can draw is that if you follow your nose you and your family may have a day at the races for nothing. Of course you must have the right nose, like those chaps with clinical intuition.

* * *

Whether Her Majesty's Government would consider helpful advice from the U.S.A. to convert the alleged loss of the second battle of Trafalgar¹ into a victory, or at least a stalemate, I don't know. But I venture to draw their attention to a recent communication on the Use of a Specific Sound to Repel Starlings (*Sturnus vulgaris*) from Objectionable Roosts.²

The authors found that when starlings were held by the legs or wings, they emitted a piercing shriek. This distress call caused other starlings to leave their roosts and not return even after some months. This suggested that a recorded distress call might be used as a repellent. Accordingly, wild starlings were induced to give distress calls by holding their legs and shaking them roughly. The calls were recorded with a tape recorder. When the distress call was broadcast a heavily infested roosting area was cleared in 4 nights.

But I'm not clear whether that segment of Her Majesty's Government that has to maintain the traditions of Trafalgar, Nelson, et al. would consider a victorious end worth the employment of such one-sided means as holding the starlings' legs and shaking them roughly; or would agree with my implied classification of Trafalgar Square and appurtenances as "objectionable roosts."

* * *

Diagnosis in the Bus Queue

1ST LADY: "Have you been to the doctor's yet?"

2ND LADY: "No, not exactly. You see, I'm goin' an' I'm not goin'—that's how I am."

1. *Lancet*, Feb. 27, 1954, p. 463.

2. Frings, H., Jumber, J. *Science*, March 5, 1954, p. 318.

Letters to the Editor

THE BOMBS

SIR.—Many of your readers had been eager to hear your comments on the situation revealed by the recent "successful" experiments with hydrogen bombs; but some of us were conscious of an element of disappointment in our reactions on first reading your leading article of April 17. You did not try to present us with an analysis to which we could expect a large majority of our profession to agree. You did not put before those who crave decision and action a clear-cut choice between a heroic disarmament and an all-out support of the American policy of "negotiation from strength." You did not even encourage us to believe that members of our profession have as such no special duty in this matter.

But you did remind us that doctors are accustomed, more than most people, to face the facts of a dangerous situation realistically, and to do their best for everyone involved in the danger; and that a realist need not be a cynic. Realists who point out that war, having lost its survival value, is unlikely itself long to survive, seem to be on unassailable ground; the trouble is that it may nevertheless survive long enough to destroy all that we value in our world, and perhaps life itself.

Dr. Duncan Leys and Dr. Alex Comfort, in their letters last week, express grave doubts about the emotional balance of those in control of thermonuclear research in America. Dr. Leys thinks that "neither fear of retaliation nor any moral considerations will restrain the desperate"; he implies that those in effective control of thermonuclear weapons in the U.S.A. are, or may become, so desperate with guilt-ridden fear as to be inaccessible to any rational restraint; and there is evidence to support such a view. At least there can be little doubt that ever since the comparatively harmless pioneer atomic bombs were dropped on Japan there have been evidences of abnormal guilt-reaction in America. The danger of the devastation of Britain by hydrogen bombs or other thermonuclear weapons is vastly greater than the corresponding danger in America, while the fear-reaction is greater in America.

Dr. Comfort uses the ugly word "paranoia" in referring to the mentality of those who inspire and direct these activities; similarity between the emergent action and that recognised in individuals as paranoid is certainly striking. There is the same persisting terror of persecutory aggression, the same unrestrained violence of defensive response to it, the same effective planning in complete secrecy. It will be said that the paranoid protects himself against non-existent dangers, while the enmity directed against the U.S.A. is real; and there is evidence of emotional imbalance in Russia too. However true this may be, it emphasises beyond everything else the need for the sane and benevolent forces in the world to assert themselves.

It is common knowledge that when all are afraid, as before the outbreak of a panic, those who are most afraid take the lead. I have become accustomed to think of fear and flight as the least worthy emotional reaction to danger, with escape to anger and counter-aggression as a more admirable, as well as a more comfortable, alternative. It is perhaps unreasonable to expect a group which has risen from fear to successful aggression voluntarily to abandon a security based upon fighting strength in favour of a greater security which may have the appearance of weakness. But the urge to survival, applied through the less frightened and more rational members of the community, may supply the necessary compulsion; and there is for the individual, and no doubt for a nation, a stronger defence than counter-aggression. If he can find courage enough to study, without preconceived fear and enmity, the motivation of his enemy, he can usually—not always—

find so much in common with his own that the mutual enmity is mutually disarmed, to the benefit of everyone concerned.

Those who have never used this method cannot be expected to value it, but they might nevertheless be ready to see that pride in fighting-strength may not be the final consideration in human values. It seems that the time has come to revise that valuation, in the interests of our friends and of our enemies as well as in our own. Personal pride, classified by Aristotle as a virtue, is a vice by Christian standards; national pride may be due for a similar revaluation. I like to feel still at liberty to be proud of our national achievements, and I would certainly find conquest from abroad more offensive if the occupying troops were non-English-speaking; but I should like to place it on record that if given the choice between this and victory over the foreigner by the snuffing out of his civilian population I should hope and expect myself to choose the former.

London, W.1.

J. NORMAN GLAISTER.

SIR.—Dr. Comfort's letter based its main argument, however sincerely, upon a major misconception. No matter how much one may detest war and desire reconciliation between nations, it is sheer speciousness to infer that for Britain there is less menace from Russia than from the United States. The North Atlantic Treaty Organisation is probably the only thing that has stood between Russia and the subjugation of Western Europe, and to attempt to confuse this particular issue is to play into the hands of Communist propaganda. Quite apart from this, it is a matter of historical fact that it was the United States who proposed, and still propose, international control of the production and development of atomic weapons, while the Soviet Union have consistently refused to accept such control.

For Britain now publicly to dissociate herself from her greatest ally—for that is what Dr. Comfort's proposition would in fact amount to—would be to present the world as a free gift to tyranny. Of course we must continue to press for international control and inspection of all atomic weapons, with a view to their ultimate abolition—and we should be well advised to extend this to submarines and rockets, both of which are the subject of intensive Soviet research and would be obvious weapons to deploy against our island. More important still, we must do all we can to achieve a permanent reconciliation between nations. But to suggest in this context that we have no more reason to trust the United States than the Soviet Union is precisely the kind of misguided propaganda which Dr. Comfort so rightly deplores.

Guy's Hospital,
London, S.E.1.

DAVID STAFFORD-CLARK.

SIR.—I wonder how many people really believe that the hydrogen bomb is a blessing in disguise, that it presents a compelling safeguard beneath a horrible threat? Politicians in plenty are expressing this curious idea, and Professor Haddow's appeal to a more enlightened section of society is amply justified on this ground alone. The potential blessing of so uncontrollable a weapon will surely escape the comprehension of men and women who have been nurtured on Christian ethics and Greek culture. The humanitarian professions, then, are armoured against such dangerous heresies; it is mainly from them that any resistance to a universal moral landslide must derive.

There must be many within medicine and its outlands who, having long held that the desperate state of human affairs has sprung from a lack of religious faith (Christianity in particular), now see a second cause—mental aberration. Dr. Comfort is one of a great company who hold this a very serious development. The priest and the psychiatrist must now work hand in hand for the healing of the nations. All who face the ideal of physical, mental, and spiritual health must find a new poignancy

in the situation, for today the power of a psychopath in a high place is such that he need ask no man's leave before he precipitates horrors.

There are millions of sane and charitable human beings whose endurance must outlast that of Damocles. Most of them are lonely and inarticulate; they derive new hope and vigour from any who will stand up and voice their fears for them, and convince them that their thoughts are in fact being broadcast and therefore not hopelessly drowned in the shouts of maniacs. There is some sort of moral obligation upon those professional men and women who believe that mankind must settle its disputes peacefully to express the goodwill and the moral scruples of the inarticulate, for theirs is the authority and the ability, by reason of the service they render to society. Only if such men and women accept this responsibility and act upon it, will there be mobilised a force capable of outlawing war itself and seizing, at this eleventh hour, our one chance of civilised survival.

Pharmaceutical Department,
Southmead Hospital,
Bristol.

PETER COOPER.

TUBERCULOSIS YARDSTICKS

SIR.—Dr. Stewart and Dr. van Zwanenberg, in their letter of April 17, have drawn attention to a difficult and topical problem—namely, the criteria which should now be adopted in assessing the "activity" of a case of pulmonary tuberculosis. They suggest that assessment must depend largely on the results of bacteriological examination, but they then proceed to produce some evidence which implies that bacteriology is no longer wholly reliable. We are certainly becoming increasingly familiar with the patient who presents the X-ray appearance of cavitation coupled with an impressive series of negative sputa, and as a result the *cachet* formerly conferred by the production of a negative culture or animal inoculation test has lost a little of its lustre. It is perhaps going too far to say that such desirable bacteriological findings can be produced at will by juggling about with the chemotherapy; but they can be influenced very appreciably, and consequently negative bacteriological findings should now be accepted with great reserve, unless the clinical and radiological evidence is completely in keeping.

In the official definition of quiescence pride of place is given to improvement in the patient's general condition, to the absence of toxæmia, and to negative sputum examinations, while the evidence provided by other clinical examinations and by serial radiographs brings up the rear. A readjustment of these criteria is overdue; and, while all the factors mentioned should continue to be given adequate consideration, increasing emphasis might with advantage be placed upon the radiological findings, including tomography, which at present appear to be the most reliable index of potential infectivity which we possess.

If the number of patients admitted to hospital for the treatment of pulmonary tuberculosis, who have received chemotherapy before any attempt has been made to confirm the diagnosis by sputum examination, can be accepted as a guide, then the popularity of bacteriological investigation has declined even further than many of us would have supposed.

Red Cross Sanatoria of Scotland,
Tor-na-Dee, Milltimber, Aberdeenshire.

R. Y. KEERS.

TUBERCULOSIS IN ADOLESCENCE

SIR.—Most of the measures Dr. Bentley suggests in his letter last week are, of course, long overdue, largely because the dangers of an unrecognised primary infection during puberty are not always appreciated, because the value of B.C.G. in preventing adolescent phthisis^{1,2} is

underrated, and because the relative rarity of the disease is allowed to conceal its importance. (In England and Wales 3–9% of children dying between the ages of 10 and 14 years do so as the result of respiratory tuberculosis.) Incidentally, the "inevitable deterioration" mentioned by Dr. Bentley is distressingly obvious in recorded experience of the disease: half the patients used to die within 2 years, and three-quarters within 5 years, of diagnosis.

The use of tuberculin testing before mass radiography is obviously rational, and probably economical. It should prevent the false sense of security sometimes engendered by a report that the chest radiograph is normal in a tuberculin-negative adolescent. The measures suggested (tuberculin testing, radiography, and vaccination) may be criticised as impracticable, uneconomical, and unnecessary. But they would certainly be more rewarding than, for example, the prolonged surveillance of healthy tuberculin-positive children between the ages of 5 and 10 years, still practised in many centres. Moreover, disease discovered at the asymptomatic stage is likely to be amenable to treatment within a reasonably short time, thus avoiding the expense of a long stay in hospital (providing too sanguine a view is not taken of minimal lesions³). Furthermore, the final years of school life are the last occasions when all the youth of the country is readily available for epidemiological study and the practice of preventive medicine on a large scale.

Dr. Bentley's suggestions should be implemented first in girls' schools, for phthisis is 3 times more common in girls than in boys between the ages of 13 and 15 years.⁴

In North-eastern England most children who develop this adult type of pulmonary tuberculosis are treated at one centre (Poole Hospital, near Middlesbrough). Here, as recommended by the National Association for the Prevention of Tuberculosis,⁵ the children's hospital is not isolated, but is an annexe of the main establishment, which is fully equipped for thoracic surgery. A recent survey⁶ of cases seen at this centre showed that early diagnosis and chemotherapy, combined with rational collapse and surgical procedures, have more than trebled the immediate expectation of life in childhood phthisis. But prevention is still far better than cure.

BISHOP AUCKLAND.

J. P. ANDERSON.

CANADIAN APPOINTMENTS

SIR.—Your issue of March 27 contains an advertisement for a consultant post in Canada at a salary of \$10,000 per annum. The notice indicates that this is approximately equivalent to £3700 sterling.

I feel strongly that prospective candidates for the post should be made aware that in terms of living standards \$10,000 is equivalent to nothing like that sum. The present rate of exchange (\$2.80 to the pound) is unrealistic; to provide a closer approximation to reality a figure in the region of \$5.00 should be cited. This post, which appears to be far more highly remunerated than one of equal status in England, is thus very much on the same level. \$10,000 will provide a reasonable standard of living, but it is far from wealth: radiologists in private practice in this country can make two to three times that figure and commonly do so.

This is not the first advertisement in *The Lancet* to mislead British doctors with ambitions to emigrate by proffering apparently generous salaries in terms of dollars; but I believe it is the first to translate dollars into pounds in this way.

3. Hyge, T. V. *Acta tuberc. scand.* 1949, 23, 153.

4. Anderson, J. P. *Ibid.* 1952, i, 876.

5. National Association for the Prevention of Tuberculosis. Design for Sanatoria. London, 1951.

6. Anderson, J. P. Phthisis in Childhood. M.D. thesis, University of Durham, 1953.

1. Hyge, T. V. *Acta tuberc. scand.* 1949, 23, 153.
2. Wallgren, A. *Tuberculosis and other Problems of Pediatrics.* Baltimore, 1950.

I would therefore urge, Sir, that some editing of Canadian advertisements be made, or that the large difference in the cost of living be drawn to the attention of applicants.

M.D.

Canada.

* * * A similar letter of warning about the cost of living in Canada appeared in our issue of Sept. 27, 1952 (p. 640).—Ed. L.

RHEUMATOID ARTHRITIS AND ALLERGY

SIR.—The inter-relationship of rheumatoid arthritis and various allergies has often been discussed, and any such claims have usually been rejected, as was the case of the statistical investigation by the Empire Rheumatism Council in 1950. The alternation, however, of various allergies, the duodenal syndrome, and psycho-neurotic states is, I believe, not uncommon.

In an examination of the case-histories of 1000 rheumatoid arthritics, 6 were found in whom the arthritis began at exactly the time that an asthmatic state disappeared. Unfortunately, not every patient was specifically questioned about the presence or absence of any asthmatic tendency, and therefore no data are available about the incidence of asthma in this series. The occurrence of 6 cases in which rheumatoid arthritis appeared to replace the asthmatic state is of interest and seems to merit further investigation by others when analysing future series of cases. We would be very grateful to hear from anyone interested in either the rheumatic diseases or psychosomatic and allergic conditions, whether their experience confirms or refutes this finding.

Rheumatism Research Unit of the
South West and Oxford Regions,
Royal National Hospital for
Rheumatic Diseases, Bath.

G. D. KERSLEY.

AVERTING POLIOMYELITIS

SIR.—Now that the threat of poliomyelitis is again upon us, may I, like Cromwell, beseech you, in the bowels of compassion, to think it possible that it may be averted?

These facts are authoritatively stated :

(1) "Poliomyelitis is an infection of the lining of the bowel, prone to pass more deeply into the body."¹

(2) "Infection is only occasionally manifested by nervous illness."²

(3) "There is now agreement that poliomyelitis is essentially spread by human contact and that stools form the main source of the virus."²

(4) "Human faeces are the most significant source of the virus; the period of communicability may extend for longer than a few days after onset; the mouth is the usual portal of entry."²

The secret of the control of poliomyelitis is to make sure that all who are at risk from contact with a known case, direct or remote, shall have clean fingers after emptying their bowels. Anyone with a lump of wet mud and a piece of toilet paper can demonstrate how toilet paper is permeable to moist faeces and must allow the fingers to be contaminated at defaecation. One way to keep the fingers clean is to substitute cotton-wool for toilet paper or to use toilet paper in three thicknesses. Another is to use an effective antiseptic. The virus of poliomyelitis "is readily destroyed by oxidising agents such as hydrogen peroxide and potassium permanganate,"³ and an ounce of permanganate crystals, costing 5d. will make fifty gallons of potent solution. I suggest that by the side of every school and public lavatory in a threatened area we should place permanganate solution in 3-lb. jam-jars. On the toilet paper should be printed some simple words such as these :

This district is threatened with the disease called poliomyelitis. The germ that causes this illness lives in the bowels

1. Burnet, F. M. *Brit. med. Bull.*, 1953, 9, no. 3.

2. Rhodes, A. J. *Ibid.*

3. MacCallum, F. O. *In Viruses and Rickettsial Diseases*. London, 1950.

of ordinary men, women, and children, but only a few of them become ill. These germs are so small that they can easily get through a piece of toilet paper, so use it in three thicknesses. Then dip your hands in the jar of red water by the lavatory seat for a few moments. Then with wet hands pull the chain and open the door, and go and wash them thoroughly.

The matter could be made an interesting subject for science lectures in schools. Science masters and mistresses and their pupils should undertake the meticulous management of school lavatories; there is nothing degrading in fighting the causes of death and crippledness, and there need be as little sentiment on this subject as there is on any other part of the sewage system. Above all there should be the enthusiasm of a campaign—a campaign for a season, against a known enemy and with clearly defined methods of confining it.

In the broad stream of infection by poliomyelitis few are stricken: if we narrow the stream, fewer will be stricken; in the presence of a virulent strain this narrowing is a matter of grave urgency.

Beckley, Rye.

C. G. LEAROYD.

TREATMENT OF VARICOSE ULCERS

SIR.—I agree with Dr. Rivlin (April 17) that the key to success in healing gravitational ulcers is adequate elastic support, but the elastic support need not be maintained by an adhesive bandage. Over ten years ago, woven elastic web bandages were introduced in our department by my colleague, Dr. H. R. Vickers, and we have found that they have all the advantages of an elastic adhesive bandage with none of the disadvantages of skin sensitisation or the sweat-retention syndrome.

The bandages are put on like a puttee from toes to calf; they have the advantage over elastic stockings that at the part where most support is needed, around the malleoli, extra turns of bandage can be applied if necessary, and any form of dressing can be used on the ulcer area.

One important feature is that most patients will continue to wear the bandages after the ulcer has healed. They come to look on them as a talisman which keeps the ulcers away, and the relapse-rate is considerably cut down.

I have never been able to discover why these bandages have not been used more generally in this country.

Rupert Hallam Department of
Dermatology, Sheffield.

I. B. SNEDDON.

SIR.—May I reply to the letter from Mr. Murley (April 10)? In doing so, I shall be replying too to Mr. Roland Jones and Dr. Rivlin (April 17) and Mr. Rowden Foote (April 24).

Firstly, there is the question of arterial spasm accompanying a deep thrombosis. I believe that arterial spasm does occur in deep thrombosis, and my belief is based on clinical observation.

I have observed that, in many patients giving a history of deep thrombosis from whatever cause, the toes are often cold and blue, indicating diminished blood-flow to the periphery. I have also found that there is very often a poor femoral pulse, and in some cases no pulse at all. Furthermore, I have sometimes been unable to introduce a fine needle into the artery, when attempting to inject tolazoline ('Priscol'), because the vessel was too small. Again, to prove that arterial spasm does exist, I have performed a clinical test in many cases. A skin thermometer is applied to the thigh and another to the dorsum of the foot; and the intra-arterial injection of tolazoline is then given. In nearly all cases the thermometer on the thigh shows a rise in temperature, and a great many show a rise in temperature in the foot as well.

The second point Mr. Murley raises is the question of lumbar sympathectomy for varicose ulcers. I myself have never done this operation for varicose ulcers, and in my letter of April 3 I do mention that, in the often

fat and flabby patient who has a varicose ulcer, a lumbar sympathectomy would not be without its risk. But lumbar sympathectomy does (and Mr. Murley will, I am sure, agree with me) raise the temperature of the limb. The first answer I get from a patient who has had a successful lumbar sympathectomy always confirms that the limb feels warmer. It is also taught that sympathectomy has its maximum effect in dilating the skin vessels as opposed to the vessels of the muscles and other deeper structures. Surely an increase of skin blood-flow will promote healing of skin ulcers? Tolazoline will temporarily have the same effect as a lumbar sympathectomy.

Mr. Murley's third point is the question of pain in leg ulcers. I have observed that in many women the pain is worse before ulceration has occurred. The pre-ulcerated leg feels hard and brawny in its lower third, and sometimes the pain is so severe that the patient is reluctant to let anyone touch the leg. In contrast to these painful brawny legs ("inverted Guinness-bottle legs") there are those with considerable ulceration where pain is slight or even absent. Surely it is the strangulation of the leg inside the resistant skin which is giving rise to this dreadful pain.

Finally, I would like to say something about skin-grafting of ulcers. One has to be guarded in saying how long a graft will last, for many do break down sooner or later. The darn graft which I have mentioned elsewhere, and which I believe originates from an idea of Mr. Dickson Wright, has a place in the treatment of varicose ulcers. Its main use is in those ulcers which are wide in area and which are not punched out. The punched-out ulcer, on the other hand, is more difficult to heal, and should respond better to hyaluronidase plus injections into the femoral artery. I must make it clear that I advocate this treatment only when compression bandaging is not having the desired effect. As I said in my letter, firm bandaging still remains the basis of all treatments, and it is when healing is slow or non-existent that I advocate these extra measures.

London, W.1.

MAURICE LEE.

SPONDYLOPSIS

SIR.—In his Heberden oration, published in your issue of April 3, Sir Russell Brain has given a brilliant exposition of disc lesions at the different spinal levels. He draws particular attention to the dural root-pouch—an important structure in explaining symptoms. Clinical grounds had enabled the presence of this pouch to be inferred¹ and the deduction drawn² that at lower lumbar levels the investment is not less than an inch long.

Sir Russell points out that disc lesions give rise to pain that appears to follow the myotome rather than the dermatome, but this is not the full explanation. Dural reference is often entirely extrasegmental and, when pressure is exerted on the dura mater, the symptoms often spread far beyond any relevant myotome. Thus, an early cervical disc lesion at any level may give rise to pain spreading to the head (C1-2 dermatomes) no less than to the scapular area (T3-6 dermatomes). Similarly, the pain arising from the dura mater³ in lumbago caused by, say, a 5th lumbar disc lesion, often reaches to the mid-thorax posteriorly, or to the abdomen, or to the groins, or to the coccyx, or to any aspect of the lower limbs. This represents reference far beyond both dermatome and myotome.

When the protrusion moves a little to one side, the dural investment of the nerve-root comes to be compressed. Now segmental reference appears, occupying

the myotome proximally and the dermatome distally. By contrast, impingement on a nerve-trunk seldom gives rise to any local symptoms at all. Constant pressure leads to a painless paresis; intermittent pressure to distal paraesthesiae (most severe during a period of recovery), in due course followed sometimes by vague aching in the affected limb.

This difference in the order in which symptoms appear provides a useful pointer in diagnosis; for pressure on dura mater and then nerve-root leads to pain in the trunk (though often in the "wrong" place), later spreading to the limb, whereas local discomfort is absent when a nerve-trunk is compressed.

The practical lesson to be drawn from Sir Russell's research on cervical myelopathy is that cervical and thoracic disc lesions are potentially dangerous. Hitherto it has been the practice to leave early protrusions to themselves, to get larger or smaller as fortune dictates. If, however (as has been the practice at St. Thomas's Hospital in our department for the last ten years), all cervical and thoracic disc lesions are reduced early on—when reduction is easy—the posterior longitudinal ligament escapes prolonged stretching and the likelihood of eventual myelopathy will clearly be diminished. Careful manipulation without anaesthesia during traction scarcely ever fails when the protrusion is small and recent, and it now appears to be not merely the useful pain-relieving measure I have so far regarded it as, but of far greater importance in the prophylaxis of eventual crippledom. Happily, therefore, Sir Russell's research points to an immediate therapeutic application.

London, W.1.

JAMES CYRIAX.

CLINICAL TESTS FOR KETONURIA

SIR.—The article by Dr. Nash and his colleagues in your issue of April 17 cannot be allowed to pass without comment. They describe the advantages of a tablet test for ketone bodies in the urine, and this is a praiseworthy contribution to chemical pathology. But they think it necessary to introduce a contrast by decrying the ways of discovering ketonuria used hitherto.

They state that there is uncertainty as to whether the colour given by the nitroprusside reaction is due to acetone or due to aceto-acetic acid. It has, in fact, been known for many years that the colour in the test is given by both compounds, but that the sensitivity of the test was such that it gave stronger reactions with aceto-acetic acid. Hurtley gave an elaborate account of the tests for acetone and aceto-acetic acid in *The Lancet* in 1913.¹ He pointed out that the Rothera test was about 20 times more delicate for aceto-acetic acid than acetone. Cole,² in the 5th edition of his book on *Practical Physiological Chemistry*, states that acetone can be detected at 1 : 20,000 and aceto-acetic acid at 1 : 400,000.

The authors find that the Rothera test is too sensitive. Kennaway showed in 1913³ that the speed of colour development depended on the aceto-acetic acid concentration. If this was 1 part in 200,000, the pink colour did not appear for some minutes. Ever since, it has been accepted that what Kennaway called the "slow-weak" reaction (i.e., when the colour does not appear for some minutes) was of no clinical importance.

The statement that Harrison⁴ does not "indicate that the urine must be saturated with ammonium sulphate to give the maximal sensitivity" is incorrect. He explicitly writes: "Saturation with ammonium sulphate removes interfering substances making the test more delicate."

Dr. Nash and his colleagues say that few textbooks adequately describe the details of Gerhardt's test: in fact, Harrison's textbook,⁴ which is only one among many, states the exact strength of ferric chloride to be added in the test—namely, 10%—and the quantity is described as "sufficient

1. Hurtley, W. H. *Lancet*, 1913, i, 1160.

2. Cole, S. W. *Practical Physiological Chemistry*. Cambridge, 1919.

3. Kennaway, E. L. *Guy's Hosp. Rep.* 1913, 67, 161.

4. Harrison, G. A. *Chemical Methods in Clinical Medicine*. London, 1947.

1. Cyriax, J. *St. Thom. Hosp. Rep.* 1949, 5, 68.

2. Cyriax, J. *Orthop. Med.* 1954, 1, 382.

3. Cyriax, J. *Lancet*, 1945, ii, 426.

drops to be added to completely precipitate the phosphates." It is well known that any excess of ferric chloride is liable to render the test insensitive. In the same textbook it is said that boiling is to be *thorough* (italics by Harrison), and it is specifically stated that it should be done in a boiling-tube or open vessel. If the writers are correct (and we are prepared to doubt this) that the boiling is usually done only momentarily in a narrow test-tube, this would be quite contrary to the established descriptions of the technique. A recent article⁵ goes as far as emphasising the need for prolonged boiling by prescribing a 50% evaporation.

We are looking forward with interest to the advantages of the tablets described, but we maintain that the present tests for ketonuria are effective, and also that, as far as we know, they are adequately performed throughout the country. The tablet test appears to be in fact a "dehydrated," slightly less sensitive Rothera test. If this was so, it would have no advantages in the laboratory but might be found to be convenient in the consulting-room.

Department of Pathology,
St. Bartholomew's Hospital,
London, E.C.1.

H. E. ARCHER
H. LEHMANN.

SIR.—In an otherwise excellent and informative article Dr. Nash and his colleagues seem to have overlooked a simple expedient for reducing the sensitivity of Rothera's test—namely, dilution. A 1 in 5 dilution of urine brings the test into the desired range of sensitivity and, for students, perhaps this is a useful manoeuvre. In practice, however, the rate of colour development is a sufficiently reliable index for the experienced.

Secondly, no mention is made of the use of a crystal of sodium nitroprusside, which, as far as I know, is reliable, is certainly simpler, and probably saves several seconds.

Department of Clinical Pathology,
St. Thomas's Hospital,
London, S.E.1.

H. E. M. KAY.

PRESCRIBING AUREOMYCIN

SIR.—I wonder how many of your readers in hospital practice know that aureomycin cannot be prescribed by the general practitioner except by a very devious route—a restriction which applies neither to erythromycin nor to chloramphenicol. The effect can only be to further the use of an antibiotic known to be associated in some cases with the development of blood dyscrasias,⁶ where antibiotics carrying no such risk are equally effective. The continued existence of this regulation is a matter of grave concern.

Wallington, Surrey.

H. BARRIE.

NURSING BY THE MOTHER

SIR.—Dr. Lowenfeld, in her letter of April 10, urges the need for fresh and creative thinking on the treatment of sick children in hospital. The Nuffield Provincial Hospitals Trust shares this view and has, in fact, initiated a study on the care of children in hospital. This study will be made on behalf of the Trust by the Nuffield Foundation's Division for Architectural Studies, the establishment of which was announced in your issue of Feb. 6 (p. 319).

This study of the child in hospital will follow the lines established by the Trust's investigation into the functions and design of general hospitals. These were similar to those suggested by Dr. Lowenfeld—that is, preliminary research by a team of people with appropriate experience, followed by experimental building to test and demonstrate the conclusions. It is hoped that work on this project will begin in the autumn of the present year.

L. FARRER-BROWN
London, N.W.1.

Director of the Nuffield Foundation.

5. Archer, H. E. *Brit. med. J.* 1953, ii, 1211.
6. Hodgkinson, R. *Lancet*, Feb. 6, 1954, p. 285.

Obituary

WILLIAM HENRY SNYDER NICKERSON
V.C., C.B., C.M.G., M.B. Manc., D.P.H.

Major-General W. H. S. Nickerson, a former director of Army Medical Services in India and one of the distinguished band of medical holders of the Victoria Cross, died at his home at Kintyre, Argyllshire, on April 10.

He was born at New Brunswick, Canada, in 1875, the son of the Rev. D. Nickerson. He came to this country to go to school at Portsmouth Grammar School, and to study medicine at the Victoria University of Manchester, where he graduated M.B. in 1896. Two years later he joined the R.A.M.C., and he served in South Africa from 1899 to 1902. He was repeatedly brought to notice for good work done under fire in the battle of Stormberg and elsewhere, and in 1900 he was awarded the V.C. and promoted captain. The following citation describing the award appeared in the *London Gazette*:

"At Wakkerstroom on the evening of 20 April 1900 during the advance of the infantry to support the mounted troops, Lieut. Nickerson went in a most gallant manner, under a heavy shell and rifle fire, to attend a wounded man, dressed his wounds, and remained with him until he had him conveyed to a place of safety."

In 1909 he received his majority, and during the 1914–18 war he served at first in France, taking part in the retreat from Antwerp and in the battles of Ypres, Neuve Chapelle, and the Somme. In 1915 he was transferred to Salonika and later he served with the Egyptian Expeditionary Force as D.D.M.S. For his war services he was appointed C.M.G. in 1916, and C.B. in 1919. He also received the Greek Medal for Military Merit.

His promotion had been rapid, and he attained the rank of major-general in 1925 at so early an age that he was allowed to postpone his retirement for four years, during which he served as director of medical services in India. When he retired in 1933 he was made colonel commandant of the R.A.M.C., an office which he held till 1945. During the late war he was medical officer to an Atlantic convoy, to the Port of London Authority River Emergency Service, and with the Home Guard.

A colleague writes: "It was most fortunate that Nickerson was appointed director of medical services of the Army in India when he was, because it was largely due to his influence that exceptionally cordial relations were established between the civil and military medical services. But for this it would not have been possible to offer so effective a resistance to the attack made on both services by the retrenchment committee set up to cope with the severe financial crisis which occurred during these years. Insidious attempts were made to encourage and exploit conflicts of interests between the two medical administrations, both of which owe a great debt of gratitude to Nickerson for the part he played in their united defence of the policy of maintaining an adequate reserve of medical officers in India. Like the other medical friends of mine who have won the V.C., he was modest and unassuming, and utterly incapable of harbouring unworthy feelings of personal vanity. His selection on his retirement for the coveted distinction of colonel commandant of the R.A.M.C. reflected the affectionate esteem in which he was held by his fellow officers, and indeed by everyone who knew him well."

Major-General Nickerson married in 1919 Miss Nan Waller, who survives him with a son and daughter.

HAROLD PARNELL JAMESON
M.D., B.Sc. Birm., M.R.C.P.

Dr. H. P. Jameson, consulting physician in geriatrics to St. Albans City Hospital, died on March 31 at the age of 50.

In 1925 he graduated M.B. with first-class honours at Birmingham University, and after holding house-appointments at the General Hospital and Children's Hospital in Birmingham he moved to London, where he worked under Sir Robert Hutchison at the London Hospital and at Great Ormond Street. In 1928 he proceeded to the degree of M.D., choosing as the subject of his thesis the Remote Prognosis of Pneumonia in Childhood.

In 1929 he settled in practice at St. Albans with Dr. J. W. Hope Simpson, largely because of the opportunity for paediatric work offered by the children's beds at St. Albans City (then Osterhills) Hospital. He had full clinical charge of these beds for ten years, and the new children's block was built under his direction.

For many years he was medical officer to the Honourable Artillery Company, and a week before the outbreak of the 1939–45 war he was called up. He served in India, Teheran, and Ceylon. With the rank of lieut.-colonel he was officer-in-charge of the medical divisions of Indian and British hospitals and consultant to a wide area.

After the war he returned to St. Albans, but shortly afterwards gave up his practice to take up his post as consultant in geriatrics at the St. Albans City and Hitchin Group of hospitals. He was a foundation member, and for the past year secretary, of the Medical Society for the Care of the Elderly.

An enthusiastic sportsman, Dr. Jameson was a keen and expert rider and he supported the Aldenham Harriers Hunt for over 20 years. He was medical officer to their point-to-point races, and to those of the Hertfordshire Hunt at Friar's Wash. Rock-climbing and mountaineering fascinated him, and only ten days before his death he had been rock-climbing in Wales with his eldest son. He was also a keen tennis player.

E. D. H. C. writes: "Jameson brought to his post as consultant physician in geriatrics at St. Albans and at Hitchin a definite and lively personality and outstanding organising ability. He had real sympathy for the needs of the sick, and I know that the general practitioners of the neighbourhood will feel the poorer for the loss of such a 'whole man' at such an early age."

In 1932 he married Joan Isabel Colthurst, who survives him with a daughter and two sons, the elder of whom is a medical student.

MATTHEW H. LOGG

M.D. Aberd.

Dr. M. H. Logg, senior physician and medical administrator of Grove Park Hospital, London, died on April 20 at the age of 56.

After graduating in 1921 at the university of his native city of Aberdeen, he became a house-physician at the Aberdeen Royal Infirmary, and in 1923 he proceeded to the degree of M.D. He came to London to specialise in tuberculosis work, and after holding a house-appointment at the Brompton Hospital he entered the service of the old Metropolitan Asylums Board at Colindale Hospital. In 1926 he was appointed to Grove Park.

His long tenure of office there was, in microcosm, the history of the tuberculosis service in London, to which he gave so much of his energies. He was particularly interested in the problem of pregnancy in the tuberculous patient. He contributed to many discussions on this topic, particularly at the British Tuberculosis Association, of which he was a founder-member; and he published a review of the subject in the *N.A.P.T. Bulletin* in 1946. His other writings included papers in our own columns on the use of para-aminosalicylic acid in pulmonary tuberculosis.

Dr. Logg leaves a widow.

Appointments

- BARRETT, AILEEN V., M.B., B.Sc. Glasg., D.O.B.S.T.:** asst. M.O., area No. 4, Middlesex.
FISHER, DOREEN M., M.B.: asst. county M.O. and school M.O., West Riding of Yorkshire (Batley and Heckmondwike).
FITZPATRICK, R. H. P., M.R.C.S., D.A.: consultant anaesthetist, Sidcup and Swanley H.M.C. group.
FLINT, F. J., M.A., D.M. Oxf., M.R.C.P.: consultant physician, Sheffield No. 1 H.M.C. group.
FRY, E. N. S., M.B. Edin., D.A.: consultant anaesthetist, Tees-side H.M.C. group.
HAGAN, J. G., M.B.N.U.I., D.P.H.: deputy M.O.H. and deputy principal school M.O., Northampton county borough.
HICKEY, J. B., M.B.N.U.I.: registrar in ophthalmology, Norfolk and Norwich Hospital.
JOHNSTON, N. G., M.B. St. And., D.A.: consultant anaesthetist, W. Durham H.M.C., Bishop Auckland General Hospital.
KOTOWSKI, JAROSLAW, M.B. Polish School of Medicine, Edinburgh: senior casualty officer, Barry Accident Hospital.
MACGILLIVRAY, R. C., M.B. Edin., F.R.F.P.S., D.P.M.: consultant psychiatrist, Little Plumstead Hospital.
SANDFORD, F. M., M.R.C.S., D.A.: consultant anaesthetist, Dartford H.M.C. group.
ZABORSKI, EDWARD, M.D. Warsaw: asst. orthopaedic surgeon, London Road Hospital, Boston.

Diary of the Week

MAY 2 TO MAY 8

Monday, 3rd

- POSTGRADUATE MEDICAL SCHOOL OF LONDON**, Ducane Road, W.12
 4 p.m. Dr. Edwin Clarke: Cervical Spondylosis with Cord Compression.
INSTITUTE OF CARDIOLOGY, National Heart Hospital, Westmoreland Street, W.1
 9.30 a.m. Dr. K. W. Donald: Exercise in Heart-disease.
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children, Great Ormond Street, W.C.1
 5 p.m. Prof. G. Frontali (Rome): Proteins in Child Nutrition.
INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1
 5 p.m. Prof. Klaus Conrad (Homburg-Saar): New Problems of Aphasia.

Tuesday, 4th

- ROYAL COLLEGE OF SURGEONS**, Lincoln's Inn Fields, W.C.2
 3.45 p.m. Prof. M. F. Lucas Keene: Development of the Pharynx. (Arnott demonstration.)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
 5.30 p.m. Dr. E. J. Moynahan: Urticaria.
INSTITUTE OF NEUROLOGY
 5 p.m. Dr. I. Wickbom (Sweden): Choice of Encephalography or Ventriculography for Examination of Intracranial Tumours.
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
 5 p.m. Sir Wilfred Fish: Dental Research in the Inoculation Department.

Wednesday, 5th

- POSTGRADUATE MEDICAL SCHOOL OF LONDON**
 2 p.m. Dr. Martin Bodian: Hirschsprung's Disease and Chronic Constipation in Childhood.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
 5.15 p.m. Section of History of Medicine. Sir Charles Dodds, F.R.S.: Christopher Merritt (1614–1695), First Harveian Librarian. Mr. J. B. Oldham: Two Eighteenth-century Liverpool Surgeons—Park and Alanson.
INSTITUTE OF DERMATOLOGY
 5.30 p.m. Dr. H. Haber: Lichen Planus and Lichenoid Eruptions.
MANCHESTER MEDICAL SOCIETY
 4.15 p.m. (Medical School, University of Manchester.) Sir Heneage Ogilvie: Future of Surgery.
UNIVERSITY OF EDINBURGH
 5 p.m. (University New Buildings, Teviot Place.) Prof. Henry K. Beecher (Harvard): Resuscitation and other Early Care of the Severely Wounded Man. (MacArthur lecture.)
MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
 8.30 p.m. (18, Nicolson Street, Edinburgh.) Dr. A. G. Cruikshank Prescribing in General Practice.

Thursday, 6th

- ROYAL COLLEGE OF SURGEONS**
 3.45 p.m. Prof. G. W. Causey: Sterno-mastoid Muscle. (Arnott demonstration.)
 5.30 p.m. Prof. G. A. G. Mitchell: Sympathetic Nervous System in Relation to Throat, Nose, and Ear.
INSTITUTE OF CARDIOLOGY
 9.30 a.m. Dr. Maurice Sokolow (California): Quinidine Therapy.
UNIVERSITY OF EDINBURGH
 5 p.m. Prof. Gerhard Domagk (Wuppertal-Elberfeld): Chemotherapy in Tuberculosis.

Friday, 7th

- POSTGRADUATE MEDICAL SCHOOL OF LONDON**
 2 p.m. Mr. E. T. C. Milligan: Surgery of Anal Canal and Fistula-in-ano.
 4 p.m. Dr. Henry Miller: Allergic Disorders of Nervous System.
ROYAL SOCIETY OF MEDICINE
 10.30 a.m. Section of Otology. Dr. J. C. Seymour: Circulation of Cochlea. Wing-Commander P. F. King: Psychogenic Deafness.
 2.30 p.m. Section of Laryngology. Mr. Dudley Ashcroft, Dr. A. L. Peeney: Management of Haemorrhage after Tonsillectomy.
 5.30 p.m. Section of Anaesthetics. Dr. J. J. Bonica (Washington): Role of Anaesthetist in Management of Intractable Pain. Dr. E. H. Seward: Wasp Venoms and Anaesthesia.
INSTITUTE OF DERMATOLOGY
 5.30 p.m. Dr. M. S. Thomson: Lichen Planus.

Saturday, 8th

- SOUTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY**
 11 a.m. (Preston Hall, Maidstone, Kent.) Dr. A. Stocker (Illinois): Preferences in Surgery for Tuberculosis.
MIDLAND TUBERCULOSIS SOCIETY
 11 a.m. (Cheshire Joint Sanatorium, Loggerheads, Market Drayton, Salop.) (Joint meeting with North-Western Tuberculosis Society.) Dr. E. Snell, Dr. R. Walshaw, Dr. L. A. McDowell, Dr. George Luntz: What is the Place, if any, of Mass Radiography.
 2.15 p.m. Dr. Clark Penman, Dr. T. W. Lloyd, Dr. G. S. Erwin, Dr. V. Cotton Cornwall: Analysis of Place of Artificial Pneumothorax in Treatment of Pulmonary Tuberculosis.

Births, Marriages, and Deaths

MARRIAGES

- ZEITLINE—ROBERTS.**—On April 2, at the Paddington Registry Office, Dr. L. L. B. Zeitline, of 16, Norfolk Place, Hyde Park, W.2, and Miss Jane Roberts, of 30A, Sussex Place, Hyde Park, W.2.

Notes and News

EMPIRE RHEUMATISM COUNCIL

In his report to the annual meeting of the Empire Rheumatism Council on April 28, Dr. W. S. C. Copeman, the chairman, paid tribute to the work of his predecessor, Lord Horder, who had held office since the inception of the Council in 1936. During the year a chair of rheumatology, the first of its kind in the Commonwealth, had been founded by the Council at Manchester University; and Dr. J. H. Kellgren had been appointed to this chair. In May, 1953, a medical deputation had been sent to the Minister of Health, in order to obtain a statement of future policy, and to secure Ministerial recognition of rheumatology as a specialty within general medicine.

Research activities continued to absorb the major part of the Council's slender financial resources. Work by Mr. A. A. Henly, Ph.D., at the Hospital of St. John and St. Elizabeth, London, suggested that in rheumatoid arthritis such changes in steroid metabolism as were found resulted from metabolic abnormalities associated with the disease process, and that primary adrenal dysfunction was not a causative factor in its development. Among other research projects one on the long-term treatment of rheumatoid arthritis, carried out by Dr. J. M. Tweed at the West London Hospital, was made possible by a Philip Gray fellowship founded by the Shell Petroleum Company. Two E.R.C. fellowships for specific researches had been awarded. One fellow, Dr. J. K. Norymberski, working at the chemical research laboratory of the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases, had developed an analytical method for the simultaneous determination of formaldehydogenic and 17-ketogenic steroids, and a routine procedure for the estimation of the latter in urine.

The financial report reveals a total income in 1952-53 of £10,019 (exclusive of legacies), compared with £13,453 in the previous year. Medical expenditure was £8127, compared with £7220 in the previous year.

University of London

Dr. J. W. Landells, senior lecturer in pathology at London Hospital Medical College, has been appointed to the university readership in morbid anatomy at the college.

On March 24 the degree of M.D. was awarded to B. W. Lacey.

Ciba Foundation

Sir Macfarlane Burnet, F.R.S., director of the Walter and Eliza Hall Institute of Medical Research at Melbourne, will deliver a lecture at 5 p.m. on Tuesday, May 11, at 26, Portland Place, London, W.1, on the Problem of Virulence in Virus Disease.

Medical Women's Federation

The annual general meeting of this federation will be held on Thursday, May 6, at 8.15 p.m., at the Grand Hotel, Sheffield, when Dr. Annis Gillie will give a presidential address on Motive and Momentum.

Tribute to Dr. Thomas Anderson

A company of fifty attended a dinner held at Ruchill Fever Hospital, Glasgow, on April 20, to celebrate the 25th anniversary of the date when Dr. Thomas Anderson, now reader in infectious diseases in the university, joined the staff of Ruchill Sanatorium. Dr. James Lawson, medical superintendent of the hospital, presided. Prof. James Howie, proposing Dr. Anderson's health, remarked that his "powerful and successful resolve to upgrade the practice of infectious diseases was and is one of the real attractions of being a bacteriologist in the city of Glasgow." Professor Howie continued:

"Sometimes people say: 'Where are the great characters now?' The answer is that they have a different and a more difficult function to perform. Many of the great characters of the past were great dictators. Nowadays dictators are out of fashion. A great dictator in British medicine today would achieve only a great fall. Great achievement is harder today; it requires the patient man, the man who is able to sense the pace at which he can work the complex, still imperfect, still new, machinery of the health service. Our Dr. Anderson is one of these. His objectives are right, his ideals are high and unselfish, and he has a limitless capacity to hold on and to pull long and steadily in the right direction. Such qualities are less obvious and less spectacular than the fireworks of a great dictator. But the results may well prove to be equally valuable and perhaps of longer duration."

Gifts were presented to Dr. Anderson and to Mrs. Anderson, whose health was proposed by Dr. Peter McKenzie.

Royal College of Obstetricians and Gynaecologists

At a recent examination for the diploma in obstetrics the following were successful:

Pauline A. Adams, D. A. Aiken, D. J. M. Allan, N. J. W. Allan, G. A. Ames, W. M. Anderson, Liselotte Asch, Swayamprabha Bajpal, G. S. Banwell, D. W. Barnes, Rosalind A. Barnes, Margaret N. Barr, Mary M. Baxter, Jean M. Beecroft, Elspeth V. Beveridge, J. C. H. Bird, W. P. Black, A. S. Blake, Richard Blight, M. L. Bloom, F. P. Brown, J. W. Browning, Hilda M. Brunt, Marjory M. Buchanan, A. M. Burnford, Nancy I. Cardno, Kim Choy Chong, Marjorie Coates, Arnold Cohen, T. I. Cope, C. E. Cosgrove, Mary G. Coyle, Audrey N. Crocker, Kusum Amerchand Dalal, Charles Dansie, Alan Davies, Jean M. Davies, J. I. W. Davies, Joan V. Davis, G. B. Davison, V. E. Dean, J. Y. N. Devine, J. Y. J. Devine, R. D. P. Druitt, Bernard Dudley, Domnall Duffin, John Dunlop, C. P. Evans, Elliott-Binns, J. J. Enright, D. L. Evans, Mary E. L. Evans, Jeannette G. Eveson, M. A. Fenton, Isabella C. Ferguson, Jack Fine, Alison M. Fleming, Margaret B. Fox, Mary U. Franklin-Evans, J. A. Girling, Ivan Goldman, J. H. Goode, P. M. Goodrich, P. D. Grant, Elizabeth D. Grassie, Hilary A. Hagan, Elizabeth M. Haines, C. J. J. Herlihy, K. M. Hewitt, Frances M. Hill, Sheila H. Hoey, Catharine E. Hollman, J. M. H. Hopper, John Houston, Edmund Howarth, T. M. Howell, D. C. Hudson, Doreen R. Hyder, Sylvia R. Ingold, Harry Jackson, R. F. Jackson, Lelia Jennings, I. M. Johnstone, Karthigesu Kanagasingam, D. P. J. Kelleher, E. I. Kohorn, Koussa Tadros Koussa, S. R. S. Laing, J. S. P. Lane, June P. Lawson, W. R. Lee, P. A. Lowe, Gwladys N. McCoach, J. Q. McCubbin, Jill MacDonald, Margaret R. MacD. McGilvray, Catriona D. McLeod, R. N. Lalins, C. F. R. Mallett, G. C. Mansfield, John Manuel, Patricia L. Martin, C. J. G. Menzies, Barbara I. Miller, J. S. M. Mitchelson, I. A. Moellan, Donald A. Morgan, Mavis H. Mortimer, A. L. I. Murphy, Rathindra Nath Nag, T. M. O'Brien, J. F. O'Kelly, E. G. Old, Chiew Seng Oon, Elspeth M. Orr, Margaret O'Sullivan, D. N. H. Owen, N. S. Painter, C. E. Parr, K. C. Parsons, Diana Patuck, Harrigar J. B. Pershad, William Peter, C. D. Peters, P. B. Poole, Sylvia E. Proble, J. F. Prece, W. E. B. Preston, D. S. Racliffe, T. F. Regan, Jean E. Ritchie, Kathleen M. Robb, T. E. Roberts, K. F. Robinson, Patricia M. Russell, Iqbal Sahney, J. F. Scarlett, Roy Schofield, Albert Schutz, F. G. M. Seager, Janet Shaw, R. G. Sinclair, G. D. Smellie, Janet U. A. Smith, S. A. Smith, Carol M. S. Spence, T. J. Stanton, Mary J. Starbuck, J. K. Steel, Michael Steele, D. H. Stewart, I. A. Stewart, W. M. B. Struteways, Mary W. Sturges, J. S. V. Surman, Muriel M. H. Sutcliffe, W. R. Swaffield, G. S. Tapsall, M. K. Thompson, N. A. Toes, Dorothy I. Troup, A. G. Turner, Sam Vakil, M. H. Vickery, J. do M. Vink, P. O. Wakelin, Phyllis M. Wallington, D. G. Walker, A. G. Wallace, I. H. Watson, Josephine P. Werren, Susanne M. Williams, A. C. Wilson, D. G. Wilson, G. C. Winch, Hazel G. Wiseman, K. A. Wood, D. W. B. Woolven, E. G. B. Worthington, A. P. Wright, M. A. Young.

Radcliffe Infirmary

Lord Nuffield has given £15,000 to provide an operating theatre for the Nuffield professor of surgery.

Poliomyelitis Vaccine

The National Foundation for Infantile Paralysis has given its approval for the start of the poliomyelitis vaccine trial in the U.S.A. (*Times*, April 27). The first inoculations were given to children in Virginia and Alabama on April 26.

Welfare of Handicapped Children

The National Committee for the Defence of Children is holding a conference on this subject at Church House, Westminster, on Saturday, May 8, at 2.30 p.m. Further information may be had from the secretary of the committee, Dr. Simon Yudkin, 23, Tillingbourne Gardens, London, N.3.

Varrier-Jones Lecture

Dr. Harold G. Trimble, associate professor of clinical medicine at Stanford University, California, will give this lecture at 26, Portland Place, London, W.1, on Friday, May 14, at 5 p.m. He has chosen as his subject Current Therapy in Pulmonary Tuberculosis.

Lebanon Hospital for Mental and Nervous Disorders

The annual meeting of this hospital will be held on Friday, May 7, at 5 p.m., at the Cora Hotel, Upper Woburn Place, London, W.C.1. The speakers will include Prof. Alexander Kennedy, F.R.C.P., and Dr. Alfred Torrie.

Rockefeller Grants

The grants to British organisations announced this week by the Rockefeller Foundation of New York include one of \$125,000 to the Medical Research Council for fellowships in the medical sciences. This grant assures the continuance of the M.R.C.'s programme for travelling postgraduate fellowships until 1959.

The Fever Nurse

The general-trained nurse is allowed to take her training to qualify as a fever nurse in one year instead of the usual two years. Her training allowance has been amended (N.M.C. circular no. 36), and in future she will receive for the year £335 (the usual second-year allowance) instead of £320 (the first-year allowance).

Dr. Dennis Geffen is visiting Greece, Cyprus, and Turkey on behalf of the British Council.

ARTIFICIAL RESPIRATION BY INTERMITTENT POSITIVE PRESSURE IN POLIOMYELITIS AND OTHER DISEASES

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NEUROLOGIST

RADCLIFFE INFIRMARY, OXFORD

THE commonest cause of death from poliomyelitis is respiratory insufficiency. This may be due to spinal paralysis affecting the primary muscles of respiration directly, and it is in such cases that tank respirators have proved of value. In other cases "bulbar" involvement leads to paralysis of the pharynx and larynx, and there is then grave danger of pharyngeal secretions or vomit being inhaled, and causing fatal pulmonary complications. In this type of case the skilled use of postural drainage often enables unobstructed breathing to be maintained (Russell 1952).

By far the most difficult and critical problem in management is presented by the "combined case," in which the paralysis is both bulbar and spinal. Some form of artificial respiration is then essential; yet, in spite of postural drainage, the uncompromising inspiratory effort of a tank respirator leads, in the absence of the power of swallowing, to inhalation of secretions and a fatal result. In some American clinics such patients have been nursed in tank respirators, with a tracheotomy; but this method involves great difficulties, notably in establishing an airtight seal at the neck without interfering with the tracheotomy.

Recently we have treated patients with combined bulbospinal paralysis by artificial respiration with intermittent positive pressure (I.P.P.), a method used by Lassen (1953) during the severe epidemic in Denmark in 1952. This method has great advantages, and we describe here how four patients were treated in a small Respiratory Unit established at Oxford to deal with cases of respiratory insufficiency. Not only cases of poliomyelitis but also cases of acute toxic polyneuritis were treated, and the unit has indeed been available for the treatment of respiratory insufficiency from any cause—e.g., after head injury or neurosurgical intervention, in drug intoxication, and in tetanus.

Case-records

The following cases are the first four we have treated in this way, and we hope that this description will be helpful to other workers.

FIRST CASE

On Aug. 17, 1953, a schoolgirl, aged 16, developed a heavy cold and cough beginning with a rigor. These symptoms disappeared within twelve hours, leaving her with a sense of lassitude. This persisted, and after nine days she developed a stiff neck; but, though feeling very unwell, she played tennis in the morning and afternoon.

Ten days after the onset she remained in bed, and during the day her legs became so weak that she could not stand. In the evening she was admitted to an isolation hospital, where she was found to have considerable weakness of all limbs, especially at the proximal joints. During the night she developed dysphagia, and her voice became only a whisper. She was seen by one of us (A. C. S.) on the morning of Aug. 28 and transferred in the prone position under his supervision to the Radcliffe Infirmary.

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On admission [R.I. 179909] she was alert but very apprehensive. Her temperature was 97°F, pulse-rate 82, and respirations 26 per min. She could not swallow, her voice was a hoarse whisper, and she could not close her larynx. The other cranial nerves were normal. The diaphragm was weak, but the intercostal muscles contracted satisfactorily. There was considerable generalised weakness of all the limbs, but some movement was still present at all the joints.

Treatment

She was nursed in the prone and semi-prone or "tonsil" positions, and the head of the bed was tipped down 10–15° to ensure drainage of secretions from her mouth. During the next twelve hours her condition remained substantially unchanged, but at the end of that time her *alæ nasi* and accessory muscles of respiration were working. Her blood-pressure had risen from 130/75 to 160/80 mm. Hg, and she was becoming cyanosed.

An attempt was made to treat her in the Siebe Gorman modification of the Drinker tank respirator, in which a patient can be nursed in the prone or semi-prone positions. These positions were adopted, and the head was lowered 10–15°. The pharynx was aspirated frequently, but three cyanotic attacks during the night made it plain that this régime did not provide a clear airway, and that artificial

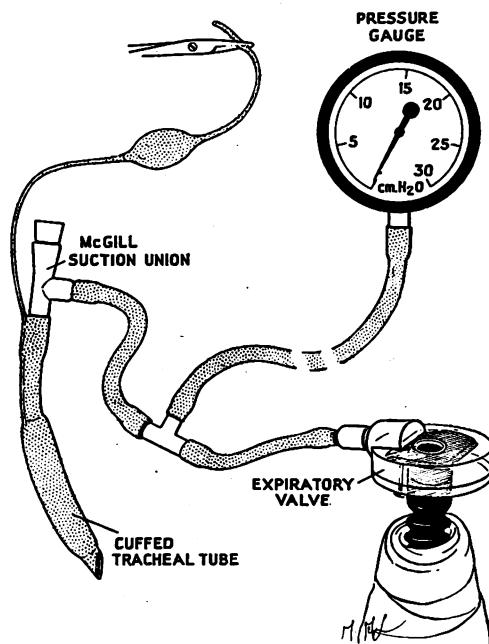


Fig. 1—Expiratory valve, pressure gauge, McGill suction union, and cuffed tracheal tube. End of lagged breathing-tube from humidifier is also shown.

respiration was defeating its object by causing secretions to be inhaled.

We therefore decided to establish I.P.P. respiration through a cuffed tracheotomy tube. The patient was removed from the tank respirator, and the respiration was maintained with an Oxford inflator (Macintosh and Pratt 1939) and face-mask. Bronchoscopy was performed under thiopentone anaesthesia, and the bronchi were cleared of secretions. During this procedure I.P.P. respiration from the Oxford inflator was given as required down the bronchoscope. A cuffed endotracheal tube was then passed, and with it efficient I.P.P. ventilation was maintained. This enabled a formal and unhurried tracheotomy to be done; and, as the endotracheal tube was removed, a short cuffed tracheal tube (fig. 1) was inserted through the tracheostoma.

For four weeks thereafter the patient received I.P.P. respiration from Radcliffe respiration pumps A and B (Russell and Schuster 1953) through an expiratory ("flutter") valve * (fig. 2). A humidifier (Marshall and Spalding 1953) was used.

* This valve was designed by Dr. F. D. Stott as an interim measure. He is of the opinion that it can be further improved.

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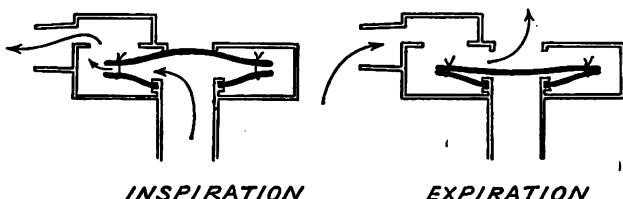


Fig. 2.—Diagrammatic representation of mechanism of expiratory valve. Case is made of plastic, and valve of rubber.

to warm and humidify the gases to the extent which is found in the normal trachea. On the day after tracheotomy (the third since the onset of paralysis) the patient had complete paralysis of all voluntary movements throughout her body except external ocular movements.

Respiration

The respiratory exchange required was assessed by clinical judgment and by the patient's subjective reactions, which proved both sensitive and reliable. It is relatively easy to provide adequate oxygenation by the means used if there is no severe pulmonary collapse, but it is desirable to avoid over-ventilation and hence chronic respiratory alkalosis. Biochemical investigations indicate that this took place to some extent, as exemplified by the progressive rise in the pH of the urine (fig. 3).

A pressure-gauge included in the system close to the tracheal tube provided a continual visual check of pressure during inspiration and expiration.

Pulmonary Complications

Particular attention was paid to the early diagnosis of areas of pulmonary collapse. The chest was frequently examined clinically, and radiographs were taken almost daily for the first three and a half weeks. Indirect indications that some collapse had taken place were (1) anxiety on the part of the patient; (2) her dissatisfaction with a setting of the respirator which had previously satisfied her; (3) increase in the pressure shown on the gauge; or (4) increase in the pulse-rate. Direct indications of collapse were obtained by auscultation and radiography. From the fourth day after I.P.P. respiration was begun the patient received vibration and light percussion to the chest from a physiotherapist. This was done every four hours, during the acute stage; and, when any degree of collapse occurred, particular attention was directed to the lobe concerned. The trachea and bronchi were aspirated during physiotherapy, and Tiemann's catheters proved very suitable for this. If these measures failed to clear the airways bronchoscopy under thiopentone anaesthesia was performed; but with increasing experience it came to be required less and less often.

Blood-pressure

Throughout the acute stage the blood-pressure was measured half-hourly. This provided an early indication of inadequate ventilation, which causes the blood-pressure to rise promptly owing to retention of carbon dioxide. It also demonstrated the mechanism of sudden episodes of unconsciousness, which first came on during the early morning of Aug. 30, when the patient had been having I.P.P. respiration for thirteen hours. In these episodes, without warning, she became unrousable, and at the same time her blood-pressure fell from the normal level of 125/75 mm. Hg to a systolic level of 80–60 or less. Her pulse-rate, which was consistently above 90 during the first four weeks of the illness, was unchanged or fell slightly during these hypotensive attacks (fig. 4). These attacks

lasted from a few minutes to a few hours; and, as soon as she became rousable, her level of consciousness returned to normal, as though she were awakening from sleep. It was impossible to correlate these attacks with any change in the artificial respiration, and they were characterised by a sudden fall in blood-pressure in contrast to the rise that is typical of over-ventilation.

Feeding

As soon as the cuffed tracheotomy tube was in place the pharynx was closed from the bronchial tree, and the possibility that the patient might vomit was no longer alarming. She was fed through a 'Polythene' stomach-tube (size 3 or 4). At first she received 4-oz. feeds hourly, comprising milk 2 oz., water 1 oz., Ringer-Fischer solution 1 oz., and two level teaspoonsfuls of glucose (10 g.). No residuum could be aspirated from the stomach an hour after each feed, and twenty-four hours later an extra ounce of milk was added to each feed. On this régime an ounce or two of fluid could be aspirated occasionally, but nearly 6 pints was absorbed daily, and the specific gravity of the urine fell rapidly (fig. 5). On the seventh day of paralysis, the fluid balance having been restored to normal and absorption being good, 8 oz. of the feeds was given two-hourly, and next day were started two-hourly 8-oz. feeds of "higher protein diet no. I" (Higgins et al. 1954). The increase in dietary protein was followed by a rise in the blood-urea level (fig. 5). When this had again fallen to 40 mg. per 100 ml., "higher protein diet no. II" was begun. The patient remained on this with some additions by mouth until Sept. 25, a month after the onset, when she could be fed entirely by mouth. While she was on these diets, the electrolyte balance was maintained by varying the amount of Ringer-Fischer solution used to dilute the feeds according to the plasma-chloride level.

Fig. 4—Blood-pressure and pulse-rate in case I during first and longest hypotensive attack (on Aug. 30).

Drugs

Large doses of antibiotics were given, mainly penicillin but also aureomycin when bronchial swabs grew penicillin-resistant organisms. Sedation was produced at first with phenobarbitone and later with chloral hydrate.

Nursing

The patient was nursed on a tipping bed with its head about 10° down. She remained mainly in the two lateral positions and sometimes in the theoretically better semi-prone position. The last, however, she found very uncomfortable. She was turned every two hours throughout her illness, and the routine for turning during the acute stage was as follows: (1) the trachea and bronchi were aspirated; (2) the expiratory valve was changed; (3) the patient was turned; and (4) the trachea and bronchi were aspirated again. The act of turning often liberated a considerable amount of secretions. Every four hours, at alternate turnings, vibration and percussion were given to the chest by a physiotherapist at stages 1 and 4. At alternate turnings, when physiotherapy was not being given, the bed was tipped steeply head down, the pharynx was aspirated, and the cuff of the tracheal tube was deflated. After a minute the cuff was re-inflated enough to prevent air from leaking past it, and the bed was returned to its usual tilt of 10°.

Investigations

Radiographic investigations have already been referred to. Cerebrospinal fluid (Sept. 7): no cells; protein 150 mg. per 100 ml. Electrocardiogram (Sept. 1 and Oct. 1): sinus tachycardia. Urine (twenty-four-hour specimen Oct. 5): coproporphyrin excretion less than 40 µg.; no porphobilinogen. Paul-Bunnell test (Oct. 30): negative.

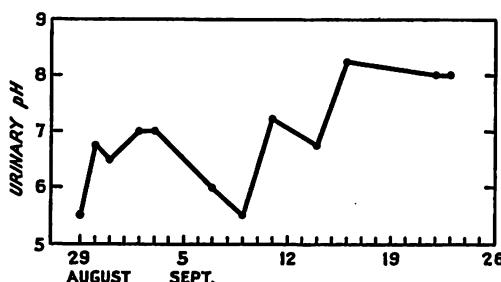


Fig. 3—Urinary pH in case I, showing rise to maximum of 8.3 attributable to respiratory alkalosis caused by over-ventilation.

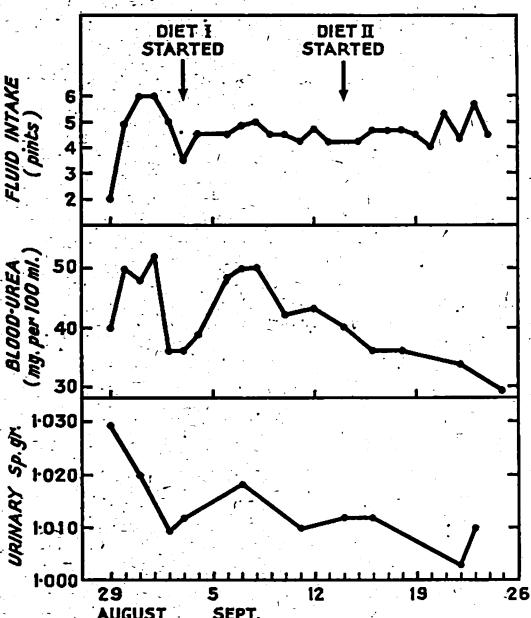


Fig. 5.—Fluid intake, blood-urea level, and specific gravity of urine in case 1

Progress

On Aug. 30 the patient had total paralysis of all voluntary movements except external ocular movements, and this persisted till Sept. 2, when feeble rotation of the neck became possible. Thereafter muscle power throughout the body rapidly recovered. By Sept. 21 she could breathe unassisted for thirty-five minutes, and the partial recovery of facial as well as other muscles made it easier to communicate with her. Sensory testing now showed that she had considerable loss of appreciation of posture and vibration in all her limbs, and some peripheral superficial sensory loss, considerable on the feet and slight on the hands. By Sept. 30 she could breathe unassisted. The cuffed tube was removed, and a Durham's tube was substituted. A few days later the tracheotomy was allowed to close.

She was discharged home on Nov. 18, and on March 11, 1954, her tendon reflexes were diminished, but there were no other abnormalities.

Diagnosis

In view of the profound lower motor-neurone paralysis, the peripheral sensory loss, and the large amount of protein in the C.S.F., a diagnosis of acute toxic polyneuritis was made, and her complete recovery was in accordance with this.

SECOND CASE

On Sept. 7, 1953, a schoolgirl, aged 13, developed pyrexia (100°F) and felt "a lump in her throat." Her appetite was poor, but she ate and drank at all meals. Two days later she drank about 10 oz. at breakfast with some difficulty and thereafter developed complete paralysis of swallowing. She was admitted to another hospital that evening and was found to have, besides dysphagia, weakness of the left face, the palate, the sternomastoid muscles, and the muscles of the shoulder girdles and upper arms. Anterior poliomyelitis was diagnosed.

Next morning she had a cyanotic attack which rendered her temporarily unconscious. She was lying supine at the time, and it seems likely that it was due to inhalation of secretions or of vomit, fluid being aspirated from her nasopharynx. A similar attack occurred three hours later. She was first seen by one of us (J. S.) four hours after the second attack. She did not respond to painful stimuli, and her respirations were extremely shallow and irregular at a rate of about 14 per min. She was receiving 100% oxygen through a mask, and her colour was satisfactory, but her ventilation was manifestly too small to prevent retention of carbon dioxide.

Treatment

A cuffed endotracheal tube was introduced and respiration maintained with an Oxford inflator. The patient was trans-

ferred in this way by ambulance to the Radcliffe Infirmary, a journey of some fifty minutes. During the journey she began to move her limbs and to open her eyes when told to do so.

On admission [R.I. 180349] bronchoscopy was performed, but no considerable amount of inhaled material was within reach. It was thought that when she recovered from the effects of under-ventilation she might be able to breathe spontaneously. An endotracheal tube was therefore replaced, and positive-pressure respiration was instituted down this tube from Radcliffe respiration pump A.

Next day an attempt was made to let her breathe spontaneously, but she could not. A formal tracheotomy was therefore done as in case 1, and I.P.P. respiration continued with Radcliffe respiration pump A. Two hours later, twenty-two hours after I.P.P. respiration was begun, her blood-pressure dropped to 40 mm. Hg systolic, her nail-beds and subsequently her lips became deeply cyanosed, and she died.

Investigation

Radiography of the chest on admission had showed mottled shadowing throughout the lung fields.

Necropsy Findings

The diagnosis of anterior poliomyelitis was confirmed. The endotracheal tube had been in position for twenty hours, and there was considerable ulceration of the larynx. An intense haemorrhagic consolidation involved about five-sixths of the lungs, and the relatively normal fifth was situated anteriofly. Presumably this hopeless state of the lungs was a consequence of secretions, and perhaps vomit, being inhaled on the day before death.

THIRD CASE

On Oct. 11, 1953, a schoolgirl, aged 17, developed a slight cold in the head. On Oct. 16 she noticed numbness and paraesthesiae of both feet and the left hand. She was admitted to another hospital and three days later developed some weakness of the left upper and lower limbs and left side of the face, which was greater next day, when diplopia also developed. There was slight enlargement of the glands of the neck, a blood film showed atypical glandular-fever cells, and a positive Paul-Bunnell test subsequently confirmed the diagnosis of infective mononucleosis with the rare complication of acute toxic polyneuritis.

On Oct. 22 she had a brief cyanotic attack after vomiting, and soon afterwards developed manifest dysphagia. On Oct. 24 her intercostal muscles and diaphragm became weak and, when she was first seen by two of us that afternoon, her respirations were very shallow and she was cyanosed. Within twenty minutes the cyanosis increased, she sweated profusely, and consciousness became impaired.

Treatment

An endotracheal tube was passed, respiration was maintained with an Oxford inflator, and she quickly became alert. Under this form of positive-pressure respiration she was transferred by ambulance to the Radcliffe Infirmary, a journey of one and a quarter hours, without incident.

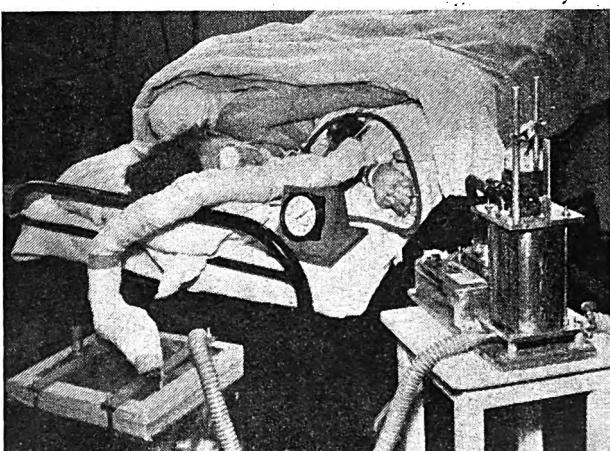


Fig. 6—Case 3 receiving treatment, showing Radcliffe respirator pump B, humidifier, lagged breathing-tube, expiratory valve, and pressure gauge. Patient's head is at "foot" of bed, where rail is lowest.

On admission [R.I. 182462] bronchoscopy was performed under thiopentone anaesthesia, and the bronchi were cleared of secretions. An endotracheal tube was replaced, tracheotomy was performed, and a cuffed tracheal tube was inserted. Respiration was maintained with Radcliffe respiration pump B, and subsequently respiration pump A, through a humidifier and expiratory ("flutter") valve (fig. 6).

At this stage, besides complete paralysis of the intercostal muscles and diaphragm she had bilateral impairment of ocular movements, a severe left and moderate right facial weakness, gross weakness of the tongue, weakness of both upper limbs, which was severe at and below the right elbow and moderate elsewhere, and severe weakness of both lower limbs. No objective sensory loss was demonstrable at this stage, but by Oct. 29 peripheral sensory impairment to light touch was demonstrable on the hands and feet.

Respiration

The respiratory exchange was more satisfactorily controlled than in case 1, and the urinary pH showed no constant trend in either direction, remaining between 5.6 and 7.0 (fig. 7).

Since the volume of gas delivered by a pump does not satisfactorily indicate the volume of air actually ventilating the patient, we collected the expired air with a spirometer and an expiratory valve with a suitable connecting-piece on the expiratory side. The patient required 7-8 litres per min. to maintain equilibrium.

Pulmonary Complications

There were poor air entry and radiographic opacity at the left base before I.P.P. respiration was begun. Four-hourly percussion and vibration to the chest were begun at once, and the pulmonary condition never gave rise to alarm. The value of physiotherapy was well illustrated on one occasion when air entry disappeared over the left lower lobe. Percussion and vibration enabled a plug of mucus to be aspirated with a Tiemann's catheter, and air entry was immediately restored.

Blood-pressure

No hypotensive attacks occurred. The blood-pressure was usually about 100/55 mm. Hg. On her first day the patient was receiving respiration at 5.6 litres per min., and her blood-pressure gradually rose, indicating under-ventilation, and settled again when respiration was increased to 8 litres per min. (fig. 8).

Feeding, Drugs, and Nursing

In feeding, the same principles were followed as in case 1. Milk, water, and glucose were given for the first day and a half; and thereafter, since the blood-urea level was normal and fluid was well absorbed from the intestine, "higher protein diet no. I" was begun. The resulting rise in blood-urea to 56 mg. per 100 ml. settled within two days, and six days after her admission to this hospital she began to receive "higher protein diet no. II."

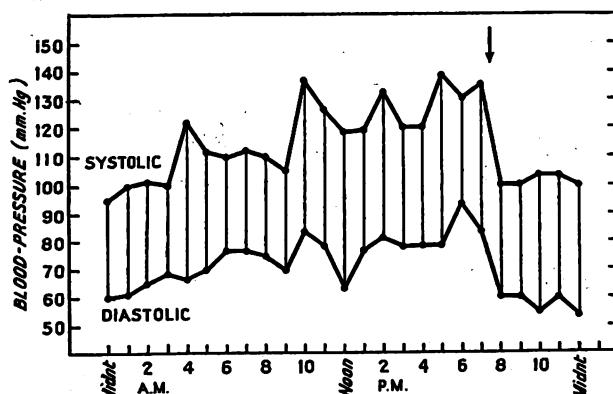


Fig. 8—Blood-pressure in case 3, beginning 6 hours after I.P.P. respiration was begun. At arrow, ventilation was increased from 5.6 to 8 litres per min.

She received penicillin and chloral hydrate. A course of aureomycin was stopped after two days, owing to a mild toxic reaction.

The same nursing routine was applied as in case 1.

Progress

On the fifth day after I.P.P. respiration was begun the first signs of recovery were observed. She could make a few feeble respiratory movements, and there was a little recovery of the cranial nerves and the right deltoid muscle. Muscle power recovered quickly, with the result that on Nov. 3 she could breathe spontaneously for ten minutes. By Nov. 10 she required no respiratory assistance, the tracheal tube was removed, and the tracheostoma was allowed to close. There was still impaired sensation of light touch and pinprick in a "glove-and-stock" distribution in all her limbs and considerable impairment of vibration sense and appreciation of passive movement in the lower limbs. By Dec. 9 she was walking about, and the only abnormalities were slight weakness of the left shoulder and hand, the pelvic girdle, and quadriceps muscles. Complete recovery took place later.

FOURTH CASE

A well-built man, aged 32, developed a headache on Nov. 5, 1953, and next day complained of weakness of his right arm. During the next night he had dysphagia and respiratory difficulty. He was first seen by two of us next morning, when he was breathing with difficulty and became cyanosed on the slightest exertion. His pharynx contained a pool of secretion, and there was no air entry over the left lower lobe. There

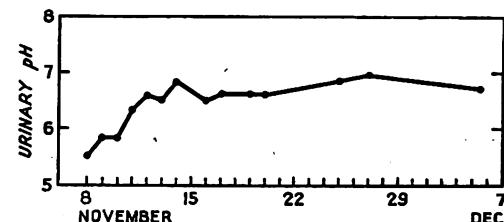


Fig. 9—Urinary pH in case 4. Initial rise is due to rehydration of patient. Thereafter pH remains slightly acid, indicating that ventilation is not excessive.

was very little movement of the left chest, and paradoxical movement on the right side indicated that the right diaphragm was functioning but the right intercostals were not. There was generalised weakness of the right upper limb, less marked weakness of the left upper limb, and a moderate weakness of both lower limbs. The ankle-jerks were the only tendon reflexes obtainable. There was no sensory loss. The C.S.F. (examined elsewhere) contained protein 95 mg. per 100 ml. and 405 cells per c.mm. (lymphocytes 347, polymorphs 45, macrophages 12). A diagnosis of anterior poliomyelitis was made.

Treatment

He was transferred to the Radcliffe Infirmary by ambulance under the supervision of one of us (A.C.S.)—a journey of thirty-five minutes. An endotracheal tube was not passed, but apparatus for intubation and I.P.P. respiration was available in the ambulance.

On admission [R.I. 183157] bronchoscopy was performed under thiopentone anaesthesia with succinylcholine iodide, and a considerable quantity of secretions was removed from the bronchi. An endotracheal tube was then passed, a tracheotomy was done, and I.P.P. respiration established with Radcliffe respiration pump A through a humidifier and expiratory valve as in the previous cases.

Next day the paralysis of the limbs had increased considerably. A trace of movement persisted in the right diaphragm, but the vital capacity was only 200 ml.

Respiration

This patient was known to have a psychopathic personality with hysterical features, and his subjective sensations were worse than useless as a guide to adequate ventilation, because he contradicted himself. For the first fourteen hours he received ventilation of 7.5 litres per min. This was thought insufficient in view of an estimated partial pressure of carbon dioxide in capillary blood of 60 mm. Hg, and the ventilation was increased to 9.8 litres per min. Thereafter he continued to receive about 10 litres per min, and this kept him almost

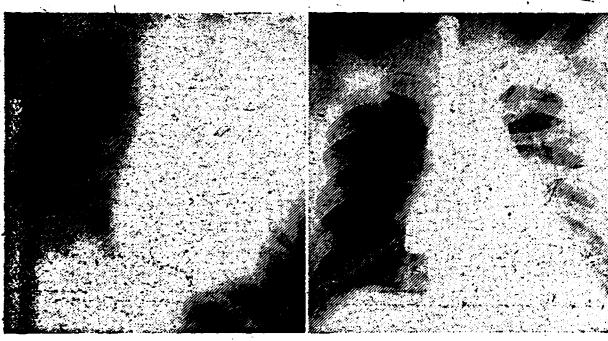


Fig. 10—Case 4 : a, on admission ; b, 5 days later, showing resolution of severe abnormalities on left side.

in respiratory equilibrium, judged by his blood chemistry and urinary pH (fig. 9).

Pulmonary Complications

The abnormalities at the left base, which were considerable when he was first seen, cleared up with routine physiotherapy and suction, and no serious pulmonary complication developed (fig. 10).

Blood-pressure

There were no hypotensive attacks. For the first week the patient's blood-pressure remained about 110/60 mm. Hg., but thereafter it began to rise very gradually; two weeks later it was between 140/100 and 200/130. The ventilation was increased from 10 litres to 13 litres per min. for twelve hours, and this produced biochemical evidence of hyper-ventilation but did not lower the blood-pressure. The hypertension gradually diminished, and two months after the onset the blood-pressure was 130/80.

The patient's psychiatric abnormalities made it difficult at times to interpret changes in blood-pressure. For instance, when he was being weaned from artificial respiration, his blood-pressure used to rise sharply as soon as the pump was turned off. Within half an hour it returned to its previous level and he would often fall asleep. Clearly this hypertension was psychogenic, and not the result of carbon-dioxide retention.

Feeding, Drugs, and Nursing

The same principles were applied as in cases 1 and 3.

Progress.—By Nov. 28 he could breathe spontaneously for five and a half hours out of the twenty-four, and by Dec. 28 he could breathe unassisted by day and night.

Discussion

The method of artificial respiration used for these patients has three great advantages: first, a cuffed tube inserted through a tracheotomy wound separates the pharynx from the trachea so that there is no danger of inhalation of foreign material even if the patient vomits; second, it permits secretions to be aspirated readily from the trachea and bronchi; third, it provides a route for artificial respiration by I.P.P. with the attendant advantages, compared with respiration in a tank, of ready access to the patient and of low cost of apparatus.

Patients with paralysis causing respiratory embarrassment are critically ill, but, as illustrated above, if they survive, even those with both bulbar and spinal involvement may make an excellent recovery. Their treatment is a specialised matter and presents many problems which are not commonly met with in other branches of medicine. It is therefore best carried out in a special unit whose doctors and (very important) whose nurses are experienced in treating this type of case. A considerable staff of doctors and nurses is required to give adequate treatment in the acute stage; and, since the number of cases requiring treatment, and therefore the number of staff required, varies greatly from time to time, a unit that is to treat such cases is most conveniently situated in a large hospital which can support a drain on its resources. Moreover it is in large hospitals that the ancillary services required are available.

This recommendation is in accordance with the policy put forward by the Royal College of Physicians (1953) and the Ministry of Health (1953). Whether the unit should be situated at a general hospital or a hospital for infectious diseases depends on local conditions.

TRANSPORT

A patient with paralysis may develop respiratory embarrassment with little warning, and this may happen when the patient is at home or in a hospital which has neither the equipment nor the organisation to deal with this condition. This fact has in the past militated against the formation of special units for these patients, but it now appears that it is relatively simple to transport them. Any unit intending to treat cases of this type must be prepared to send out a team, consisting of an anaesthetist and a physician, to provide for the safe transport of the patient. This team must be prepared to intubate the trachea with a cuffed endotracheal tube under either local or general anaesthesia, and to provide a portable source of I.P.P. respiration and of suction. The Oxford sucker-inflator unit (supplied by M.I.E. Ltd., 12, New Cavendish Street, London, W.1) has proved very suitable for this purpose. The requisite equipment can be carried in any car and should be kept ready for immediate use. It will often be unnecessary to intubate the patient for transport, as in cases 1 and 4, but it is nevertheless essential for the anaesthetist to travel with the patient in the ambulance and to be prepared to intubate if necessary.

For transport, we prefer intubation through the mouth to tracheotomy, since it enables the patient's condition and therefore the need for tracheotomy to be reassessed after a period of satisfactory ventilation. Moreover, if tracheotomy is required, a formal and unhurried operation can most easily be performed in the respiratory unit by a surgeon experienced in this operation. Tracheotomy must not, however, be unnecessarily delayed, owing to the danger of ulceration of the larynx if an endotracheal tube is left in situ for even a few hours.

I.P.P. RESPIRATION

The circuit used was an open circuit with no rebreathing, and it supplied air 100% saturated with water vapour at 36°C. Additional oxygen was sometimes used. We attempted to maintain a ventilation-rate appropriate to the patient's need without excessive inspiratory pressures. During the expiratory phase tracheal pressure was atmospheric, and expiration slightly exceeded inspiration in length.

Respirators

To provide I.P.P. respiration Lassen (1953) used a semi-closed system and relied on students to squeeze an anaesthetic bag supplied from cylinders containing oxygen and nitrogen. We have used Radcliffe respiration pumps A and B (made by H. G. East & Co., Longworth Road, Oxford) (Russell and Schuster 1953) to supply positive pressure. These pumps are easy to adjust to the patient's needs, and eliminate any risk of accidental overdistension of the lungs. They give a rapid rise in pressure at the beginning of inspiration

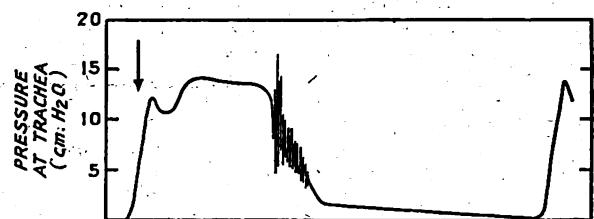


Fig. 11—Pressure record at trachea taken with a condenser manometer, with Radcliffe respiration pump A at 20 respirations a minute. Rapid rise in pressure at start (arrow) of inspiration is a feature of this pump.

(fig. 11), which ensures that the lungs are well filled for the greater part of inspiration. Maloney et al. (1953) advocate a machine which provides negative pressure during expiration. We have not had the opportunity of testing such a machine, but there is need for further study of the effects of different pressures and rates of change of pressure during both expiration and inspiration. Unfortunately the records illustrated by these workers show that this machine was compared with another which permitted only gradual expiration and with which the expiratory pressure did not fall below 5 cm. water.

Though oxygen or any other gas can be delivered by Radcliffe respiration pumps they normally use room air, which possesses the great advantage of being readily available. Lassen (1953) has described the difficulties and expense of maintaining a supply of gas cylinders when he used hand-operated I.P.P. respiration. The same problem arises in respiratory machines (Bang 1953, Macrae et al. 1953, Pask 1953) which rely for their motive power on the pressure from a cylinder of compressed gas.

Humidifier

The value of humidification to keep secretions fluid has been emphasised by Lassen (1953). It is physically impossible to produce humidification that in any way simulates that obtaining in the normal trachea, unless the humidifier also warms the air and is placed between the respirator and the patient. The simple apparatus described by Marshall and Spalding (1953) has proved satisfactory. When it has been in use, secretions have remained moist and were readily removed by aspiration. When the patients were being weaned from the respirator and were breathing spontaneously through the tracheal tube, sticky secretions sometimes occurred, and the patients complained of discomfort and difficulty in breathing, which was relieved by further humidification. To obviate this a plastic bag was placed loosely over the free end of the tracheal tube, and the pump was used to blow humidified air into it. This device enabled the patient to breathe warm humidified air mixed with room air and has facilitated the weaning phase.

Expiratory Valve

The most important feature of an expiratory valve is that it should permit perfectly free expiration; for, if the tracheal pressure does not fall to atmospheric in expiration, there is a deleterious effect on the circulation (Werkö 1947, Cournand et al. 1948, Motley et al. 1948). For this reason any form of expiratory apparatus which depends for its proper functioning on introducing resistance cannot be regarded as satisfactory. The "flutter" valve (made by Owen Mumford & Co. Green Place, Abingdon Road, Oxford) used in these cases has proved adequate. To ensure rapid opening of this type of valve to the expiratory position negative pressure from the respirator is necessary, and a non-return valve on the delivery side of the respirator must therefore not be used.

Pressure Gauge

The use of a pressure gauge (made by K. D. G. Instruments Ltd., Purley Way, Croydon) close to the tracheostoma has proved of special value because it provides a continual visual check on the working of the I.P.P. system. It shows that in inspiration the maximum safe intrapulmonary pressure is not being exceeded, and in our experience pressures above 20 cm. water are rarely required. It also gives positive evidence that the expiratory valve is opening freely. Moreover a change in the readings gives an early indication that something is wrong. A rise in pressure suggests pulmonary complications, and a fall a leak in the system, either outside the patient or beside the tracheal cuff. In either case early treatment will avoid serious mishaps.

Tracheal Tube

We have used cuffed endotracheal tubes cut to a length of about 4½ in. At the external end a McGill suction union is connected, and through the opening in this, which is normally kept occluded, aspiration can readily be applied. The lower end of the tube is also cut short immediately below the cuff, with the minimum of bevel, for this end reaches almost to the carina and, if too long, can easily enter the right bronchus, occluding the left. For the same reason tracheotomy should be as high as possible. The cuff is deflated briefly every four hours to protect the tracheal mucosa, and a fresh tube is inserted every three or four days.

Ventilation

The dangers of inadequate ventilation with hypoxia and retention of carbon dioxide are well recognised. Those of over-ventilation are not at present well defined. There are extremely sensitive mechanisms in the normal person which prevent over-ventilation, and if it occurs it produces profound alterations in body electrolytes. It therefore seems highly unwise to induce over-ventilation in a sick person, whose ability to compensate may be impaired or who may not be in a condition to withstand a change in ionic balance. The importance of maintaining electrolyte equilibrium has been increasingly appreciated in recent years in other serious conditions—e.g., diabetic coma, the postoperative state, and severe injury—and should not be neglected in this instance.

It is not easy to assess when adequate ventilation is being provided, and the patient's subjective sensations, often a most useful guide, are not available in the most difficult instances—i.e., in the acute stage, when the patient may be unconscious or incapable of co-operation, and in children. Objective criteria are therefore desirable.

We have measured in a spirometer the volume of air expired each minute, and have found this a valuable procedure. Cases 1 and 3, girls aged 16 and 17, of slight build, required 7–8 litres per minute, whereas case 4, a heavily built labourer, required about 10 litres per minute. In all the cases the respiratory rate was 16–20 per minute. A minute volume that is approximately correct can thus be assured, and it can be adjusted in the light of the patient's progress. Slight under-ventilation can be detected by a gradual rise in blood-pressure, and over-ventilation by a rise in the urinary pH. The conclusions drawn from these estimations may be confirmed by investigating the blood chemistry.

Pulmonary Complications

Patients with bulbospinal paralysis are extremely liable to pulmonary complications since they cannot cough and rid themselves of their secretions. Prophylaxis and early treatment are essential, and the following prophylactic measures have been adopted.

(1) Two-hourly changes of posture from one side to the other; these often loosen secretions so that they can be easily aspirated.

(2) Four-hourly vibration and percussion by a physiotherapist; these to a considerable extent took the place of the normal cough in removing secretions.

(3) Aspiration of trachea and bronchi with Tiemann's catheter, whenever secretions are present. This catheter is rather stiff and has a curved tip by which it is possible, with the patient lying on, say, the right side, to pass the catheter into the bronchi of the left (uppermost) lung which is receiving physiotherapy.

(4) Hydration of the patient and humidification of the inspired air. In this way the secretions are kept fluid and easy to aspirate.

(5) Antibiotic therapy.

In the presence of established pulmonary collapse these measures were intensified. If they failed, bronchoscopy was performed, but the need for this became less and less frequent as experience was gained.

Although bronchoscopy through the tracheostoma is easy, it proved impossible to ventilate an apneic patient adequately through a bronchoscope in this situation, because of leaks round the instrument. Bronchoscopy was therefore performed through the mouth, with the tracheostoma temporarily occluded. Thiopentone anaesthesia, with or without relaxants and with intermittent inflation with oxygen, proved satisfactory.

BLOOD-PRESSURE

Lassen (1953) found frequent records of the blood-pressure a useful guide to correct ventilation, since carbon-dioxide retention is quickly reflected in a rise in blood-pressure. Although in some circumstances the significance of changes in blood-pressure was sometimes difficult to determine, in most instances valuable information was obtained from half-hourly records.

FEEDING, DRUGS, AND NURSING

Feeding.—With a cuffed tube in the trachea the bronchial tree is separated from the pharynx, and the dangers and deficiencies of parenteral nourishment, which may have to be faced in some cases of dysphagia without respiratory weakness, can be avoided. Polythene nasal tubes are less irritating than rubber and require changing less frequently. In an illness of the severity and duration of most cases of bulbospinal paralysis it is important that nourishment be adequate. Not only must the intake of fluid and calories be satisfactory, but also the diet should be mixed and contain as much protein as can be metabolised, judged by the blood-urea level. We have used the diets described by Higgins et al. (1954), which provide 2200 calories or more daily. They were diluted with water or with Ringer-Fischer's solution as biochemical investigations indicated.

Drugs.—Antibiotics are required in full doses. Sedation is necessary, especially in the early stages, and chloral hydrate and phenobarbitone have both been used.

Nursing.—A severely paralysed patient requires a great deal of careful nursing, and I.P.P. respiration allows completely free access to the patient, in striking contrast to artificial respiration in a tank respirator. Patients must be nursed on a bed that can be easily tipped. They will often be slightly head down, and therefore care of the skin over the acromioclavicular joint is especially important. Since it is not one of the classical pressure areas it is liable to be overlooked.

At least two nurses are required to turn a badly paralysed patient, and during the acute stage it has been our practice to have a doctor attending to respiration during turning, and readily available at all times.

Summary

"Combined" paralysis of both the pharynx and the muscles of respiration presents a very difficult problem in treatment, for which careful preparation is desirable.

This requires the organisation of small units in a well staffed hospital, members of which are prepared to act as a mobile team to transport patients safely under conditions of full control of respiration. The transport of such patients is usually safe even when they are completely paralysed.

The method introduced by Lassen (1953) of artificial respiration by intermittent positive pressure via a cuffed tracheotomy has been found satisfactory, and four cases are described.

This method with respiration pumps now available promises to be the method of choice in the treatment of this most critical group of cases.

We are specially indebted to Mr. R. G. Macbeth, director of the department of otorhinolaryngology, Radcliffe Infirmary, for his assistance in the development of this unit. In addition, we were most dependent on expert assistance unstintingly provided by many anaesthetists, E.N.T. surgeons, biochemists, physicians, physiotherapists,

and nurses, at all hours of the day and night. Dr. G. S. Dawes kindly took the pressure record in fig. 11.

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SIDE-EFFECTS OF OXYTETRACYCLINE THERAPY

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OXYTETRACYCLINE (terramycin) has been used in this hospital to treat gastro-intestinal infections and other susceptible infections when another antibiotic has been unsuccessful. The dosage given to children was 20 mg. per kg. of body-weight daily in four equal divided doses. The course lasted five days in every case except where the oxytetracycline was discontinued owing to side-effects. The dose given to patients aged 12 years or more was 2 g. daily, and this was the largest dosage used. The oxytetracycline was given with copious fluids, usually milk. Vitamin-B supplements were also given.

Not unnaturally side-effects were observed in some cases, showing once more that antibiotics upset the complex host-parasite-drug relationship, of which we know relatively little.

Most reports on oxytetracycline toxicity refer to nausea, vomiting, heartburn, diarrhoea, and headache as the most common manifestations; but we decided not to include these symptoms *per se*, because in most cases it was difficult to determine whether such symptoms were signs of the initial disease or of drug disturbance. Another reason is that many of our patients were infants and therefore unable to complain of minor symptoms. 2 cases of acute gastro-enteritis are included, however, for reasons that will be made clear below. Also, patients exhibiting other syndromes have had concomitant vomiting and diarrhoea.

The clinical syndromes observed during the treatment of 603 patients with oxytetracycline in the fourteen months from October, 1952, to December, 1953, are shown in table I.

Illustrative Case-histories

SYNDROMES ASSOCIATED WITH COAGULASE-POSITIVE

Staphylococcus aureus

Group I : Fulminating Gastro-enterocolitis

Case 1.—A girl, aged 6 years, was admitted as a carrier of *Salmonella typhimurium*. She was physically well. On the fourth day of oxytetracycline administration she developed

TABLE I—CLINICAL SYNDROMES DEVELOPING DURING OXYTETRACYCLINE THERAPY

Group	No. of cases	<i>Staph. aureus</i>	
		Isolated	Not isolated
I: fulminating gastro-enterocolitis ..	2	1	1
II: sore throat			
With rash—i.e., staphylococcal scarlet-fever syndrome	7	6	1
Without rash	8	3	5
III: no throat lesion			
With rash—i.e., "surgical" or extrafacial staphylococcal scarlet-fever syndrome	1	1	0
Without rash	3	3	0
Totals of groups I-III	21	14	7
Group IV: pyrexia as sole clinical feature	24	0	24
Group V: urticaria	3	0	3
Group VI: transient erythema	4	0	4
Totals of groups IV-VI	31	0	31

a pyrexia of 99°F, with a little vomiting and green diarrhoea. On examination she had inflamed fauces, with white patches of exudate. Oxytetracycline was discontinued. That day the pyrexia increased to 102°F. The child had twelve loose stools in twenty-four hours, but she developed intense peripheral circulatory failure next morning and died twenty-four hours after onset of diarrhoea.

Necropsy findings.—Patchy areas of early inflammation were seen in the stomach, duodenum, jejunum, ileum, cæcum, ascending colon, and descending colon. The appearances did not indicate gross damage. The stools contained a considerable amount of mucus and were pea-green. No significant abnormality was found in any of the other systems.

Bacteriology.—Cultures made from the throat and faeces on the fourth day of therapy produced a pure growth of coagulase-positive *Staph. aureus*. Post-mortem cultures from all levels of the intestinal tract and the lungs produced a pure growth of coagulase-positive *Staph. aureus*, which was resistant to penicillin, aureomycin, and oxytetracycline, and sensitive to chloramphenicol and streptomycin.

Case 2.—A boy, aged 2 years, was admitted with a clinical diagnosis of dysentery; there was a week's history of greenish diarrhoea with mucus but no blood. He had been vomiting intermittently. His sister was known to have Sonne dysentery. Physically there was no abnormality of note. His stool cultures showed no intestinal pathogens. He had two loose stools a day until the early hours of the fifth day of treatment with oxytetracycline, when he suddenly developed profuse vomiting and diarrhoea. He had nine loose stools before 8 A.M. Signs of peripheral circulatory failure became evident, and intravenous fluids were given immediately. His watery stools continued throughout the day, but his condition deteriorated and he developed a pyrexia of 104.2°F. He died at 4 A.M. on the sixth day, just twenty-six hours after the acute onset of symptoms.

Necropsy findings.—Numerous small mucosal haemorrhages were present in the stomach. The Peyer's patches of the

ileum were swollen, many being congested. The intervening mucosa showed no abnormality. The large bowel showed nothing of note. No significant abnormality was found in any of the other systems.

Bacteriology.—No pathogens were isolated ante-mortem from rectal swabs. Post-mortem cultures from bowel showed no dysenteric, salmonella, or coliform organisms. No attempt was made to isolate *Staph. aureus* because we did not suspect this organism at that time.

Although *Staph. aureus* was not isolated from this case, we think that the similarity between this case and case 1 is such that the aetiology was probably the same in both cases.

Group II: Sore Throat

(1) **With rash.**—7 patients developed a scarlatiniform rash with throat lesions on the fourth or the fifth day of treatment with oxytetracycline, and 5 of them had severe diarrhoea simultaneously. In 6 cases a pure growth of coagulase-positive *Staph. aureus* was obtained from throat swabs (table II). The following are illustrative examples :

Case 5.—A girl, aged 2 years, was admitted with a *Salmonella enteritidis* infection of the gastro-intestinal tract. On her fourth day of treatment she developed a pyrexia of 100.6°F, her fauces being much injected. A day later her fauces were oedematous, with areas of white ulceration. She had severe diarrhoea. Oxytetracycline was discontinued. Next day her fauces and buccal mucosa were much injected, with a white glazy film over them; the ulceration of the fauces persisted, and punctate erythema appeared. The child's persistent diarrhoea had produced dehydration, which was aggravated by her inability to swallow, because of her sore throat. She was treated with intravenous fluids, intravenous sulphadiazine 1 g. four-hourly, and intramuscular antistreptococcal serum 10,000 units. The day after treatment was started the rash was fading, but the white film on the fauces and buccal mucosa had extended on to the palate. Next day the rash disappeared; but there was extensive white ulceration of the palate and fauces, although the initial fiery redness of the surrounding mucosa was subsiding. The temperature came down to normal and remained so. (The pyrexia had persisted for five days, lasting two days after the start of sulphadiazine therapy.) The diarrhoea also lessened. Since the child had been rehydrated and could swallow fluids, the intravenous therapy was terminated after four days. The white ulcerated oropharyngeal lesions steadily improved till healing was complete on the seventeenth day after the start of treatment, leaving evidence of uvular scarring.

Bacteriology.—Throat swabs on the fourth day after the start of treatment produced a pure growth of coagulase-positive haemolytic *Staph. aureus* resistant to penicillin, aureomycin, and oxytetracycline, and sensitive to chloramphenicol and streptomycin. Cultures made from the throat, sputum, and a sore on the tongue produced a pure growth of this organism for eight days after the initial pyrexia. *Staph. aureus* was not isolated from the faeces. Attempts to find *Candida* in the oropharynx and faeces were unsuccessful.

TABLE II—STAPHYLOCOCCAL SCARLET-FEVER SYNDROME

Case no.	Age (yr.)	Sex	Disease	Side-effects	Day of appearance	Bacteriology
3	1 ^{1/2}	F	Sonne dysentery	T.102°F, ulcerated throat, scarlatiniform rash, diarrhoea	5	T.C., pure growth of <i>Staph. aureus</i>
4	3	F	" "	T.102°F, inflamed throat, scarlatiniform rash See text	5	T.C., pure growth of <i>Staph. aureus</i>
5	2	F	Infection with <i>Salmonella enteritidis</i>	T.100.4°F, inflamed throat, scarlatiniform rash, diarrhoea	4	T.C., pure growth of <i>Staph. aureus</i>
6	3	F	Infection with <i>Salmonella enteritidis</i>	T.100.4°F, inflamed throat, scarlatiniform rash, diarrhoea See text	4	T.C., pure growth of <i>Staph. aureus</i>
7	3 ^{1/2}	F	Sonne dysentery	T.100.4°F, inflamed throat, scarlatiniform rash See text	4	T.C., pure growth of <i>Staph. aureus</i>
8	7 ^{1/2}	F	" "	T.100.4°F, inflamed throat, scarlatiniform rash	4	No culture made
9*	16	F	Gangrenous appendicitis	T.103°F, ulcerated throat, scarlatiniform rash	4	T.C., pure growth of <i>Staph. aureus</i>
18	5	M	Clinical dysentery	T.100°F, balanitis, scarlatiniform rash	7	Culture from balanitis, pure growth of <i>Staph. aureus</i>

* Case 9 had 250 mg. of oxytetracycline six-hourly for forty-eight hours followed by 'Distaquaine' penicillin 600,000 units twice daily and streptomycin 0.5 g. twice daily.

T.C., throat culture.

TABLE III—OTHER SYNDROMES ASSOCIATED WITH COAGULASE-POSITIVE *Staph. aureus*

Case no.	Age (yr.)	Sex	Disease	Side-effects	Day of appearance	Bacteriology
1	6	F	Infection with <i>Salmonella typhimurium</i>	Ulcerated throat and gastro-enteritis	4	See text
10	5	F	Sonne dysentery	T.100·2°F, inflamed throat	4	T.C., <i>Staph. aureus</i>
11	5	M	" "	Vomiting and diarrhoea, T.100·2°F, inflamed throat	5	T.C., <i>Staph. aureus</i>
12	3	F	Infection with <i>Salmonella typhimurium</i>	T.102°F, inflamed throat with white exudate	4	T.C., pure growth of <i>Staph. aureus</i>
19	2	M	Sonne dysentery	Urinary infection	8	U.C., pure growth of <i>Staph. aureus</i>
20	52	F	Infection with <i>Salmonella typhimurium</i>	Urinary infection	3	U.C., pure growth of <i>Staph. aureus</i>
21	1½	M	Gastro-enteritis	Urinary infection	5	U.C., pure growth of <i>Staph. aureus</i>
2	2	M	Clinical dysentery	Gastro-enteritis	5	No organism isolated
13	2	M	Sonne dysentery	T.100°F, inflamed fauces	4	Not examined
14	1¼	M	" "	T.100°F, inflamed throat	4	Not examined
15	12	F	" "	Inflamed throat	4	Not examined
16	2½	F	Flexner dysentery	T.100°F, inflamed throat, vomiting, and diarrhoea	4	Not examined
17	5	F	Sonne dysentery	Injection of buccal mucosa and inflammation of throat	8	Not examined

T.C., throat culture. U.C., urine culture.

Case 6.—A girl, aged 3 years, sister of case 5, presented a similar clinical picture with similar bacteriological findings.

Case 7.—A girl, aged 3½ years, was admitted with Sonne dysentery. On the fourth day of oxytetracycline therapy she developed pyrexia (99°F), with vomiting and diarrhoea. A macular erythema appeared which became a generalised punctate erythema. Intense petechial congestion of the pharynx and rhagades of the lips were present. The oxytetracycline was discontinued. Next day the rash was not so intense. The child had occasional bouts of vomiting but was not dehydrated. The pharyngeal congestion had extended forwards on to the palate and buccal mucosa. The following day the oropharyngeal congestion persisted, and there were white glazy patches of exudate on the anterior pillar of the fauces and on the palate. The vomiting and diarrhoea ceased. More exudate developed in the pharynx in the next twenty-four hours when the last remnants of the rash were seen. The throat exudate persisted for nine more days before clearing. During this time the lips became ulcerated, especially at the angles of the mouth.

Bacteriology.—Throat culture on the first day of the throat infection produced a profuse pure growth of haemolytic coagulase-positive *Staph. aureus* resistant to penicillin, aureomycin, and oxytetracycline, and sensitive to chloramphenicol and streptomycin. A pure growth was obtainable from the throat for five days, and the staphylococcus was the predominant organism in the throat for seventeen days. *Staph. aureus* was not cultured from the faeces. A search for candida in throat and faeces was unsuccessful. A skin test for sensitivity to oxytetracycline was negative.

The following was a presumptive case :

Case 8 developed pyrexia, injected throat, and generalised punctate erythema on the fourth day of treatment. No bacteriological examination was made in this patient, but the clinical features and time of onset indicate that the aetiology was probably the same as in the cases already mentioned.

(2) Without rash.—A febrile disturbance with infection of the oropharynx developed in 8 patients on the fourth or the fifth day of treatment (apart from case 17), and in 3 of them a coagulase-positive *Staph. aureus* was isolated as a pure growth on throat culture (table III).

Case 10.—A girl, aged 5 years, with Sonne dysentery developed pyrexia (100·2°F) and had enlarged and inflamed tonsils and uvula on the fourth day of treatment.

Bacteriology.—Throat culture produced a pure growth of *Staph. aureus* sensitive to chloramphenicol and resistant to penicillin, aureomycin, oxytetracycline, and streptomycin.

This patient had another course of oxytetracycline later with no untoward effect, the staphylococcus having been eliminated.

Case 11.—A boy, aged 5 years, with Sonne dysentery developed pyrexia (100·2°F), vomiting, and diarrhoea on the

fifth day of treatment. His pharynx and tonsils were red. His pyrexia settled in twenty-four hours, but his throat did not clear for four days.

Bacteriology.—Throat culture produced a pure growth of coagulase-positive *Staph. aureus* resistant to penicillin, aureomycin, oxytetracycline, and chloramphenicol, and sensitive to streptomycin.

Case 12.—A girl, aged 3 years, sister of case 1, developed pyrexia (102°F) on the fourth day of treatment with oxytetracycline. She had neither vomiting nor diarrhoea, but she had an intensely inflamed throat, with white glazy patches of exudate. The pyrexia settled in forty-eight hours, and the throat cleared in four days.

Bacteriology.—Throat culture produced a pure growth of coagulase-positive *Staph. aureus* resistant to penicillin, aureomycin, and oxytetracycline, and sensitive to chloramphenicol and streptomycin.

The 5 patients in whom no bacteriological examination was made are presumed to have had a similar infection to that in the 3 described because they had a remarkably similar time of onset, and clinically they presented an indistinguishable picture.

Group III : No Throat Lesion

(1) With rash.—Case 18 presented as a scarlatiniform syndrome of extrafaucial or "surgical" scarlet-fever type, his infective lesion being a balanitis from which a pure growth of coagulase-positive *Staph. aureus* resistant to oxytetracycline was isolated.

(2) Without rash.—3 patients developed urinary infections due to a coagulase-positive *Staph. aureus* resistant to oxytetracycline. One of them (case 21) required a further course of oxytetracycline after the urinary infection was treated, and had no upset during this second course (table III).

SYNDROMES NOT ASSOCIATED WITH COAGULASE-POSITIVE *Staph. aureus*

Group IV : Pyrexia

24 patients developed pyrexia (at least 99°F) without other signs or symptoms during treatment with oxytetracycline. The remarkable feature about these cases was the similarity of the time of onset : they all occurred from the third to the sixth day (20 of them on either the fourth or the fifth day) after the start of oxytetracycline therapy (table IV). The coincidence of the time of onset of pyrexia with time of onset of the staphylococcal lesions reported above suggests a similar aetiology. No definite clinical sign apart from pyrexia was observed in these patients, and no bacteriological examinations

TABLE IV—PATIENTS WITH PYREXIA BUT NO OBSERVABLE LESION

Case no.	Age (yr.)	Sex	Type of dysentery	Pyrexia (°F)	Days of appearance
22	4 ^{1/2}	F	Sonne	99.2	3-5
23	5 ^{1/2}	F	Flexner	99.4	4
24	2	F	Sonne	99.6	5-7
25	3	M	Clinical	99.0	5
26	44	F	Flexner	99.0	6
27	4	F	Sonne	99.2	4
28	2 ^{1/2}	M	Clinical	99.8	4-5
29	5	M	Sonne	99.8	4-5
30	1	M	Sonne	99.0	5
31	2	F	Sonne	100.0	4-5
32	4	M	Sonne	99.0	4-5
33	6	F	Sonne	99.0	5
34	2	F	Sonne	101.0	3-4
35	1 ^{1/2}	M	Sonne	99.0	4-6
36	17	F	Sonne	99.2	6
37	2 ^{1/2}	F	Sonne	99.2	5
38	1 ^{1/2}	F	Sonne	100.0	3-4
39	4 ^{1/2}	M	Sonne	99.0	4-6
40	9	F	Sonne	99.4	6
41	3	M	Sonne	99.0	6-8
42	5	F	Sonne	99.0	5
43	1	M	Sonne	100.2	4
44	5	M	Sonne	99.0	4-5
45	4	M	Flexner	99.0	5

were made; so we cannot attribute the pyrexia to any known cause. The investigation of these cases was mainly retrospective, which fact explains the lack of bacteriological examinations made to find an aetiological agent. The time of onset of the pyrexia was earlier than would be expected if the pyrexia was due to drug allergy. A similar number of cases of gastrointestinal infections treated with other drugs were surveyed, but no evidence of pyrexia on the fourth or the fifth day was found.

Group V: Urticaria

3 patients (table v) developed urticarial lesions in association with oxytetracycline therapy. One of them (case 15) had had a throat infection on the fourth day of treatment. Another (case 47) exhibited the appearances of serum-sickness, with massive urticaria, circumoral and circumorbital oedema, and pains in his joints.

Group VI: Transient Erythema

A transient erythema was seen in 4 patients (table v); it came on from the eighth to the tenth day after the start of oxytetracycline therapy. In 3 of these cases throat cultures were made, but no organisms were isolated.

Discussion

In this series of 603 patients side-effects other than mild gastro-intestinal upsets developed in 51 patients on 52 occasions. This represents an incidence of about 8%.

The scarlet-fever syndrome observed in 8 cases is of interest because *Staph. aureus* was the only organism isolated in 7 of them. Staphylococcal scarlet fever is not unknown and has been described by several workers. Aranow and Wood (1942) reviewed the published reports on staphylococcal scarlet fever and made reference to the isolation of the erythrogenic toxin. We have found 6 published cases of this syndrome complicating antibiotic therapy.

Finland (1951) cites Chang and Jackson as having noted it in 3 patients under treatment for either pertussis or diphtheria with some of the newer antibiotics (unspecified), and stating that the rapid disappearance of *Hæmophilus pertussis* and *Corynebacterium diphtheriae* from nasopharyngeal cultures was promptly followed by the development of typical scarlet fever, pharyngeal swabs showing pure cultures of haemolytic *Staph. aureus* and no haemolytic streptococci. Finland mentions another case of staphylococcal scarlet fever in a patient receiving prophylactic penicillin for an extensive burn, the organism being cultured from the throat and the surface burn.

Hazen et al. (1951) record 2 cases. In one a scarlatiniform rash developed on the third day of therapy with oxytetra-

cycline, and proceeded to ulcerative stomatitis, pharyngitis, diarrhoea and vomiting. This case corresponds closely to those we report here. The second case is stated to have developed the same signs and symptoms on the ninth day of aureomycin therapy.

The syndrome appears to consist of fever, throat lesions (sometimes very severe), scarlatiniform rash, and (in 5 of our cases) concomitant vomiting and diarrhoea. However, we think this infection is analogous to the modern concept of haemolytic streptococcal scarlet fever, in which may be found infectious sore-throat syndromes, and the erythema only appears if the patient is sensitive to the erythrogenic toxins. Case 18 appears to be an example of extrafacial or "surgical" scarlatina with the balanitis as the site of infection. This case occurred on the seventh day after the start of oxytetracycline therapy; but, as several of our cases show, *Staph. aureus* may persist in a pure culture from an infected site for several days after the cessation of treatment.

Seven of the throat infections (cases 1, 3, 5, 6, 7, 9, and 12) had intense congestion of the fauces and buccal mucosa and white glazy patches of exudate, which resembled moniliasis. In view of published reports suggesting that moniliasis might complicate the use of broad-spectrum antibiotics (Harris 1950, Woods et al. 1951, Tomaszewski 1951, and others), attempts were made to find candida in the mouth, throat, and rectum by culture on Sabouraud's medium but without success. In these cases a pure growth of *Staph. aureus* alone was obtained from the oropharynx.

Vomiting and diarrhoea were additional signs in 6 cases to other symptom complexes, but in 2 cases vomiting and diarrhoea on the fourth and the fifth days after the start of oxytetracycline therapy led to the death of the children within a very short period from the onset of these signs, in spite of intravenous fluids and anti-shock treatment. In only 1 of them (case 1) did we isolate *Staph. aureus* from the bowel.

Reports from many workers indicate that staphylococcal gastro-enterocolitis is a serious complicating factor in antibiotic therapy, particularly during therapy with oxytetracycline (Jackson et al. 1951, Janbon et al. 1952, Terplan et al. 1953, Dearing and Heilman 1953, Fairlie and Kendall 1953, Gardner 1953). These cases occur both with and without the finding of a *Staph. aureus*; and pathologically some are described as having pseudomembranous ileocolitis, whereas others show no disturbance of the mucosa. Little abnormality was noted in the mucosa of case 2, but case 1 showed patchy areas of early inflammation throughout the gastro-intestinal mucosa and watery pea-green stools. Many workers suggest that the sudden onset, dramatic progress, and clinical features of this gastro-enterocolitis resemble

TABLE V—SYNDROMES NOT ASSOCIATED WITH RESISTANT *Staph. aureus*

Case no.	Age (yr.)	Sex	Disease	Side-effects	Day of appearance	Bacteriology
15	12	F	Sonne dysentery	Urticaria	10	..
46	4	F	Sonne dysentery	Urticaria	7	..
47	43	M	Pneumonia	Urticaria, angio-oedema, joint pains	4	..
48	8	F	Sonne dysentery	Transient erythema	8	T.C., no growth
49	5	F	Sonne dysentery	Transient erythema	8	..
50	4	F	Sonne dysentery	Transient erythema	9	T.C., no growth
51	2 ^{1/2}	M	Sonne dysentery	Transient erythema	10	T.C., no growth

T.C., throat culture.

Asiatic cholera, and Janbon et al. (1952) call this syndrome *le syndrome cholériforme de la terramycine*.

The pathogenesis of these conditions is not yet clear. At present most workers consider that the resistant staphylococci become pathogenic when the other organisms are suppressed by broad-spectrum antibiotics or by the combination of penicillin and streptomycin. The view has been advanced that these drugs might actually stimulate the organisms to pathogenicity or to the production of toxins (Fairlie and Kendall 1953, Prissick 1953). Fairlie and Kendall support this view because some of their patients exhibited symptoms as early as twenty-four hours after antibiotics were first given. However, in our cases, where a resistant staphylococcus was involved, the onset was usually on the fourth or fifth day after the start of antibiotic therapy. Since Linsell and Fletcher (1950) and Di Caprio and Rantz (1950) found that the normal flora present before therapy was either eliminated or much reduced shortly after the start of therapy (Linsell and Fletcher stated that coliform bacilli and faecal streptococci were entirely eliminated in all of their cases by the third day), we are of the opinion that the staphylococci isolated in our cases became pathogenic after the normal flora had been suppressed. The gastro-intestinal upsets observed suggest that the staphylococci might secrete an enterotoxin similar to, or the same as, that observed in food-poisoning due to staphylococcal enterotoxin. This well-known syndrome is clinically similar to the staphylococcal gastro-enterocolitis we describe.

Hofer and McCaskey (1954) summarised the many mechanisms which may play a part in an antibiotic-resistant "superinfection" into three groups: (1) environmental factors (e.g., where suppression of sensitive organisms upsets possible symbiotic states); (2) stimulation of bacterial growth by antibiotics; and (3) tissue alterations. Under this last heading they point out that aureomycin, oxytetracycline, and chloramphenicol may cause clinical vitamin deficiency. They suggest that the alteration of the bowel flora resulting in vitamin-B deficiency may also favour acute enterocolitis as a result of local tissue alteration and, perhaps, decreased body resistance.

3 of our patients developed urinary infections due to resistant staphylococci; these cleared up on therapy with antibiotics to which the staphylococci were sensitive. The predominance of this organism in the urine after the use of oxytetracycline has been noted by other workers (Finland et al. 1950, Jackson et al. 1951, Womack et al. 1952).

It will be observed that the 5 cases in which phage-typing was done indicate that three different organisms were involved. Indeed, cases 1 and 12, sisters who were admitted together and who developed side-effects on the same day, acquired their "superinfections" from two different phage-pattern strains.

We suggest that the organism was probably harboured by the patients on admission, because these cases occurred in different wards, at different times, and with different nurses. On two occasions 2 sisters have been admitted to hospital and have developed syndromes due to oxytetracycline-resistant staphylococci with the same chronological sequence of events (cases 5 and 6; and cases 1 and 12). In addition, the resistant organism was not isolated from the upper respiratory tract of the nurses and doctors in contact with the latter 2 sisters.

Dearing and Heilman (1953) treated gastro-enterocolitis due to resistant staphylococci by discontinuing the oxytetracycline and giving erythromycin, obtaining good clinical results and the elimination of the staphylococci from the bowel. However, they cite the finding of a strain of *Staph. aureus* resistant to erythromycin in a patient in whom this drug was used, and forecast that more resistant strains will develop. So it appears that

TABLE VI—RESISTANCE TO ANTIBIOTICS OF STAPHYLOCOCCI ISOLATED

Case no.	Resistant to	Sensitive to	Phage-type
1	P, A, O	C, S	7/54/77
5	P, A, O	C, S	..
6	P, A, O	C, S	..
7	P, A, O	C, S	75/77
9	P, A, O, S	C	75/77
10	P, A, O, S	C	..
11	P, A, O, C	C, S	75/77
12	P, A, O	C, S	6/47/53/75 +
18	P, A, O	C, S	..
19	P, A, O, C	C, S	..
20	P, A, O	C, S	..
21	P, A, O	C, S	..

A, aureomycin. C, chloramphenicol. O, oxytetracycline. P, penicillin. S, streptomycin.

disturbances of the host-parasite-drug relationship are not going to be overcome by finding new antibiotics.

Finland et al. (1954) raise a doubt about the value of erythromycin in staphylococcal diarrhoea, stating that in most of these cases the stopping of treatment with the offending antibiotic leads to fairly prompt cessation of diarrhoea, and the staphylococci clear readily from the stools, even when staphylococci are still being obtained from cultures of other infected materials. We cannot comment on the rate of clearance of this organism from the bowel; but, as cases 5 and 7 showed, *Staph. aureus* persisted for a considerable time (eight and five days respectively) as a pure growth on throat culture. In view of this we think it is probably advantageous to the patient to be given an antibiotic to which the organism is sensitive. The clinical management of the diarrhoea caused by resistant organisms is stated by Hofer and McCaskey (1954) to be extraordinarily difficult. However, Finland et al. (1954) have shown that the incidence of watery diarrhoea associated with the administration of oxytetracycline or of aureomycin can be materially reduced, although not entirely prevented, by decreasing the dosage of these antibiotics. They also draw attention to the precipitating effect of the administration of cathartics in producing this diarrhoea, and state that cathartics should be avoided.

We wish to point out that 2 of our patients developed syndromes due to a resistant staphylococcus, but on the elimination of this organism they had a second course of oxytetracycline with no ill effects (cases 10 and 21).

Dearing and Heilman (1953) state that in their locality it was only after several years' use of oxytetracycline and aureomycin that resistant strains of *Staph. aureus* were produced, but the resistant strains we have observed were found in the first fourteen months (from October, 1952, to December, 1953) of the use of oxytetracycline.

The resistance and sensitivity of the staphylococci to different antibiotics are shown in table vi. Of fourteen staphylococci isolated twelve were cultured to assess their resistance to antibiotics: they were all resistant to penicillin, aureomycin, and oxytetracycline; two were resistant to streptomycin in addition; and a further two were resistant to chloramphenicol in addition.

3 urticarial reactions were noted: one on the fourth day, one on the seventh, and one on the tenth. Case 47 had severe angioedema of face and eyes as well as an urticarial reaction. Johnston and Cazort (1953) report a case similar to this but with severe cyanosis of extremities, lips, and face; it developed on the eighth day of therapy, and the patient had had a previous course of oxytetracycline.

Transient erythema was observed in 4 cases, sometimes with mild pyrexia but with no throat lesions. The rash cleared in all cases within twenty-four hours, and usually there was no general upset. Throat cultures in 3 of these patients were negative. These signs were

observed from the eighth to the tenth day. It therefore seems that, although there are exceptions, syndromes caused by resistant staphylococci develop before the eighth day after the start of treatment (most commonly on the fourth or the fifth day) and syndromes due to drug sensitivity develop on the eighth day or later.

There were 2 deaths, and 2 children with the scarlatinal syndrome were sufficiently ill to cause anxiety. These 2 girls, sisters, had severe diarrhoea causing dehydration, and their throat lesions prevented them from swallowing; accordingly they needed intravenous fluids for several days. One of the deaths (case 1) was particularly tragic because the child was only a carrier of *Salmonella typhimurium* and on admission was clinically healthy.

This report emphasises that the broad-spectrum antibiotics are not without their dangers, all the more so because we do not yet fully understand the reasons for some of the upsets involved. Our mortality is 0·3%. Jackson et al. (1951), treating 91 pneumonia patients with oxytetracycline, observed diarrhoea in 37 cases, a resistant staphylococcus being the only, or the predominant, organism in 12 out of 18 cases in which cultures were attempted. It was thought that the staphylococcal gastro-enterocolitis might have been an important contributory factor in the fatal outcome of at least 3 of the 7 patients who died. We emphasise that the broad-spectrum antibiotics should not be used for trivial and minor illnesses.

Is the relative benignity of the side-effects we observed due to the fact that we used a smaller dosage than is generally used? Or do our local staphylococci possess invasive, pathogenic, or toxin-producing qualities different from those of brethren elsewhere? Or is it because most of our patients belonged to the younger age-groups and had not got debilitating disease? The answer to these and other questions lies in the search ahead of us.

Summary

An incidence of about 8% of side-effects was observed in 603 cases treated with oxytetracycline.

The side-effects were divided into those associated with coagulase-positive staphylococci resistant to oxytetracycline and those in which no resistant organism was isolated.

Broad-spectrum antibiotics should not be used in minor illnesses.

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SEE-SAW RELATIONSHIP BETWEEN HYPERTHYROIDISM AND MYASTHENIA GRAVIS

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HYPERTHYROIDISM with myasthenia gravis has rarely been reported. Rennie (1908) described the first recorded case in Australia and referred to previous publications by Meyerstein (1904), Loeser (1904), and Brissaud and Bauer (1905).

It was later realised, as pointed out by Brain and Turnbull (1938), that external ocular paresis in association with thyrotoxic myopathy was often confused with myasthenia gravis in the past. Doubt must therefore be cast on all reported cases in the absence of confirmatory neostigmine tests. Allowance must also be made for the observation by McEachern and Ross (1942) that thyrotoxic myopathy itself shows a limited neostigmine response. Thus Thorner (1939), listing 24 reported cases, could find only 7 where the diagnosis was beyond doubt. It has been suggested that Rennie's original case was really one of exophthalmic ophthalmoplegia with thyrotoxic myopathy (Cohen 1946).

In proved cases of the combination of these two diseases there has been considerable divergence of findings as regards the effect of anti-thyroid treatment on the signs of myasthenia gravis. Partial thyroidectomy has either relieved or cured the myasthenia gravis (Kowallis et al. 1941, Thorn and Eder 1946, Sheldon and Walker 1946). Bartels and Kingsley (1949) found in a series of 12,962 cases of exophthalmic goitre 4 with complicating myasthenia gravis; they considered that anti-thyroid treatment produced no change in the myasthenic picture.

On the other hand, a "see-saw balance" between the two conditions has been described, the signs of myasthenia gravis increasing as the signs of thyrotoxicosis diminish, and vice versa. Thorner (1939) recorded a case of myasthenia gravis where the onset of thyrotoxicosis was attended by a lessening in the myasthenia, and radiotherapy of the thyroid gland made the myasthenia worse. Carrying his trial further he found that the myasthenia gravis improved under treatment with thyroid extract, but at the expense of inducing thyrotoxicosis. Thyroidectomy has been shown by Cohen (1946) and McEachern and Parnell (1948) to worsen the myasthenia gravis; and thiouracil therapy has been shown by Thorn and Eder (1946), Cohen (1946), and McEachern and Parnell (1948) to increase the myasthenia gravis. Greene (1949) has also pointed out the see-saw balance.

The case presented here shows clearly the see-saw relationship between these two conditions.

Case-report

A woman, aged 29, first reported to the medical outpatient department in August, 1948, with four months' history of illness. Three months after a normal confinement she had developed typical thyrotoxicosis, with sweating, tremors, nervousness, weakness, loss of weight, diffuse thyroid enlargement, and bilateral exophthalmos. Her doctor started treatment with methyl thiouracil 300 mg. a day for four weeks followed by a maintenance dose of 100 mg. a day. In eight weeks the patient had gained 7 lb. in weight and was feeling much steadier, but her thyroid had become larger. At that time, however, she developed a drooping of the right eyelid, more pronounced at the end of the day, when her legs felt weak and she had difficulty in swallowing. It was because of the ptosis that she was referred initially to the eye department, and thence to the medical outpatient department. Her mother had developed at puberty non-toxic thyroid enlargement, which has persisted until now. A sister in 1950

had thyrotoxicosis necessitating thyroidectomy. Two other siblings are alive and well. On examination the patient was well built, with moderate bilateral exophthalmos but no clinical signs of thyrotoxicosis. There was ptosis of the right upper eyelid, more pronounced after repeated movements. Vision was normal, and nothing abnormal was detected elsewhere in the body. A Wassermann reaction was negative, and a radiograph of the skull was normal.

Treatment.—A test dose of neostigmine 1.5 mg. by injection abolished the ptosis completely for an hour. Thiouracil was therefore discontinued, and two or three tablets daily, each containing prostigmine 15 mg., were sufficient to control the signs of myasthenia gravis.

November, 1948.—The patient had again begun to lose weight, with signs of thyrotoxicosis, the plasma-cholesterol level being 135 mg. per 100 ml. Exophthalmos was more severe, and there was constant diplopia, with paralysis of the left superior oblique muscle. The pulse-rate had risen to 122. An injection of neostigmine 1.5 mg. caused retraction of the previously ptosed lid to a greater extent than on the other side, exposing a band of sclera. Potassium iodide gr. 6 daily was given with little or no improvement in the thyrotoxic picture.

January, 1949.—Thiouracil was again exhibited in full dosage. Within six weeks the thyrotoxicosis was satisfactorily under control, but the myasthenia gravis had become extreme, with drooping of both eyelids, general weakness, and slurring of the speech.

May, 1949.—Thiouracil was again discontinued, and the myasthenia gravis gradually improved at the expense of a mild recurrence of thyrotoxicosis. Radiography of the chest showed mild bilateral tracheal compression. The urinary excretion of creatinine was 176 mg. per 100 ml., the plasma-cholesterol level was 155 mg. per 100 ml., a glucose-tolerance test was normal, and the basal metabolic rate (B.M.R.) was +29%. Small doses of thiouracil were given in an attempt to strike a balance but had to be reduced when the myasthenia became more severe.

January, 1950.—The B.M.R. was +18%, and plasma-cholesterol level 300 mg. per 100 ml.; diplopia was still present, but evidence of thyrotoxicosis was minimal. Thiouracil therapy was again stopped.

March, 1950.—Thyrotoxic signs had reappeared, and for a fourth time thiouracil was used, with resultant control of the thyrotoxicosis and a worsening of the myasthenia gravis.

April, 1950.—Small doses of thiouracil were again given.

August, 1950.—Thiouracil treatment was stopped. The patient's appearance in October, 1950, is shown in fig. 1.

January, 1951.—Thyrotoxicosis was again manifest. Thiouracil was given once again, with improvement in the thyrotoxicosis and increase in myasthenia.

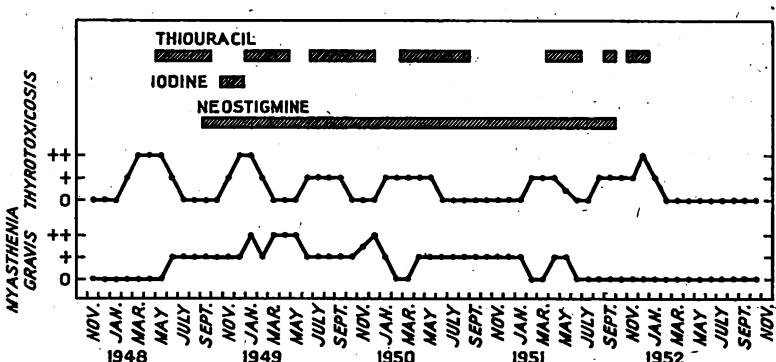


Fig. 2.—Effect of treatment on combined thyrotoxicosis and myasthenia gravis: note see-saw relationship.

From June, 1951, the requirements of neostigmine, which was originally instituted in September, 1948, decreased progressively. Although a further course of thiouracil was given in November and December, 1951, myasthenia gravis did not recur. The effect of the treatment is shown in fig. 2.

February, 1952.—The patient appeared to have achieved natural recovery, and she has needed neither thiouracil nor neostigmine since then.

Follow-up.—Neither thyrotoxicosis nor myasthenia gravis has recurred. The patient's present condition is good. The exophthalmos persists, together with slight ptosis of the right upper eyelid. The patient's appearance in September, 1953, is shown in fig. 3. Eye movements are full, and the patient's weight is steady. The thyroid enlargement has regressed slightly.

Discussion

McEachern and Parnell (1948) have classified the neuromuscular disorders that may complicate thyrotoxicosis as follows:

- (1) Exophthalmic ophthalmoplegia, with oedema, fatty infiltration, and swelling of the extraocular muscle-fibres.
- (2) Acute thyrotoxic encephalomyopathy, presenting with bulbar palsies and relieved by anti-thyroid measures (Waldenström 1945).
- (3) Chronic thyrotoxic myopathy, characterised by weakness, wasting, and fasciculation of voluntary muscles.
- (4) Familial periodic paralysis.
- (5) Myasthenia gravis.

The present case and previously published cases (see table) supply apparently contradictory evidence about the effect of anti-thyroid treatment on myasthenia gravis. It seems therefore relevant to consider in detail the diagnostic criteria upon which the differentiation is



Fig. 1.—Patient in October, 1950.



Fig. 3.—Patient in September, 1953.

EFFECT OF ANTI-THYROID TREATMENT ON MYASTHENIA IN THYROTOXICOSIS

Authority	Case no.	Age (yr.)	Sex	Disease first appearing	Treatment	Effect on myasthenia gravis
<i>Thyrotoxic myasthenia</i>						
Kowallis et al. (1941) ..	1	39	F	Thyrotoxicosis	Partial thyroidectomy	Recovery
Carson and Keynes (1942) ..	2	?	?	?	Partial thyroidectomy (toxic adenoma removed) and thymectomy	Improved, remained thyrotoxic
Sheldon and Walker (1946) ..	3	50	F	Thyrotoxicosis	Partial thyroidectomy	Recovery
Thorn and Eder (1946) ..	4	50	F	?	Partial thyroidectomy	Improved
<i>Myasthenia gravis</i>						
Thorner (1939) ..	5	20	F	Myasthenia gravis	X rays	Worse
Carson and Keynes (1942) ..	6	?	M	?	Partial thyroidectomy Thymectomy	Worse Improved
Thorn and Eder (1946) ..	7	59	F	Myasthenia gravis	Thiouracil	Worse
Cohen (1946) ..	8	27	F	Myasthenia gravis	Iodine Thiouracil Partial thyroidectomy	Worse Worse Appears to have died of myasthenia
McEachern and Parnell (1948)	9	38	F	Thyrotoxicosis	Partial thyroidectomy	Worse
	10	32	F	Myasthenia gravis	Iodine Thiouracil Thyroid	Worse Worse Improved
Greene (1949) ..	11	?	?	Thyrotoxicosis	Thiouracil Partial thyroidectomy Thymectomy	Worse Worse Improved
Maclean and Wilson (present case) ..	12	29	F	Thyrotoxicosis	Iodine Thiouracil	No change Worse

made between true myasthenia gravis and thyrotoxic myopathy :

Myasthenia gravis

Creatinuria
Perhaps thymic enlargement
Lymphocytosis
Perhaps ocular palsies
Weakness worse at end of day
Drooping of eyelids
Frequently bulbar palsies
Much relief from neostigmine

Thyrotoxic myopathy

Creatinuria
Perhaps thymic enlargement
Lymphocytosis
Perhaps ocular palsies
As weak in the mornings
Retraction of eyelids
Occasional bulbar palsies
Limited relief from neostigmine

It has been held that bulbar palsies do not occur in thyrotoxic myopathy (Greene 1949), yet acute thyrotoxic encephalomyopathy does, and Laurent (1942) records 2 cases of severe thyrotoxicosis in which pronounced dysphagia, dyspnoea, and weakness, relieved by neostigmine, developed a week or two before death. Creatinuria, thymic enlargement, and lymphocytosis are common to both conditions. In myasthenia gravis the myasthenia is more severe at the end of the day, and the eyelids droop, whereas in thyrotoxicosis they are retracted. It seems not impossible, however, that myasthenia may relax the levator palpebrae spasm.

Response to neostigmine is usually held to be pathognomonic of myasthenia gravis, yet neostigmine has been observed to relieve the myasthenia in thyrotoxic myopathy (McEachern and Ross 1942, Waldenström 1945), and this cannot therefore be used as an undisputed means of differentiation.

Myasthenia in association with thyrotoxicosis may be divided into two main groups :

(1) Thyrotoxic myasthenia responds to neostigmine and is relieved or cured by anti-thyroid treatment.

(2) Myasthenia gravis is in most cases relieved by the onset of thyrotoxic symptoms and made worse by anti-thyroid measures. Thymectomy sometimes improves it (Greene 1949, Carson and Keynes 1942). They show a definite see-saw relationship between thyrotoxicosis and myasthenia gravis, the one waxing as the other wanes.

The present case is therefore clearly one of myasthenia gravis, being produced at will by initiating anti-thyroid treatment, and resembling the case reported by Thorner (1939), who achieved remission of myasthenia gravis with thyroid extract at the expense of inducing thyrotoxicosis.

The muscular weakness and easy fatigability in myasthenia gravis are due to a muscular metabolic defect

leading to failure in chemical transmission at the neuromuscular junction, where normally acetylcholine is liberated. The administration of the anticholinesterase neostigmine, by protecting acetylcholine from destruction, rapidly alleviates the symptoms. Normal blood and muscle cholinesterase levels have been obtained in such cases, and the cause must be either deficient production of acetylcholine or the presence of a curare-like substance. If such a substance does exist, the cuff experiments of Walker (1938) would indicate that it is locally produced by muscular activity. A raised blood-thyroxine level either diminishes the production of, or inactivates, such a curare-like substance, leading to improvement in the myasthenia.

The rôle of the thymus in myasthenia gravis is obscure. It has often been found enlarged, but its size seems to have no bearing on the duration or the extent of the clinical picture according to Carson (1942). Keynes (1949), reporting on 120 survivors of thymectomy who did not have tumours, showed that 65% were virtually cured, 25% improved, and 10% unchanged. The improvement, however, is gradual, and may take a year before the optimal benefit is received.

Thyrotoxic myasthenia responding to neostigmine must be presumed to have a similar differential aetiology. No cuff experiment seems to have been done here, and the constant level of the myasthenia through the day argues a central rather than a local cause. Perhaps a constantly high blood-thyroxine level causes deficient production or rapid destruction of acetylcholine at the motor nerve-endings, thus resulting in myasthenia.

The coincidence of myasthenia gravis and malignant exophthalmos in the absence of thyrotoxicosis reported by Zondek and Ticho (1951) seems to incriminate the pituitary gland, and both conditions were in fact improved by X-ray therapy to the pituitary region. We therefore make the following suggestions :

(1) That thyrotoxic myasthenia is due to rapid destruction or defective production of cholinesterase at the myoneural junction, secondary to a high circulating thyroxine level.

(2) That myasthenia gravis is due to a curare-like substance produced locally at the site of muscle activity, and inactivated or not produced when the blood-thyroxine level is high.

(3) That there is a direct inverse relationship between the thyroid and the thymus glands, probably both under influence of the pituitary gland.

(4) That the action of the thymus gland in the production of myasthenia gravis is still obscure and appears to be secondary.

Summary

A case is presented showing the typical "see-saw" relationship between thyrotoxicosis and myasthenia gravis.

Such a relationship is always present when these two conditions are found together, and surgical intervention must therefore be regarded as dangerous.

The condition is self-limiting, and in the present case a middle course was steered between the exhausting effects of both diseases by the intermittent use of thiouracil.

Myasthenia coincident with thyrotoxicosis may be either thyrotoxic myasthenia or true myasthenia gravis. Anti-thyroid measures have directly opposing effects in these two conditions, relieving the thyrotoxic myasthenia and worsening the myasthenia gravis.

A possible mechanism by which myasthenia is produced in these diseases is suggested.

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SURGICAL TREATMENT OF ACUTE OSTEITIS IN CHILDHOOD

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BOTH the urgency and the extent of the optimal surgical treatment of acute haematogenous osteitis have been sharply disputed for over twenty years (*Proceedings of the Royal Society of Medicine* 1932). The introduction of penicillin, which made possible remarkable control over staphylococcal infections as a whole, intensified this controversy. Wilkinson (1951) remarked that the question whether the administration of penicillin should be accompanied by extensive emergency surgical procedures "could be settled with certainty only by a large series in which alternate patients were operated on. Experience is still fallacious and judgment difficult even after the advent of the antibiotics."

We describe here a trial planned to decide this question. The trial covered three years from January, 1949. At that time there seemed to be considerable differences between the practice of different groups of experienced workers. Agerholm and Trueta (1946), Trueta and

Agerholm (1948), and Tucker and Hollenberg (1948) held that penicillin treatment had not eliminated the need for extensive emergency surgery, but that incision of the abscess and drilling of the affected bone could be followed by primary closure of the wound. Dennison (1948) had advocated a similar procedure, without drilling of the bone. By contrast, Altemeier and Helmsworth (1945) and Altemeier and Wadsworth (1948) had decided that "emergency surgical intervention is usually unnecessary" in cases adequately treated with penicillin; they believed in allowing a clinically demonstrable abscess to form, which could be evacuated days or weeks after admission. Aird (1946), Hudson (1946), and Wilkinson (1948) appeared to agree broadly with this more conservative approach. Most conservative of all, Higgins et al. (1947) claimed that, in children, it was necessary only to aspirate pus which "formed outside the bone," at an unspecified stage of the disease. Unfortunately we felt unable to accept their conclusions at that time, because more than half their patients were less than a year old, several had already been ill for some weeks at the time of admission, and the small doses of penicillin which they recommended suggested that they had been dealing with relatively mild cases.

We found it impossible satisfactorily to assess the relative merits of these two contradictory schools of thought, because of two main omissions from their reports: there was no clear clinical definition of the type of cases treated, and the evidence did not suffice for realistic and objective comparison of the results. We therefore decided to treat a consecutive series of suitably defined cases alternately by Trueta's method and by a more conservative method (calling the two treatment groups "drilled" and "conservative"), and to try to find a satisfactory criterion for assessing and comparing the results.

Our trial was planned to supply the answers to the following three practical questions:

1. What are the clinical indications for local intervention to remove pus?

2. Where indicated, how urgent is this local intervention?

3. Should the local intervention consist in incising the abscess and drilling the affected bone, or can an open operation be avoided altogether?

Methods

SELECTION OF MATERIAL

We felt strongly that the cases for inclusion in the trial must be carefully selected from the full range of cases of acute osteitis admitted to hospital, with two main requirements in mind: (1) our series must be sufficiently uniform for comparison of results between one case and the next to be valid; and (2) the question of surgical treatment must be a real issue in every case, both so that the trial should be really critical and so that there should be no ethical objection to operation if so indicated by our method of random selection.

We selected for the trial all cases which on admission satisfied the following criteria:

Age: 2-12 years.

Grade: severe (see below).

Duration on admission: 48-168 hours.

Bone involved: major long bone of a limb.

Treatment before admission: no antibiotics.

Organism: sensitive to penicillin.

The lower age-limit was set at 2 years in accordance with the views of Green (1935); and although we do not fully agree with these views, our original decision proved satisfactory for the purposes which we had in mind. The upper age-limit was determined by the fact that our experiment was confined to cases in the children's wards.

Grade was judged in terms of a clinical classification of the disease which we had devised for ourselves, for lack of a satisfactory one in published reports. This classification will be described fully elsewhere, together with the details of the 96 cases of acute osteitis admitted during the trial. The severe case over the age of 1 month is defined as one in which

all the essential symptoms of the disease are fully developed within 72 hours of the onset of pain. These symptoms are taken to be: complete disability of the affected limb, pain sufficient to interfere seriously with sleep, complete anorexia, malaise sufficient to suppress all interest in recreation of any kind, and obvious feverishness. Of 50 consecutive such cases, delirium occurred in half and vomiting in a third; their temperatures on admission were 101°–107°F, and the blood-culture on admission was positive in 30. Possibly our mild cases (in which these symptoms never became fully established, or did so after more than 72 hours) correspond roughly with the "subacute" cases of some workers (*Proceedings of the Royal Society of Medicine* 1932, Dennison 1948). Such cases were excluded from the trial because we knew that in them rapid recovery could be expected with penicillin alone, without any local intervention.

Duration.—Those whose penicillin treatment was started within 48 hours of the onset were excluded for the same reason. (Of 14 such patients only 1 required local intervention.) Those whose illness was of more than a week's duration on admission were excluded because we felt that after this stage the nature of the surgical treatment was unlikely materially to affect the local lesion: the prognosis was known to be very bad, and we hoped that there would be too few such cases for purposes of comparison. Only 1 case had to be excluded on these grounds; this was a severe case of acute osteitis of the humerus of 15 days' duration, in which the abscess burst through the skin on the evening of admission.

Only *major long bones* were included because the surgical problems raised by osteitis of small and flat bones are very different, and are often individual to the particular bone.

Patients who had had any significant *antibiotic therapy* before admission were excluded because their inclusion would have introduced a variable factor which we could neither control nor allow for properly in the final assessment.

The *sensitivity of the organism* had to be defined because penicillin was regarded as an essential part of the treatment: only 1 case had to be excluded because of a resistant organism (*Staphylococcus aureus* resistant to 2000 units per ml.).

By this method of selection the number of cases included in the trial was 31 of a total of 96 cases of acute osteitis seen during the 3 years. This could hardly be described as the "large series" called for by Wilkinson (1951); but we believe it to be a far more informative series, in relation to the questions which we were trying to answer, than a much larger unselected series would have been.

The selected cases were allotted on admission alternately to one of the two treatment groups—"drilled" and "conservative"—according to the next available symbol on a chart prepared with a statistician's advice.

ASSESSMENT OF RESULTS

Our second major problem was to devise a satisfactory way of measuring the success of treatment, so that the results in our two treatment groups could be objectively compared. The method of radiographic comparison used by Agerholm and Trueta (1946) was rejected as insufficiently precise, and of doubtful relevance to the patient's welfare provided the end-result was satisfactory. The criteria described (*Proceedings of the Royal Society of Medicine* 1932) were rejected as irrelevant to cases treated with penicillin in adequate dosage. We eventually decided to try to measure the effect of the operative treatment (or lack of it) on the duration of the disease, by recording the number of days which elapsed after admission to hospital until the patient was allowed to use the limb normally, without splints (always provided that the decision to allow full activity was vindicated by satisfactory subsequent clinical and radiographic progress during a reasonable follow-up period). McAdam (1945) had published this information about some of his cases.

This method appeared to have the advantages that the result could be expressed numerically; it was an expression of what mattered most to the patient; and, above all, it was a fact and not a personal impression. Of course personal judgment did enter into the decision to allow full activity; but the decision in each case was made

by the same group of three people and in accordance with well-defined clinical and radiographic signs (Neligan and Warrick 1953), so that there was a high degree of uniformity and minimal scope for any unconscious personal bias. The method appeared to us to be satisfactory in practice. In 1 "drilled" case (table I, case 9) infection recurred two weeks after the patient was first allowed to walk; a further period of restricted activity was necessary, and the duration of disability was reckoned to the end of this second period.

When it came to the final assessment, however, it was clearly unrealistic to compare the results in a weight-bearing bone, such as the tibia, with those in the arm-bones or fibula; so the series was ultimately reduced to the 23 cases in which the femur or the tibia was involved. This need had been foreseen, and the chart used for allocating the selected cases to the two treatment groups on admission was designed accordingly, with separate subgroups for each bone.

General Management

The penicillin therapy and general management of the cases in the two treatment groups was identical in all respects, except for minor differences implicit in the different surgical techniques:

Penicillin.—50,000 units intramuscularly was administered 3-hourly for 21 days at least, and thereafter until the bone was free of tenderness and the erythrocyte-sedimentation rate (E.S.R.) was decreasing steadily and had reached about 20 mm. in 1 hour (Westergren).

Intravenous Therapy.—Plasma, blood, or electrolyte solutions, as indicated, were given in 2 "drilled" and 3 "conservative" cases.

Immobilisation was achieved by padded plaster back-splint or a sling in all cases where it could make the patient more comfortable. To avoid disuse osteoporosis, such immobilisation was stopped as soon as the limb was free of pain and any wound was healed. But in 5 cases the limb was put into a plaster cast when the patients were sent home at the end of the course of penicillin, because we thought that these patients were unlikely to keep off the leg voluntarily until we gave permission for weight-bearing.

Free Activity.—The decision to allow this depended on a satisfactory clinical condition and certain radiographic criteria (Neligan and Warrick 1953). Absence of any decalcification within 28 days of the onset, or the first signs of recalcification in previously decalcified areas, were taken to indicate that a fracture need not be feared. The only exception was case 14 (in the "conservative" group), where decalcification was so gross that we waited for the third set of films showing recalcification before regarding the tibia as safe for weight-bearing.

Surgical Treatment

In the "drilled" group the surgical treatment was that described by Trueta and Agerholm (1948). But we have subsequently found out (Trueta 1952) that in two details our technique differed from that used by these workers:

1. In many of our cases the wound was not examined until the 10th day after operation, when the stitches were removed. This omission, however, does not appear to have been directly related to delay in healing; and a haematoma was evacuated on the 4th day in the only case where the wound broke down completely and required secondary suture (case 12).

2. In 9 of the 12 cases interrupted catgut sutures were used to approximate the periosteum or the muscle sheath, or both, before closing the skin. This procedure was very definitely related to delay in healing of the wound (see table I); but in no case did this delay cause postponement of weight-bearing. Trueta states that he too had noted this tendency of buried catgut to interfere with the healing of the wound, and had eliminated periosteal sutures from his technique some years previously.

In the "conservative" group, by contrast, there was no detailed description of any accepted method of local treatment for us to follow. Table II shows that in the first 5 cases in this group we failed to achieve the objective of avoiding open operation. In these 5 cases aspiration was omitted or done in a way which we now regard as

half-hearted and ineffective; but the operation was confined to incision of the periosteum and evacuation of the underlying pus, followed by suture of the wound. When once we had realised that the subperiosteal abscess could be adequately emptied by thorough aspiration, carried out as soon as possible and repeated if necessary, the whole picture altered. We were able, by this means, to avoid operation in 4 of the last 6 cases (the remaining 2 required no local treatment for the evacuation of subperiosteal pus). A further 15 similar cases have since been treated satisfactorily by aspiration alone.

Where indicated, we now carry out the first aspiration within hours of starting penicillin treatment. The patient is given an appropriate dose of sodium quinalbarbitone ('Seconal Sodium') orally and morphine hypodermically about three-quarters of an hour before the aspiration. With a full aseptic technique, and using autoclaved instruments, a short, wide-bore needle (a "taking" transfusion-needle, B.S.W.G. 13, 3.5 cm. long,

has proved suitable and convenient) is plunged through the tissues into contact with the bone at the site where the abscess is judged to be maximal; the thick pus may flow out slowly under pressure, or may need to be aspirated. If no pus is found at the first attempt, the needle is withdrawn slightly and reinserted down to the bone at a different angle. Where the abscess is very extensive we have thought it wise to aspirate it at two separate sites, to ensure adequate emptying; but this may not be necessary at subsequent aspirations, when the material is more fluid. A small dressing is placed over the puncture-hole for a few hours afterwards. We have not injected penicillin into these abscesses; but when an infected joint has been aspirated penicillin has been injected in the usual way (cases 14 and 21).

The unequivocal indication for initial local intervention is, we believe, the presence of a subperiosteal abscess; but we have not found it necessary to wait for the formation of an abscess demonstrable on ordinary

TABLES I AND II—23 SELECTED CASES OF SEVERE ACUTE OSTEOITIS OF FEMUR AND TIBIA OF MORE THAN 48 HOURS' DURATION IN PATIENTS AGED 2-12 YEARS

Case no.	Age (yr.)	Duration on admission (hr.)	Site	ml. of pus (estimated)	" DRILLED " GROUP						Follow-up	
					Period (days) from admission till					Duration (yr.)	Latest radiographs	
					Wound healed	Afebrile	Free of tenderness	Penicillin stopped	Weight-bearing allowed		Sclerosis	Broadening
1	4	50	Femur upper shaft	2	11	4	16	35	72	4	None	Mild
2	8	104	Tibia lower shaft	75	28*	5	10	28	61	4½	None	Mild
3	5	50	Tibia lower shaft	5	11	4	11	21	33	4	None	None
4	8	56	Femur upper shaft	0	9*	6	13	22	36	4	None	None
5	9	82	Tibia lower shaft	0	25*	7	16	21	47	4	None	Mild
6	6	145	Tibia upper shaft	50	11	3	11	21	22	3½	None	Mild
7	8	96	Femur upper shaft	5	26*	7	10	26	55	2½	None	Mild
8	9	144	Tibia lower shaft	10	28*	4	15	29	42	2½	Mild	None
9	3	70	Tibia bipolar	60	32*	10	25	(32) (+24)	(62) 152	3	None	Mild
10	9	144	Tibia lower shaft	30	19*	5	20	23	74	2	None	Mild
11	11	57	Tibia lower shaft	15	55*	7	14	30	61	2	Mild	Mild
12	10	120	Femur lower shaft	2	73*	6	?	34	80	2	Mild	Mild
<i>Average</i>	..	91	27	6	15	29	61

* Interrupted catgut sutures used to close either the periosteum or the muscle sheath.

" CONSERVATIVE " GROUP

Case no.	Age (yr.)	Duration on admission (hr.)	Site	Period (days) from admission till						Follow-up		
				Aspiration (ml. of fluid in parentheses)	Operation	Afebrile	Free of tenderness	Penicillin stopped	Weight-bearing allowed	Duration (yr.)	Latest radiographs	
											Sclerosis	Broadening
13	11	144	Tibia lower shaft	1(4), 2(0)	2	4	22	24	80	4	Mild	None
14	3	120	Tibia upper shaft	16, 18 (knee)	9	18	26	32	121	4½	None	None
15	11	108	Femur lower shaft	..	2	4	37	37	65	4	None	Mild
16	7	130	Tibia upper shaft	4(25)	7	3	17	22	69	4	None	Moderate
17	12	104	Tibia lower shaft	2(25), 4(20)	5	6*	13	21	54	3½	None	Mild
18	12	108	Femur neck	8	20	31	68	3	None	None
19	3	56	Tibia upper shaft	1(10), 3(10), 5(14), 11(20), 16(10)	..	7	25	35	79	2½	None	Moderate
20	8	100	Tibia lower shaft	2(15)	..	5	17	23	31	2½	None	None
21	10	86	Tibia lower shaft	2, 3, 4, 5 (ankle)	..	8	16	22	35	2	None	None
22	2	90	Tibia upper shaft	1(30), 2(23), 4(35), 6(40), 8(33), 14(20)	..	8	11	27	46	2½	None	Mild
23	10	120	Tibia lower shaft	0(50), 1(8), 5(35), 8(30), 12(25), 16(48)	..	9	30	30	61	1½	Moderate	Mild
<i>Average</i>	..	106	7	21	28	64

clinical examination, as suggested by Altemeier and Wadsworth (1948), nor does our experience in case 14 suggest that it is safe to do so.

The difficulty is that it is usually impossible to detect fluctuation on ordinary clinical examination when the pus is in a tense collection deep to the exquisitely tender periosteum. But we know that a subperiosteal abscess is likely to be present in any severe case of acute osteitis where penicillin treatment has not been started within 48 hours of the onset of pain. If, in such a case, the tenderness extends along the shaft of the bone well beyond the limits of the affected metaphysis, with swelling of the overlying tissues, we act on the assumption that an abscess is present; for our experience suggests that this extension of tenderness is usually produced by extension of pus deep to the periosteum. If the patient is then examined under heavy sedation, so that tenderness is eliminated, the fluctuation is usually detectable. In this way the presence and the position of the abscess can be determined with certainty in the great majority of cases and the site of the aspiration planned accordingly. Failing this, we have been guided by the area of greatest tenderness, and have not failed to find the abscess with the aspirating needle since our first case.

We have repeated the aspiration as often as a fluctuant collection of fluid reaccumulates, or until the aspirated material is sterile on culture. Detection of fluctuation is much easier after the initial aspiration both because the tissues are less tense and tender and, we believe, because some of the fluid is relatively superficial, having leaked out from beneath the periosteum through the holes made by the needle.

Comparison of Results

The results of the trial, set out in tables I and II, show no significant difference between the two treatment groups, judging by our main criterion: the average number of days from admission until free weight-bearing was allowed and found to be safe was 61 for the "drilled" and 64 for the "conservative" cases. Examination of the two groups for factors likely to affect the prognosis shows only one significant difference: the average duration on admission in the "conservative" group was, by chance, some 15 hours greater than in the "drilled" group. Judging by the average duration of fever and of penicillin treatment, there is again no significant difference between the two groups. The average duration of tenderness, however, was shorter in the "drilled" group (15 as compared with 21 days); but in no case did the tenderness persist long enough to affect adversely the general management of the case, and its distribution did not suggest persistence of metaphyseal infection. A preliminary survey of the radiographic appearances up to the present time does not show any clear-cut difference between the two groups except that the amount of subperiosteal calcification is certainly greater in the "conservative" cases in the early stages. This follow-up is being continued to see whether there is any difference in the time taken for the affected bones to regain a normal appearance. The fact that in each case successive radiographs are showing a steady return towards normal is our justification for publishing the results after such a relatively short follow-up period.

In 2 cases the period of disability was unduly long:

Case 9.—This patient in the "drilled" group had a clinical recurrence of infection, as already mentioned, 2 weeks after he was first allowed to bear weight. In retrospect, we may have made a mistake in stopping his penicillin treatment on the 32nd day, after his E.S.R. had risen from 30 to 37 mm. in 1 hour (Westergren) during the previous week; but his course of penicillin was longer than the average for the series. Although the recurrence settled well with penicillin and immobilisation, and no further period of restricted activity has been necessary, he had a minor recurrence a year later during which he spontaneously discharged a minute sequestrum, and penicillin-sensitive *Staph. aureus* was grown from

material aspirated from his tibia. He had a further minor recurrence, due to the same organism, another year later, and is regarded as a possible chronic case. This result is most unsatisfactory.

Case 14.—Our failure in this case in the "conservative" group, on the other hand, can confidently be attributed to our inexperience of the method. His operation was delayed for 9 days after admission, because of severe vomiting and diarrhoea among other factors; no aspiration was carried out during this period because we had not yet realised how much can be achieved in this way. This was the one case, therefore, in which an abscess obvious on ordinary clinical examination was allowed to develop, and in the light of subsequent experience we have no doubt that this avoidable delay in local intervention caused the gross decalcification of the tibia which occurred during the next 10 weeks; this was quite out of proportion to what we saw in any other case. This was also the only case in either group in which septic arthritis developed during penicillin treatment.

Conclusions

Any conclusions are applicable only to the type of case included in the trial. Some of the most difficult surgical problems in the treatment of acute osteitis arise in the newborn, and in older children whose lesion is in the neck of the femur; our results are not strictly relevant to these problems, since the newborn were deliberately excluded and only 1 older child with a lesion of the neck of the femur chanced to qualify for inclusion. But we think that the principles suggested by our results can be applied to these problems, and to lesions of short or flat bones.

We think that these principles, in terms of our initial questions, are as follows:

1. The clinical indications for local intervention are the signs of a subperiosteal abscess, as already described. Such an abscess is likely to be present in any severe case of acute osteitis where treatment has not been started within 48 hours of the onset.

2. When these indications are present it is a matter of some urgency to evacuate the pus, and we believe this should be done within 24 hours of admission or as soon afterwards as the abscess can be accurately located.

3. There appears to be no certain advantage in open operation with drilling of the bone. By the criterion we have used, the results are as good in cases treated by thorough aspiration of the subperiosteal pus, repeated when necessary. This result is not inconsistent with the finding that a subperiosteal abscess cannot be completely emptied by a single aspiration (Agerholm and Trueta 1946, White and Dennison 1952). That the aspiration may help indirectly, by allowing escape of pus into the soft tissues, is suggested by case 4. At operation 3 days after a single aspiration, no frank pus was found; but we saw a half-inch rent in the periosteum and some bloodstained seropus in the soft tissues.

Since our experience did not suggest any essential difference in the results likely to be achieved on the one hand by extensive emergency surgery and on the other by aspiration of pus, we felt free to base our choice on a comparison of the intrinsic merits and convenience of the two methods. The more conservative method has the advantages that a major operation under general anaesthesia is avoided; that there is no risk of the troubles associated with slow wound healing; that the first aspiration can be made within a few hours of admission even in cases where the patient would not be considered fit for operation; and that the patient is left unscarred. The advantage of extensive emergency surgery is that, once the operation has been done, there is no more that can be done, and there is no need for daily reassessment of the local condition with a view to further local treatment (except such as is required by the wound). We decided in favour of the more conservative method, and the results have been satisfactory so far; but we feel that success with this method demands a high standard of clinical judgment, with daily reassessment, and may not be achieved consistently except in centres where many cases are seen.

Summary

A trial was carried out in the years 1949-51 to decide whether in the treatment of acute haemogenous osteitis in childhood administration of penicillin should be supplemented by extensive emergency operation.

Of 96 cases admitted to hospital under our care, 23 satisfied the criteria for inclusion in the trial. Consecutive cases were treated alternately: (a) by open operation, including drilling of the bone; and (b) by a more conservative method, in which we came to rely on aspiration of pus from the subperiosteal abscess as the sole surgical measure.

The main criterion for assessing the results was the duration of disability after treatment was started. By this criterion there was no significant difference between the results with the two methods, and no important difference was found in respect of any other criteria.

Because of its intrinsic advantages, we selected the conservative method for routine use; but its successful application depends on good clinical judgment and on daily reassessment in the early stages.

We thank all those colleagues, surgeons and paediatricians, who made this study possible by allowing us to assume clinical responsibility for patients who would otherwise have been theirs, and particularly to Sir James Spence and Dr. Donald Court for their constant encouragement and help. Mr. F. D. Hindmarsh, Mr. J. D. T. Jones, and Mr. J. A. Key were kind enough to operate on three patients in such a way that they could be included in the trial. We have also received invaluable help and guidance, both in the planning of the experiment and the presentation of the results, from Mr. H. Campbell, B.A., F.R.S.S. Prof. J. Trueta's interest, and his willingness to spare time to discuss this work, have been of the greatest help.

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RESISTANT VENTRICULAR TACHYCARDIA CURED WITH LARGE DOSES OF PROCAINAMIDE

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IT is now established that procainamide is superior to quinidine in the treatment of ventricular tachycardia. The effective dose, which varies considerably, is usually 300-800 mg. intravenously, but a few cases require larger doses. The case reported here illustrates the need for, and method of, administration of larger doses of procainamide than usual, and suggests that the speed of injection may be important.

Case-report

A man, aged 65, was admitted on Nov. 9, 1953, with a history of sudden onset of palpitations a week previously. These continued uninterrupted, and there was increasing dyspnoea. Two years before he had had a myocardial infarct, with subsequent angina of effort and attacks of similar palpitations lasting from two to ten minutes. He had chronic bronchitis. Before admission he had received without benefit oral quinidine gr. 6 thrice daily for five days, followed by digitalis folia gr. 1 twice daily for two days.

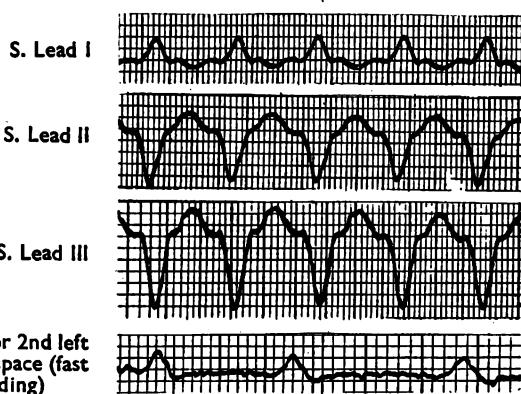


Fig. 1—Electrocardiograms on admission.

On admission he had a regular tachycardia of 180 with signs of moderately severe congestive failure, and early cure was considered imperative. Electrocardiography showed ventricular tachycardia, so the following schedule of treatment was started: oral procainamide 1 g. four-hourly; rectal aminophylline 0.35 g. four-hourly; oral promethazine 25 mg. four-hourly; phenobarbitone gr. 1/2 thrice daily; amylobarbitone sodium gr. 3 every night; and mersalyl 1 ml. intramuscularly on alternate days.

2nd day.—The heart-rate was regular at 164, and the arm-tongue circulation-time exceeded 60 sec. Intravenous procainamide 1000 mg. was given at 50 mg. a minute; and the pulse-rate and blood-pressure were recorded, and an electrocardiogram (c.r.4) was made with a standard portable electrocardiograph, at intervals of a minute. The pulse slowed to a minimum of 112 after 700 mg. of procainamide had been given, and the lowest systolic pressure was 100 mm. Hg.

3rd day.—The congestive failure had improved, and the circulation-time was 18 sec. Intravenous procainamide 1000 mg. at 100 mg. a minute was followed half an hour later by 1000 mg. at 200 mg. a minute. The pulse-rate before, between, and three hours after the injections was 160; and it slowed during each injection, reaching a minimum of 110 towards the end of the second injection. At that point the lowest systolic pressure (90 mm. Hg) was recorded.

4th day.—Intravenous procainamide 1600 mg. was given at 160 mg. a minute; the pulse-rate fell to 100 and the systolic blood-pressure to 60 mm. Hg, but within twenty minutes the pulse-rate rose to 130. A further 1200 mg. was injected at 50 mg. a minute, and the pulse-rate again fell to 100 and the systolic blood-pressure to 80 mm. Hg. Again this proved transient. After this large dose of 2800 mg. the patient complained of irritation of his back and was confused, becoming about an hour later euphoric, hyperkinetic, deluded, and hallucinated. This condition lasted until it was controlled with intramuscular amylobarbitone sodium gr. 6 and intramuscular paraldehyde 10 ml.

5th day.—The patient was greatly improved but remained euphoric, had transient diarrhoea, and was febrile. A leucocyte-count was normal, and stool culture was negative. Treatment with penicillin 250,000 units four-hourly was started.

6th day.—Intravenous procainamide 1500 mg. was given at 400 mg. a minute, and nodal rhythm was established at 80. The lowest systolic pressure (65 mm. Hg) was recorded a minute later. Nodal rhythm at 80 was still present thirty minutes later, and that heart-rate was maintained until the patient was discharged.

7th day.—A purpuric rash appeared on the patient's back, and oral procainamide was discontinued in favour of quinidine gr. 3 thrice daily. A leucocyte-count was normal, and platelets were plentiful in a film.

8th day.—Electrocardiography showed sinus rhythm. *12th day.*—The patient was quite free from cardiac failure and got up; his erythrocyte-sedimentation rate was 16 mm. in 1 hr. (Westergren).

21st day.—The patient was discharged and told to continue taking quinidine.

Electrocardiography on admission (fig. 1) showed a rapid regular succession of ectopic ventricular complexes arising in one focus, probably posterior; the main deflection in c.r.4 (fig. 2a) was a wide slurred r wave. During the

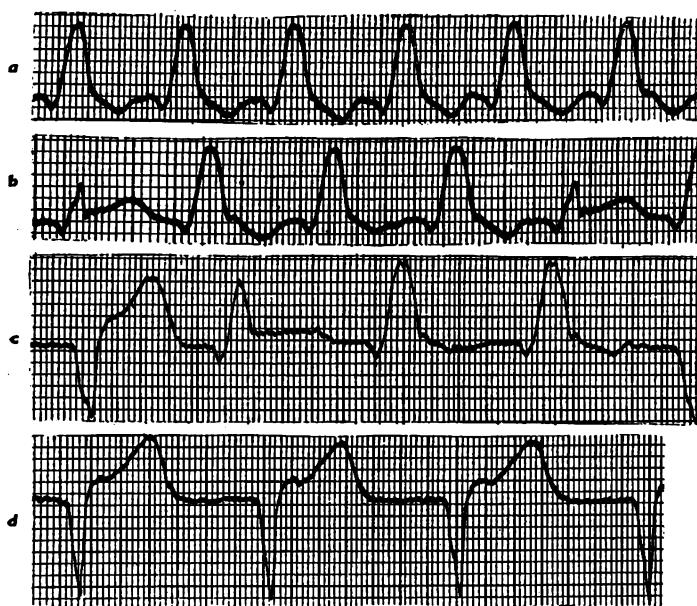
Time marker = $\frac{1}{10}$ and $\frac{1}{60}$ sec.

Fig. 2—Successive changes in C.F.4 electrocardiograms on intravenous injection of procainamide: a, simple slowing; b, sporadic substitution by complexes arising from another focus; c, appearance of isolated complexes (probably nodal extrasystoles); d, nodal rhythm.

intravenous injection of procainamide the following changes were observed successively: (1) simple slowing (fig. 2a); (2) sporadic substitution by complexes arising from another (probably also posterior) focus (fig. 2b); (3) the appearance of isolated complexes (q s lasting 0.1 sec. in c.r.4 [fig. 2c]), probably nodal extrasystoles by comparison with the next stage; and (4) nodal rhythm (fig. 2d). On the first two occasions (second and third days) changes 1 and 2 were noted; on the fourth day change 3 followed; and on the sixth day change 4 was reached. At no time was widening of the q r s complex observed. The final electrocardiogram showed evidence of old posterior infarction (fig. 3).

Comments

As previously reported by other workers, quinidine and oral procainamide failed, but intravenous procainamide eventually succeeded. The intramuscular route was not tried.

With proper precautions it was possible to give intravenous doses larger and faster than is usually recommended (1000 mg. in ten minutes). Minute-by-minute control was essential because individual tolerance varies and serious toxicity may develop with the minimal effective dose. 7300 mg. was given in five days, with a daily maximum of 2800 mg. and a maximal single injection of 1600 mg. Noradrenaline 4 µg. per ml. was immediately available in case of serious hypotension but was not needed.

The first injection was given at 50 mg. a minute (half the recommended speed). Later the dose and the rate

of injection were alternately increased. The final and curative injection, though not the largest, was the fastest (400 mg. a minute), and speed was considered an important factor in its effectiveness. Rapid injection increased the hypotensive side-effects, and there is evidence that it may delay intraventricular conduction excessively (Zapata-Diaz et al. 1952), but this was not seen here. We suggest reserving its use for cases proved resistant to injection at the usual rate. Use of direct-writing electrocardiography to detect widening of the ventricular complexes before fibrillation develops would improve the technique. The most troublesome side-effect was the hyperkinetic confusional psychosis which followed two successive large doses.

Rashes and fever have been reported following oral therapy, and there is evidence that they may be allergic. The promethazine already given may have modified their severity (Koffler 1953) in the present case. Agranulocytosis has also been reported, but we have found no previous observation of purpura with a normal leucocyte-count. Diarrhoea is also apparently a new finding.

Nodal rhythm has been produced experimentally (in dogs) with procainamide, and its transient appearance, as in the present case, noted before (Schoolman et al. 1953). It is probably due to direct suppression of the sino-auricular node.

Discussion

In resistant ventricular tachycardia intravenous procainamide appears often more successful than oral therapy (Antzis et al. 1952, Hanenson et al. 1952, and others), but oral quinidine in full doses may be as successful as oral procainamide (Antzis et al. 1952, Schaffer 1951). Schaffer states that the anti-arrhythmic activity of oral procainamide is from a quarter to a third of that of quinidine (equal absorption stated); and the rate of removal of procainamide from the blood-stream is twice as rapid as that of quinidine (Kayden et al. 1951).

In the present case the urgency did not permit trial of either massive quinidine therapy (gr. 2-6 each hour until toxicity was manifested) or intramuscular procainamide (*Lancet* 1952), either of which might have been successful.

In previous published reports the curative intravenous dose has been 300-800 mg., but some cases have needed more (Kelley et al. 1952, Schoolman et al. 1953) and some cases less—e.g., 60 mg. (Stearns et al. 1952). Our patient received 1000 mg. intravenously at 50 mg. a minute at first; next day 1000 mg. at 100 mg. a minute, this dose being repeated half an hour later at 200 mg. a minute; and the day after 2800 mg. an hour (1600 mg. at 160 mg. a minute and, after twenty minutes, 1200 mg. at 50 mg. a minute). After a day's rest 1500 mg. was given at 400 mg. a minute, ceasing immediately the pulse-rate fell to 80. The fact that speed increases the hypotensive side-effects has not been always found (Lucas and Short 1952, using smaller doses), and some workers also found that no better results followed rapid injection (Miller et al. 1951, using doses of 250-500 mg. at a rate of up to 500 mg. a minute). Further study of resistant cases treated with larger doses is needed. Two more disadvantages of rapid injection are the increased risk of intraventricular block (Zapata-Diaz et al. 1952) and the difficulty of close observation.

When procainamide is administered intravenously, the blood-procainamide level soon declines, perhaps 10-15% per hour (*Journal of the American Medical Association* 1950); and, as in previous reports (Miller et al. 1951, effect lasting from six minutes to two hours), we found its action on the heart transient, a second dose half an

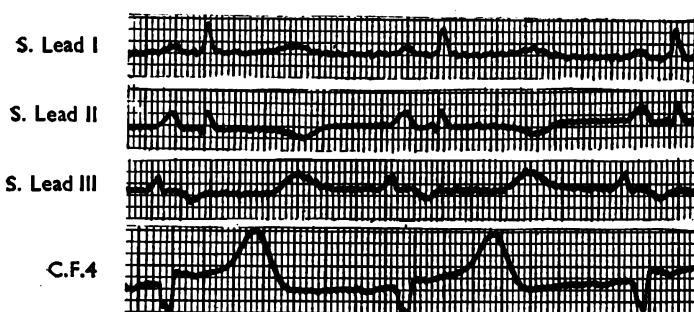


Fig. 3—Electrocardiograms showing evidence of old posterior infarction.

hour later being little more effective than the first. With these larger doses we found speed to be relatively more important than size, but owing to the considerable dangers (cardiodepression and hypotension) involved in these methods, we would restrict such doses to very special cases.

As necessary precautions against hypotension, it is essential to observe the patient closely, measuring the systolic pressure every half-minute; to have antidotes ready (e.g., phenylephrine [Stearns et al. 1952]) and/or to take prophylactic measures (e.g., slow noradrenaline drip [Schoolman et al. 1953]). The other chief danger is the production of ventricular fibrillation. The cases for treatment can first be selected by excluding those with disease of the intraventricular conducting mechanism, because of the danger that procainamide may produce fibrillation, which may be fatal (Read 1952). Ideally progress should be observed by direct-writing electrocardiography so that any widening of QRS (recommended maximum 50%), with subsequent notching or prefibrillary complexes (Denney et al. 1952), could be detected immediately and suggest caution or a halt. We merely observed the result of each injection in retrospect and, finding no such change, increased the rate and dose accordingly. Bifocal extrasystoles of ventricular origin (fig. 2b) were regarded with timidity, but the appearance of possible supraventricular complexes (nodal extrasystoles) was encouraging and suggested steady progress. It has also been suggested that the atrioventricular node is more sensitive to depression than the ectopic ventricular focus (Schack et al. 1952, Bernstein et al. 1952), but this suggestion seems to be in conflict with the appearance of nodal rhythm during cure.

As regards unavoidable toxicity, the acute confusional psychosis with prominent cerebral stimulation was not in agreement with previous experience (*Journal of the American Medical Association* 1950). This psychosis followed the administration of 2800 mg. of procainamide in an hour; so it is possible that blood-procainamide levels capable of stimulating the cerebral cortex may not have been reached before in man. In one case (Bakos and Askey 1952) restlessness and a desire to go home were manifested after oral procainamide 250 mg. had been given four-hourly for five doses.

Agranulocytosis and rashes have been reported following oral therapy with procainamide (Antzis et al. 1952), but the present case showed no blood disorder. However, immediately before the observation of petechiae both in our case and in one reported by Antzis et al. (which later developed agranulocytosis) penicillin therapy had been started for pyrexia of unknown causes. This might have been only coincidental.

Pyrexia has been severe in some cases, and for both it and other toxic effects—e.g., urticaria, malaise, and nausea—an allergic basis has been suggested (Koffler 1953, Hellman 1952). In one case (Bakos and Askey 1952) pyrexia was specifically reproducible; in others it was associated with eosinophilia (Hellman 1952 and others) and responded to anti-histamine drugs. Intravenous procainamide given to two asthmatic patients produced convulsive movements and shock (Stearns et al. 1952). If promethazine had not been used in the present case, the temperature might well have risen higher than was observed here (100.4°F), and more side-effects than irritating purpura and diarrhoea might have developed.

Perhaps the fact that these effects follow oral procainamide mainly is reason for using quinidine as much as possible for oral curative therapy, and perhaps entirely for maintenance.

Conclusions

Intravenous procainamide should only be used in urgent cases and with the greatest possible precautions;

and higher doses and speeds of administration should only be used, and then cautiously, in proved resistant cases. The use of prophylactic anti-histamine drugs during procainamide therapy is desirable, and quinidine should be used for oral therapy where possible.

Summary

A case is reported of ventricular tachycardia with cardiac failure. After other methods had failed, cure was effected with intravenous procainamide given faster and in larger dosage than is usually recommended.

We wish to thank Dr. R. Kempthorne for permission to publish this case and for helpful criticism in the preparation of this paper; Dr. J. F. Heggie for his advice about the illustrations; Dr. L. A. Hamilton for his assistance and advice; and Mrs. I. P. Vedast for preparing the electrocardiograms.

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A POTENT GROUP-O CELL-AGGLUTININ OF HUMAN ORIGIN WITH H-SPECIFIC CHARACTER

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SERA which agglutinate group-O and group-A₁ cells preferentially can be divided into two groups on the results of inhibition tests with saliva: those whose power to agglutinate such cells is inhibited by saliva from secretors belonging to any of the groups within the ABO system are designated anti-H, and those whose power is not inhibited are provisionally grouped together and called anti-O (Morgan and Watkins 1948).

It should, however, be realised that, although the latter sera are grouped together as anti-O, the results of inhibition tests with secretions from various sources, and the behaviour of the sera with the erythrocytes of group-O cord-blood (Watkins 1952), suggest that not all the sera classified as anti-O are of the same specificity. It is still not known which, if any, of these anti-O sera react specifically with the product of Bernstein's O gene.

Both O and H agglutinins are found among human sera; but anti-O sera are found more often. Both kinds of antibodies usually behave as cold agglutinins and are of low potency. The differentiation into anti-H and anti-O on the basis of inhibition by saliva is clear-cut, but it is impossible to distinguish between the two kinds of antibody on the basis of their reactivity with red cells.

TABLE I—REACTIVITY OF ERYTHROCYTES WITH SERUM "TOMLINSON" AT 21°C AFTER ABSORPTION OF SERUM WITH GROUP-A₁B CELLS

Group	No. of samples tested	No. of samples showing agglutination titre of													
		0	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512	1/1024	1/2048	1/4096	1/8192
O	39	3	3	..	1	1	2	9	7	7	5	4	28	7	..
A ₁	42
A ₂	9
B	10
A ₁ B	5	1	..	1	1
A ₂ B	2

Bhende et al. (1952) reported three examples of Indian blood with a "new" blood-group character related to the ABO system. The serum from each of the men contained anti-A₁, anti-A, and anti-B agglutinins, and the cells were not agglutinated by either anti-A or anti-B sera. Superficially, therefore, these men appeared to belong to group O, but their red cells were not agglutinated by human or by animal anti-H sera or by human anti-O sera, and their sera contained in addition group-O cell-agglutinins of greater potency than any which had hitherto been examined. Two of the sera gave a titre of 1 in 256 against group-O cells, and the third a titre of 1 in 32. Moreover these sera were active at 37°C, and the degree of agglutination was the same at 37°, 24°, 12°, and 5°C. The agglutination of group-O cells by each of the three sera was inhibited by saliva from group-O secretors; these sera were therefore classified as anti-H. The sera were not used to test the H-reactivity of red cells belonging to groups other than O, because of the presence of the anti-A, anti-A₁, and anti-B agglutinins. None of the three Indians secreted in their saliva A, B, H, or Le^b substances, but they secreted Le^a substance.

A further example of a human anti-H serum, "Warboys," has been encountered which differs in some of its properties from the Indian sera and anti-H sera of animal origin (Watkins 1952, Crumpton and Morgan 1953). The serum "Warboys" came from a group-B donor who did not secrete B or H substances in her saliva.

Serum "Tomlinson"

Recently an anti-H serum has become available to us which is considerably more powerful in its action on group-O cells than are the Indian sera. This serum was obtained from a woman, Mrs. Tomlinson, with carcinoma. The patient's blood-groups were A₁, Le (a-b-), CDe/cde, MNS, P+, Lu (a-), K-, and Fy (a+). Her red cells were not agglutinated by natural anti-H eel serum (Jonsson 1944), by immune anti-H serum prepared by the injection of rabbits with ovarian-cyst H-substance (Morgan and Waddell 1945), by natural cattle serum (Schiff 1927), by anti-H serum prepared by immunisation of chickens with *Shigella shiga* (Grubb 1949), or by anti-O sera.

Treatment of the washed cells with saline at 56°C, however, yielded an eluate which agglutinated group-O cells to a titre of 1 in 64. It therefore seems that, although unagglutinated suspensions of Tomlinson's cells could be prepared in cold saline, they were nevertheless coated with a group-O cell-agglutinin which could be removed by washing with warm saline. The cells remaining after the antibody had been eluted were not agglutinated by either anti-O or anti-H sera.

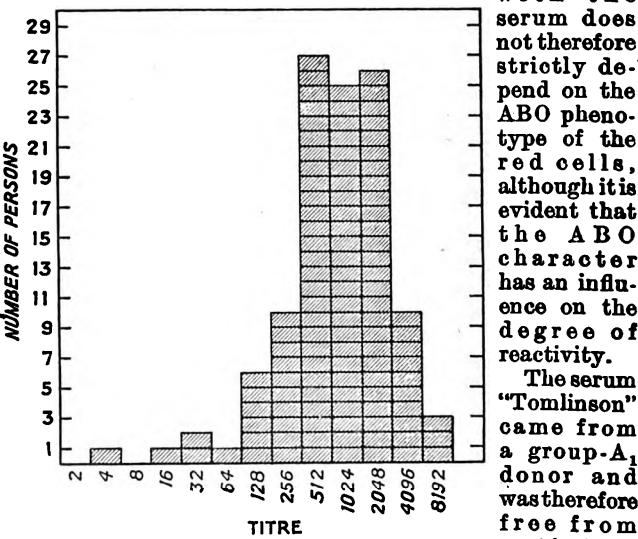
Mrs. Tomlinson's saliva contained A substance, measured in inhibition tests against human anti-A serum, and H substance, measured against rabbit, eel, and cattle anti-H sera and human anti-H serum obtained from one of the Indians. Her saliva inhibited her own serum; unfortunately she died before a second sample of saliva could be obtained to confirm these findings. It was impossible to obtain blood and saliva specimens from any other members of her family.

The serum "Tomlinson" was titrated against the red cells of 65 group-O English people selected to include

Le (a-b+), Le (a+b-), and Le (a-b-) cells. All the bloods reacted strongly and gave agglutination titres ranging from 1 in 8192 to 1 in 32,768 at 25°C. The agglutination end-points were unchanged at 13°C and were lowered by only one or two tubes when the tests were made at 37°C. Absorption of the serum with either OLe (a+b-) or OLe (a-b+) cells removed completely the agglutinin reactive with all group-O cells. Agglutination of group-O cells by the serum "Tomlinson" was inhibited by saliva from group-O secretors, by purified H substance obtained from ovarian-cyst fluids (Annison and Morgan 1952), by hog H substance, and by meconium from group-O secretor babies. The serum was thus anti-H. The human anti-H serum "Warboys" was inhibited by meconium samples from babies who did not secrete A, B, or H substance in their saliva (Watkins 1952); the serum "Tomlinson," in common with the anti-H sera obtained from the Indians, was not neutralised by meconium from babies of the "non secretor" type.

A further point in which the serum "Tomlinson" behaved like the Indian anti-H sera and unlike "Warboys" was that it reacted with group-O cells from the newborn almost as strongly as with group-O cells from adults, whereas "Warboys" did not agglutinate cord-blood erythrocytes.

A sample of the serum "Tomlinson" was absorbed with A₁B Le (a-b+) cells until there was no further reaction with the absorbing cells. The absorbed serum was then titrated against 108 bloods belonging to different groups within the ABO system. The range of agglutination titres given by the cells is shown in table I. The absorbed serum gave consistently high titres with group-O and group-A₁ cells. Group-A₁ cells showed various degrees of reactivity, ranging from no detectable agglutination up to titres nearly as high as those given by group-O cells. In each of the six phenotypes within the ABO system, including group A₁B, samples were obtained which reacted with the anti-H serum; reactivity



with the serum does not therefore strictly depend on the ABO phenotype of the red cells, although it is evident that the ABO character has an influence on the degree of reactivity.

The serum "Tomlinson" came from a group-A₁ donor and was therefore free from anti-A or anti-A₁ agglu-

TABLE II—REACTIVITY OF GROUP-A₁ CELLS WITH UNABSORBED SERUM "TOMLINSON" AT 21°C

Group-A ₁ donor	Genotype	Agglutination test												
		Dilution of serum "Tomlinson"												
		1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512	1/1024	1/2048	1/4096	1/8192
T.H.	A ₁ A ₁	3	3	3	3	3	2	1	0	0	0	0	0	0
P.W.	A ₁ A ₁	3	3	3	2	2	2	0	0	0	0	0	0	0
E.I.	A ₁ O	4	4	3	3	3	3	3	2	2	2	1	0	0
J.O'D.	A ₁ O	3	2	2	1	0	0	0	0	0	0	0	0	0
J.W.	A ₁ O	4	4	4	3	3	3	3	2	2	1	0	0	0
P.P.	..	1	tr	0	0	0	0	0	0	0	0	0	0	0

tr, trace of agglutination; 1, groups of 2-3 cells; 2, larger groups with many free cells; 3, agglutination visible to the naked eye; 4, massive agglutination.

tinins and could be used to test the H-reactivity of group-A₁ cells without prior absorption or neutralisation of the serum; group-A₁ cells from one hundred and twelve people were titrated against the unabsorbed anti-H serum. Included in the samples were specimens from two unrelated group-A₁ donors who were of authentic genotype A₁A₁; both parents of each donor belonged to group A₁B. Authentic heterozygous group-A₁O cells from three donors were also included in the test. The titres obtained with the hundred and twelve samples are shown in the accompanying figure, and the results of titration of six specimens of group-A₁ cells are given in table II. The genotype of the donor (P.P. in table) whose cells reacted most weakly with the serum "Tomlinson" is unknown. The known homozygous group-A₁A₁ cells gave strong reactions at 21°C, whereas one of the heterozygous group-A₁O specimens (J.O'D. in table) showed considerably less reactivity. Since in a hundred and twelve group-A₁ bloods one would expect about fifteen of the genotype A₁A₁, many such bloods must be reacting more strongly than a known specimen of group-A₁O cells. The capacity of the cells to be agglutinated by the anti-H serum is therefore clearly not related to their homozygous A₁A₁ or heterozygous A₁O nature. Titration of serum "Tomlinson" with the weakly reacting cells from donor P.P. in albumin, or treatment with trypsin, did not increase the reactivity. Agglutination of the homozygous group-A₁A₁ cells could be inhibited by purified human H substance and was therefore due to the anti-H agglutinin in the serum and not to some other antibody. Further, the elution at 56°C of antibody absorbed at 0°C on to group-A₁A₁ cells from the serum "Tomlinson" gave an agglutinin which behaved qualitatively like the original serum.

One hundred samples of group-B cells were tested against a 1 in 5 dilution of serum "Tomlinson" after neutralisation of the β agglutinin in the serum with human B substance free from H activity. Only one specimen did not produce visual agglutination at this dilution. Titrated against the anti-H serum this sample gave a titre of 1 in 4.

Red cells from the Indian donor Z (Bhende et al. 1952) were not agglutinated by undiluted serum "Tomlinson" at 12°, 20°, or 37°C. Agglutination with the group-A₁ cells (P.P.), which reacted weakly at room-temperature, disappeared at 37°C but was intensified at 12°C. The cells from the Indian donor were therefore the only ones, among those tested, which appeared to be completely devoid of H activity.

The serum "Tomlinson" was not inhibited by the individual sugar components (2%) (L-fucose, D-galactose, N-acetylglucosamine, and N-acetylgalactosamine) of the human H substance as are certain other anti-H agglutinins (Watkins and Morgan 1952, Morgan and Watkins 1953).

Discussion

The group-O cell-agglutinin described here presents some unique features. It is by far the most powerful human anti-H serum that has so far been found and

shows a greater range of reactivity against cells belonging to groups other than O than is shown by animal anti-H sera. The agglutination given by homozygous group-A₁A₁ cells, and the weak reactivity shown with a sample of known heterozygous group-A₁O cells, leave no doubt that this powerful agglutinin is not detecting the product of the O gene despite its preferential reaction with group-O cells. Tanaka (1952) also concluded that the capacity of an anti-H serum (eel serum) to react with red cells did not depend on the presence on the cells of the product of the O allele. Another unusual feature is that the donor of the serum "Tomlinson" was a secretor of A and H substances; this finding is at variance with the suggestion of Sanger (1952) that anti-H and anti-O may be antibodies of the same general specificity, the former occurring in non-secretor persons. The possibility cannot be excluded, however, that the development of the antibody in this instance might be an immune response in some way connected with the patient's carcinoma.

The genetical relationship of H character to the ABO blood-groups is not yet clear. The serum "Tomlinson" will provide a most useful reagent for further investigations on the distribution and nature of the H-specific material on erythrocytes and in secretions.

Summary

A powerful group-O cell-agglutinin of human origin is described.

Its behaviour in inhibition tests with the water-soluble blood-group substances in saliva and purified H substance showed that it is an anti-H agglutinin.

The antibody reacts with authentic group-A₁A₁ cells more strongly than with a sample of known group-A₁O cells.

These results confirm that anti-H agglutinin does not detect a product of Bernstein's O gene, and that within the ABO system the homozygous (AA, BB) or heterozygous (AO, BO) nature of the cells cannot be determined by anti-H reagents.

We wish to thank Dr. Dorothy Parkin, of the Medical Research Council Blood Group Reference Laboratory, Dr. Adrian Slade, and the laboratory staff of the County Hospital, York, for allowing us to investigate this serum; and Dr. R. R. Race, F.R.S., and Dr. Ruth Sanger for advice and comments.

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ADDISON'S DISEASE WITH DIABETES MELLITUS

A CASE TREATED WITH CORTISONE

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LECTURES IN THERAPEUTICS IN THE UNIVERSITY OF SHEFFIELD

THE coexistence of Addison's disease and diabetes mellitus is rare. Unverricht (1926) first described a case of diabetes in which the insulin requirements decreased rapidly with the development of Addison's disease. Soffer (1948) found only fourteen authentic cases published. In eight of these Addison's disease developed after the diabetes, in four the diseases appeared simultaneously, and in only two did Addison's disease precede diabetes.

A constant feature of cases of Addison's disease with diabetes mellitus is their extreme instability (Crampton et al. 1949). They are especially liable to develop hypoglycaemic attacks, which may cause death, as in the case described by Rhind and Wilson (1941).

The present case is an instance of diabetes mellitus in which the insulin requirements decreased considerably as Addison's disease developed. Treatment with cortisone, in addition to producing a striking improvement in the symptoms of Addison's disease, has increased the daily insulin requirements to near their former level and has greatly improved control of the diabetes.

Case-history

A housewife, now aged 42, enjoyed good health until the age of 23, when she developed diabetes and was stabilised on diet and 60 units of soluble insulin daily. Although she had a stillbirth at the age of 28, she later had two normal pregnancies at 34 and 38. Her mother and her twin sister both have diabetes mellitus. She remained well until her last pregnancy, when a gradual reduction in insulin dosage became necessary because of frequent nocturnal hypoglycaemic attacks. In a year the dosage decreased from 60 to 24 units of soluble insulin daily. Pigmentation of the skin, which developed during pregnancy, did not clear after delivery, and in the following two years the patient became progressively less energetic, her weight fell, and her appetite steadily decreased. She had occasional prostrating bouts of vomiting, sometimes associated with diarrhoea. In spite of continued reduction in insulin dosage the hypoglycaemic attacks persisted and the pigmentation deepened. A patch of intra-oral pigmentation developed.

On admission to hospital in July, 1952, physical examination revealed much wasting and extensive cutaneous and buccal pigmentation. The blood-pressure was 80/60 mm. Hg.

Investigations.—The serum-sodium level was 130 m.eq. per litre, serum-potassium level 5.3 m.eq. per litre, and fasting blood-sugar level 160–450 mg. per 100 ml. The urinary excretion of 17-ketosteroids in twenty-four hours was 1.5 mg. A blood-count showed Hb 86%, red cells 4,200,000 per c.mm., white cells 5000 per c.mm. (polymorphs 65%, eosinophils 2%, lymphocytes 26%, monocytes 7%). Radiographs of chest and abdomen were normal. Electrocardiography showed low voltage in leads I and a VL; flat T waves in leads I, II, III, a VL, a VF, V₄, V₅, and V₆; inverted T waves in V₁, V₂, and V₃; and prolongation of the s-T interval. The erythrocyte-sedimentation rate was 5 mm. in 1 hr. (Westergren). A Kepler test was abandoned because the patient could not drink the requisite volume of water without vomiting.

Treatment with added salt, injections of crude cortical extract, and deoxycortone acetate somewhat improved her general condition; but, as this was still poor, she was given oral cortisone acetate 25 mg. daily. After the second dose her urine became heavily loaded with sugar and ketone bodies. Since nausea, vomiting, and progressive drowsiness ensued, it was evident that she was on the verge of diabetic coma, and

only with difficulty was her diabetes again brought under control. After this the cortisone was withheld and 100 mg. of deoxycortone acetate implanted subcutaneously. With this treatment, the addition of 6 g. of salt to her diet each day, and restabilisation of her diabetes on 6 units of soluble insulin daily she improved slightly. After discharge she soon deteriorated once more, and her weight fell to 5 st. 4 lb. over the next year, a loss of 2 st. 10 lb. She had almost complete anorexia and was apathetic and depressed. It was felt that she was unlikely to survive many months.

Readmission to hospital was arranged in August, 1953. The signs of Addison's disease were unchanged, and her general condition was much worse. The investigations were repeated with similar results, except that the electrocardiographic abnormalities were more extensive (fig. 1a). The glucose-tolerance test is discussed below.

Treatment.—It was decided that a second attempt to introduce cortisone therapy must be made, starting cautiously with only 5 mg. daily. Accordingly this dose was started on Sept. 7, 1953. There was an immediate increase in insulin requirements from 6 to 16 units daily. By three-hourly urine testing and frequent blood-sugar estimations it was possible to make adjustments in insulin therapy promptly. Once the diabetes was stabilised, the dose of cortisone was increased to 10 mg. daily, whereupon more insulin was required. There-

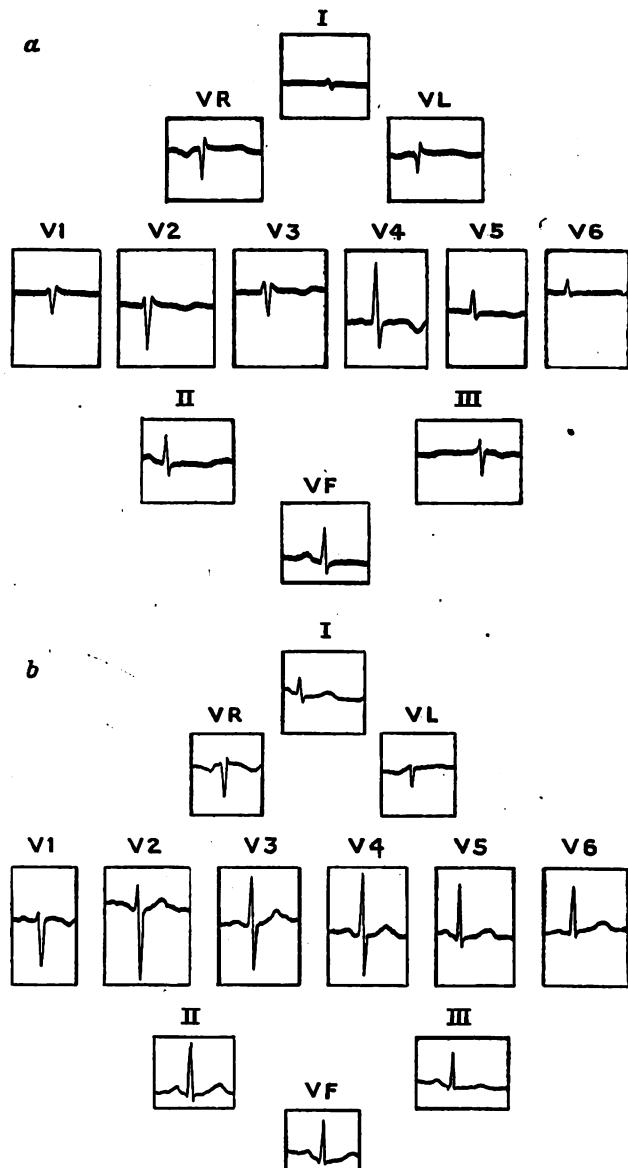


Fig. 1—Electrocardiographic changes produced by cortisone : a, a week before starting cortisone therapy ; b, after two months' treatment with cortisone.

after cortisone was increased to 12.5 and finally to 25 mg. daily, by which time the insulin dose had risen to 48 units a day. These effects are illustrated in fig. 2. During this period there was a striking improvement in the patient: her apathy vanished, she regained her appetite, her general energy increased, and her weight increased.

Follow-up.—After five weeks in hospital she has been at home for three months, making steady progress while doing her own housework and caring for her two children. The improvement can be well seen in the two photographs (fig. 3). She weighs 7 st. 6 lb., her blood-pressure is 110/60 mm. Hg., her fasting blood-sugar level is 100–140 mg. per 100 ml., and her electrocardiograms have reverted to normal (fig. 1b).

Comparison of Diabetogenic Properties

This patient presented a rare opportunity for attempting a comparison between the diabetogenic powers of cortisone and of hydrocortisone. Oral cortisone is fully effective in four hours; therefore blood-sugar curves obtained from glucose-tolerance tests done at this interval after doses of either cortisone or hydrocortisone could be compared with control tests.

Because of the profound disturbance of carbohydrate metabolism resulting from small doses of these substances we could not administer increasing doses interspersed with days on which they were omitted for control tests,

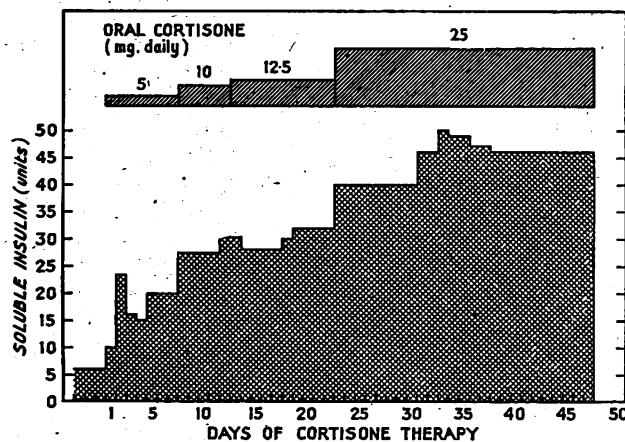


Fig. 2.—Effects of cortisone therapy on insulin requirements in Addison's disease with diabetes mellitus.

because this would have made control of the diabetes mellitus impossible.

For these reasons the following procedure was adopted:

(1) Control glucose-tolerance tests were made in duplicate before treatment was started. The results are shown in fig. 4a.

(2) A glucose-tolerance test was repeated four hours after oral administration of cortisone 5 mg. This was compared with the effect of hydrocortisone 5 mg. given next day. The result is shown in fig. 4b. It will be seen that the curve ran at a higher level after hydrocortisone.

(3) Once cortisone therapy was started with 5 mg. daily and the necessary adjustments in insulin dose were made, the dose of cortisone was raised to 10 mg. On the first day of the new dose a glucose-tolerance test was done, and a second test was done next day four hours after 10 mg. of hydrocortisone; cortisone



Fig. 3.—Patient : a, before cortisone therapy ; b, after three months' cortisone therapy, showing striking improvement in her general condition.

was omitted on this day. This gave a pair of curves contrasting the effect of 10 mg. of both substances (fig. 4c).

(4) Finally, when the time came to raise the dose to cortisone 25 mg. daily, a fourth pair of glucose-tolerance tests were completed, the first test after hydrocortisone 25 mg. (given instead of cortisone 25 mg.) and the second after cortisone 25 mg. (fig. 4d). In this way pairs of curves were obtained on successive days, contrasting the effects of 5, 10, and 25 mg. of both drugs, and these could be compared with the tests before treatment. Cortisone preceded hydrocortisone in the first two dosages; the reverse order was used in the third. The effects are illustrated in fig. 4. Hydrocortisone seems to be more diabetogenic than cortisone, apart from the last pair of curves in which there is little difference between the two; by this time the patient was already maintained on cortisone 12.5 mg. daily, and extreme sensitivity to these hormones had been lost. The blood-sugar estimations were done by the method of Hagedorn and Jensen.

Discussion

The alterations in carbohydrate metabolism that take place when a patient with diabetes develops Addison's disease have been described by Crampton et al. (1949). In Addison's disease there are a low fasting blood-sugar level, hypersensitivity to insulin, and defective storage of glycogen (Allott 1953). These effects, which are reversed by cortisone, accounted for the decrease in insulin requirements of our patient and for the abrupt increase on starting cortisone. After this second successful introduction of cortisone therapy it can be seen that the administration of cortisone 25 mg. would create an

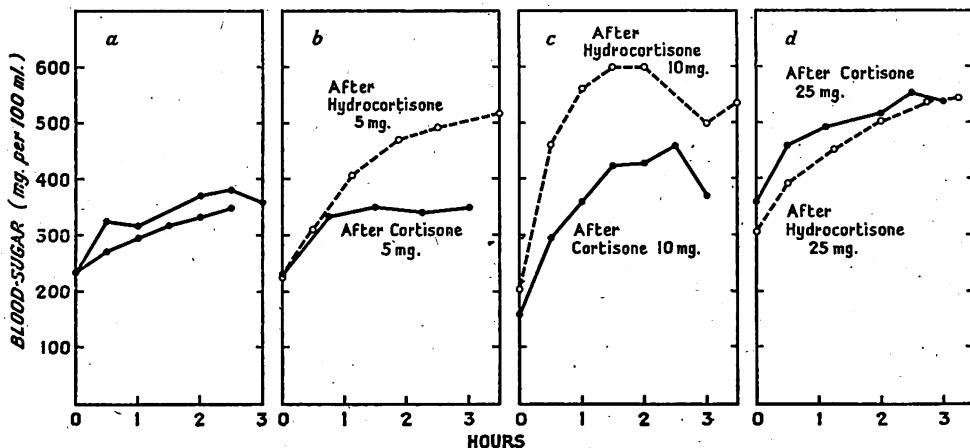


Fig. 4.—Glucose-tolerance tests after 50 g. of glucose given by mouth at 0 hours : a, two tests without previous administration of hormone ; b, after cortisone 5 mg. and after hydrocortisone 5 mg.; c, after cortisone 10 mg. and after hydrocortisone 10 mg.; d, after cortisone 25 mg. and after hydrocortisone 25 mg.

urgent need for large additional doses of insulin, and this adequately explains the rapid development of diabetic ketosis when cortisone was given in 1952.

These events closely resemble those reported by Simpson (1953) in a similar patient, in whom diabetic precoma resulted from the administration of cortisone 25 mg. daily for three days. This patient was stabilised on cortisone 12.5 mg. daily after the daily insulin needs had increased from 12 to 74 units.

Thorn et al. (1951) describe two cases treated with cortisone by subcutaneous implantation, later supplemented by oral cortisone, but no comment is made on the rate at which insulin requirements increased. The return of the electrocardiograms to normal after cortisone therapy agrees with the observations of Somerville et al. (1951).

Summary

A case of coexistent diabetes mellitus and Addison's disease is described. As the Addison's disease developed, the insulin requirements decreased. Cortisone therapy initially precipitated diabetic ketosis, but later a more cautious introduction of cortisone was successful. Clinical improvement ensued although insulin requirements increased abruptly. A tendency to develop frequent hypoglycaemic attacks was eliminated.

Experiments were made to compare the diabetogenic properties of cortisone and hydrocortisone.

We wish to thank Dr. H. P. Brody and Prof. E. J. Wayne for permission to publish this case and for their helpful advice, and Mr. Ernest Salvin for the blood-sugar estimations. Part of the expenses were defrayed by a grant from the Tuberculosis Research Fund of the University of Sheffield.

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TRANSFERENCE OF PASSIVE IMMUNITY FROM MOTHER TO YOUNG

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IN rabbits the transfer of passive immunity from mother to young occurs before birth (Brambell, Hemmings, and Henderson 1951b). There is no evidence that in this species any further transference occurs after birth, by way of the colostrum or the milk. It has been shown that transference in the rabbit is effected by the passage of antibodies from the maternal circulation into the uterine lumen and by their uptake from there by the yolk-sac of the foetus (Brambell, Hemmings, Henderson, Parry, and Rowlands 1949). Thus it is the inverted yolk-sac wall, covered with entoderm and vascularised by the vitelline circulation, which is the absorptive organ in the foetal rabbit, and not the allanto-chorionic placenta, as had been assumed previously (Brambell et al. 1951b).

The passage of antibodies into the foetus in rabbits can be studied conveniently by injecting immune serum directly into the uterine lumen, thereby avoiding complication due to passage from the maternal circulation to the uterine lumen (Brambell et al. 1949). The inverted yolk-sac wall and the chorion, forming a wide annular

zone, which is non-vascular, between the margin of the yolk-sac and the circumference of the placenta, are exposed to the immune serum in this way. The use of a mixture of immune sera, prepared in two or more species against a different antigen in each case, permits of direct comparison of the absorption of the different antibodies (Brambell, Hemmings, Henderson, and Rowlands 1950; Brambell, Hemmings, Henderson, and Oakley 1952). It was shown by this means that antibodies prepared in rabbits were absorbed by the yolk-sac wall and appeared in the foetal circulation much more readily than those prepared in cattle or horses (Brambell et al. 1952). Further work (as yet unpublished), in collaboration with Prof. C. L. Oakley and Mrs. I. Batty, has shown that antitoxins prepared in man, guineapig, and dog form a series in that order intermediate between those prepared in rabbits on the one hand, and in horses and cows on the other hand, in reference to the ease with which they are absorbed into the foetal circulation. Thus absorption by the yolk-sac is a selective process distinguishing between antibodies prepared in different species.

Antibodies from immune sera injected into the uterine lumen in pregnant rabbits also appear in the amniotic fluid of the foetus, having traversed presumably the non-vascular chorion and the amnion. Passage of antibodies from the uterine lumen to the amniotic fluid is not selective with reference to species of origin (Brambell et al. 1952). It differs in this respect from passage into the foetal circulation. Once within the amniotic fluid, antibodies can reach the foetal stomach, presumably through the gulping movements of the foetus, and may attain very high concentrations in the stomach contents. Nevertheless antibodies do not pass from the gut contents into the foetal circulation in rabbits in detectable amounts, whether they are prepared in rabbits or in other species (Brambell, Hemmings, Henderson, Oakley, and Rowlands 1951a).

It is well known that immunity is transferred from the fowl to the chick by way of the yolk of the egg. Passage of antibodies from the yolk into the circulation of the chick takes place during the later part of incubation (Brändy et al. 1946, Buxton 1952). It has been shown by one of us (J. B.) that immune serum can be injected into the yolk-sac on the 6th to 8th days of incubation and immediately after hatching and that antibodies from the serum can be absorbed into the circulation. Antibodies from immune serum prepared in fowl are absorbed readily, but those from sera prepared in rabbits, horses, or cows could not be detected in the circulation of the chick. Antibodies from serum prepared in pigeons were absorbed into the circulation in significant amounts, but less readily than those of immune fowl serum. Although the one-day-old chick can absorb antibodies from immune fowl serum injected into the retracted yolk-sac after hatching it cannot do so from the same serum administered orally, even before it has commenced to feed. The newly hatched chick resembles the foetal rabbit in that antibodies can be absorbed by the yolk-sac wall, but not by the gut wall, and absorption by the yolk-sac is a selective process distinguishing between antibodies prepared in different species.

In the rat, passive immunity is transferred mainly after birth by way of the colostrum and the milk. Moreover, transference continues for 20 days of lactation in this species. One of us (R. H.) has shown that when immune serum prepared in rats is administered by tube to the stomach the antibodies pass rapidly into the circulation of young rats at all ages from birth to 20 days. Antibodies of immune serum prepared in rabbits are absorbed from the gut into the circulation also, at least during the first 10 days of life, but much less readily than those from immune rat serum. Antibodies of immune sera prepared in cows or in fowl do not enter the circulation by this route in quantities that can be detected. Thus absorption of antibodies from the gut of the young

rat is selective, as is the absorption by the yolk-sac in the foetal rabbit or the chick.

In man transfer of passive immunity is known to take place mainly, or more probably entirely, before birth. The route is unknown, so far as we are aware. It has been assumed, though without evidence, to be by way of the allanto-chorionic placenta. This assumption is not justified any longer, in view of the discoveries outlined above concerning the route of transference in the rabbit. Yet the structure and arrangement of the embryonic membranes in man is entirely different from that in the rabbit. Transmission by way of the yolk-sac appears impossible, since this organ is rudimentary and is isolated from the periphery of the conceptus. Hence transference in man must take place by some other route than in the rabbit (Brambell, Hemmings, and Rowlands 1947). The late human conceptus is bounded by the placenta (chorion frondosum) and by the chorion laeve, consisting of the chorion to which, over almost its entire extent, the amnion is fused. Transmission of antibodies from the maternal circulation could occur either through the placenta directly into the foetal circulation, or by way of the chorion laeve into the amniotic fluid and thence by swallowing to the foetal gut. The former route appears at first sight to be the more obvious, but we know of no evidence to support it. Regarding the latter route we know that transfer is by way of the uterine lumen, not the placenta, in the rabbit (Brambell et al. 1949); that antibodies do pass into the amniotic fluid; that these are concentrated in the stomach contents of the rabbit foetus; and that antibodies are absorbed in quantity from the gut contents of newborn ruminants, horses, pigs, dogs, mice, and rats (Brambell et al. 1951b). It would be in keeping with our knowledge of other animals that the route in man should be via the chorion laeve, amniotic fluid, and foetal gut.

There is evidence that the absorption of antibody by the foetus in man is a selective process. Although the titre of the cord-blood of a newborn baby usually approximates to that of the blood of the mother, when she has been actively immunised, often equalling or even exceeding it, Hartley (1951) quotes two cases in which refined diphtheria antitoxin prepared from horse-serum did not pass from the maternal to the foetal circulation in significant amounts. Further, there is evidence that in haemolytic disease incomplete anti-D antibody reaches the foetus more readily than complete antibody (Pickles 1949). The selective absorption described above in the rabbit, fowl, and rat is mediated by an entodermal surface in each case, whether yolk-sac or gut wall. Absorption is selective in the guinea-pig also (Hartley 1951), but the arrangement of the foetal membranes in this animal is so similar to that in the rabbit that there is no reason to believe that the route of transference is different. It seems probable, if absorption is selective in man, that it occurs through an entodermal surface also and that the initial passage through the chorion laeve into the amniotic fluid is not selective. Concentration of antibody from the amniotic fluid in the stomach might occur, as in the foetal rabbit near full term (Brambell et al. 1951a). Should this be so, a considerable reservoir of antibody might be built up in the stomach contents, from which it might be absorbed into the circulation.

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Medical Societies

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

THE society's 74th annual congress was held on April 22-24 in Newcastle upon Tyne, under the presidency of Mr. ALEXANDER MACRAE. At the opening session, the Nettleship medal was presented to Dr. NORMAN ASHTON, director of pathology at the Institute of Ophthalmology, in recognition of his contributions to ophthalmology.

In the discussion on inflammatory vascular diseases affecting the eye, Mr. R. C. DAVENPORT considered in particular the condition of retinal vasculitis. He emphasised the frequent clinical association of these retinal vascular lesions with inflammation of the uveal tract; the condition was thus one that involved the major structures in the eye rather than a local vascular derangement. Dr. S. P. MEADOWS dealt with temporal arteritis. He had been impressed by how phlegmatic these patients were when confronted with sudden total blindness, an attitude which suggested that there was an associated general nervous degeneration. Other speakers confirmed this observation. Prof. J. B. DUGUID presented evidence to show that arterial occlusion was the underlying factor in various forms of acute arteritis.

Discussing the diagnosis of orbital tumours, Mr. GEORGE BLACK emphasised the value of radiography after air injection into the orbit. He preferred trans-frontal exploration rather than anterior biopsy when the tumour did not present anteriorly.

During the symposium dealing with the changes in the incidences of the eye afflictions of coalminers in the past twenty-five years, Dr. DOROTHY CAMPBELL discussed miners' nystagmus and pointed out the importance of accurate certification and of social welfare in preventing the condition. Mr. W. J. WELLWOOD FERGUSON presented statistics on the incidence and nature of ocular injuries from mining with general reference to methods of mining and methods of treatment and prevention. Dr. G. I. SCOTT drew attention to the declining incidence of hypopyon ulcers in miners during the past twenty-five years. This could be attributed particularly to the improvement of prophylactic treatment, given both as a first-aid measure at the pit-head and by the general practitioner.

A second symposium was devoted to gonioscopy after glaucoma operations. Mr. H. E. HOBBS illustrated the gonioscopic appearances after drainage operations, and assessed the clinical effects of the anatomical variants shown; and Mr. REDMOND SMITH discussed the general interpretation of broad and narrow angles and the presence of peripheral anterior synechiae.

In a series of short demonstrations, Mr. A. SEYMOUR PHILPS explained the technique of keratography and its value in recording irregularities of the corneal curvature; Mr. A. T. G. EVANS described a case of essential atrophy of the choroid with ataxia and a strong family history of similar conditions; Mr. J. FRANKENTHAL discussed a case of a large cyst of the iris following lens extraction; Mr. P. J. L. HUNTER described an unusual case of bilateral lymphosarcoma of the orbit; Mr. E. F. KING reported two cases of secondary carcinoma of the choroid, which had shown a striking regression after adrenalectomy; and Mr. P. D. TREVOR-ROPER described a case in which symmetrical metastases from a breast carcinoma had presented in the angles of both anterior chambers, strictly confined to the horizontal axes, suggesting an anatomical vagary of the retrobulbar arteries by which the metastases were diverted into the long posterior ciliary arteries rather than the short posterior ciliary arteries.

Reviews of Books

Child Health and the State

ALAN MONCRIEFF, C.B.E., M.D., F.R.C.P., J.P., Nuffield professor of child health, University of London. London : Oxford University Press. 1953. Pp. 48. 6s.

The publication of Professor Moncrieff's Newholme lectures will enable many who could not hear them to read and ponder over them with profit. He describes the evolution of the many services devoted to the promotion of health and happiness in childhood, and reviews the position of the local-authority services in relation to the National Health Service. He believes that the State is still not pursuing a sufficiently energetic child-health policy, particularly for the pre-school child. Nevertheless, it is a matter for pride that Newholme's words are still true : "In no other part of Europe has there been such wide-spread and universal organisation of special work for the infant and pre-school child as in Britain."

Professor Moncrieff also believes that the great improvement in the health of school-children in the last fifty years has not been accompanied by sufficient adjustment of the school health service to present conditions. He regrets that provision for the care and education of the maladjusted child is still inadequate, and he rightly deplores the failure to continue the reablement and training of handicapped children after they leave school. The machinery for caring for the handicapped at this crucial age is there, but it is often ignored, and he emphasises the importance of enabling the physically handicapped child to remain at home whenever possible. Some of the provisions of the enlightened Children Act of 1948 have still not been implemented, and he particularly regrets the dilatoriness in establishing temporary reception centres which would spare deprived children from facing several changes before they are settled in suitable homes. But more and more deprived children are enjoying a happy home life rather than growing up in abnormal institutional surroundings.

His emphasis on the value of a closer liaison between parents and schools, and his belief that school doctors should take more part in school activities and instruction, are sound. There will also be general agreement with his view that still more could be done to help parents to accept responsibility for home care by encouraging them to overcome their troubles by living with them instead of passing them on to someone else, and with his timely warning of the increasing danger of parents demanding as a right to have everything done for them.

Physiopathology of Cancer

Editor : FREDDIE HOMBERGER, M.D., research professor of medicine; WILLIAM H. FISHMAN, PH.D., research professor of biochemistry, Tufts College Medical School. London : Cassell. 1953. Pp. 1031. 13s.

In his introduction to this weighty tome, Dr. C. C. Little emphasises the need to have at least a speaking acquaintance with the objectives, obstacles, and advances in all possible channels to progress. To meet this need the book not only covers research on the physiopathology of cancer, but goes much beyond its title and includes contributions from biology, chemistry, physics, clinical investigations, and practical applications. The durable value of some of the articles perhaps justifies the lavish production and high price.

Inevitably there is overlapping and even a little discord among the 28 contributors. Omissions of new work are unavoidable owing to the time-lag in publication. References extend only to 1951, with a few footnotes of later date. Recent successes in grafting heterologous tumours in the cheek pouch of the hamster, which will affect opinions on the immunological basis of grafting, are not included, nor is the reported action of cortisone in increasing metastatic growth. A more serious omission, not due to a time-lag, is a discussion of the subdivision of tumour induction into stages that have been described as initiation and promotion. This analysis of tumour genesis has practical uses as well as profound theoretical value.

But the excellence of many chapters outweighs any defects. The chapter on hormonal factors in experimental carcinogenesis may prove one of the most generally useful. The

chapter on steroid metabolism gathers together widely scattered and often discrepant data.

At present our only hope of reducing the amount of human cancer is by prevention, and only precise knowledge of environmental cancer will enable us to achieve this. This is the theme of a most informative section on occupational and other environmental factors. It is supported in another section by a lucid account of the problems of collecting and interpreting data and the help that can be expected from statistical studies. Well-balanced accounts of theories of carcinogenic mechanisms, chemotherapy, and radiation therapy, and an adverse review of diagnostic tests are included. The virus theory is dealt with in lively fashion, stress being laid on known instances of non-specificity of cell infection, thus making more plausible its universal application to all morphological varieties of cancer in all classes of animals. A section on epidemiology of spontaneous virus infections in avian flocks in the U.S.A. provides new observations on the time of appearance of antibodies to the Rous sarcoma virus in young birds and on the high incidence of antiviral antibodies to three varieties of infection in older ones. This information has long been wanting on both sides of the Atlantic.

Pulmonary Tuberculosis

Pathology, Diagnosis, Management and Prevention. 3rd ed. WALTER PAGEL, M.D., pathologist, Central Middlesex Hospital ; F. A. H. SIMMONDS, M.D., physician and medical director, Clare Hall Hospital ; NORMAN MACDONALD, M.B., M.R.C.P.E., physician, Clare Hall Hospital. London : Oxford University Press. 1953. Pp. 728. 8s.

The general plan of presentation in this edition of Kayne, Pagel, and O'Shaughnessy's Pulmonary Tuberculosis is the same as in the last, but so swift have been the advances in the subject during the past five years that much of it has been rewritten—notably the sections on chemotherapy and surgical management, epidemiology, prevention, and B.C.G. vaccine. Dr. Nassau has again revised his chapter on bacteriological diagnosis. Yet the book remains the same size, and contains all the important facts. The quality of the many illustrations is high.

The authors' deep insight into the disease as a whole and into its natural progress has enabled them to maintain balance between the different aspects of the subject, and has clearly steadied them in their evaluation of such modern methods of treatment as lung excision—a radical measure which has still to win its long-term spurs. On the other hand, they are perhaps too severe in their criticism of the artificial pneumothorax, and possibly too lenient towards the pneumoperitoneum which has certainly felt the impact of chemotherapy and modern surgery much more than has the artificial pneumothorax.

Viruses

Symposia on Quantitative Biology. Vol. 18. Cold Spring Harbor Biological Laboratory. 1953. Pp. 301. \$8.00.

If the textbooks contain solid fare, the Cold Spring Harbor symposia provide exotic and highly spiced dishes unsuited to tender digestions. In this instance there are 41 papers, mainly on bacteriophages, and to a lesser extent on animal viruses, and anyone who listened attentively to all 41 papers must have emerged sadder and perhaps wiser.

The papers are grouped as follows : virus in the vegetative state (i.e., in course of intracellular development) and its maturation, including recombination and multiplication cycles in bacterial and animal viruses ; provirus (this is the state in which virus is assumed to exist in latent infections during which its development can be stimulated at any stage, although at the moment it cannot be identified in the provirus form) ; the transition from provirus to vegetative virus (both these groups of papers deal mainly with bacteriophages) ; structure of viruses ; biochemical studies of virus infections ; host-controlled variations of viruses ; and, finally, the new and rapidly developing field of animal viruses in tissue culture.

This is a unique collection of essays containing a great deal of thought-provoking stuff, but it must be read in small doses, and certainly not in bed.

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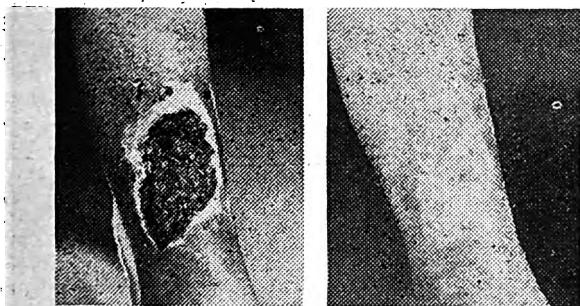
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THE LANCET

LONDON : SATURDAY, MAY 8, 1954

Hazards of Broad-spectrum Antibiotics

ON an earlier page of this issue Dr. HAY and Dr. MCKENZIE describe the side-effects observed in the treatment of 603 cases with oxytetracycline (terramycin). Their patients under 12 years of age received 20 mg. per kg. of body-weight daily in four equal divided doses; those aged 12 years and over were given 2 g. daily. The drug was given with abundant fluids, usually milk, and vitamin B was also administered. Despite these precautions the incidence of side-effects was 8%; and 2 of the patients died with fulminating gastro-enterocolitis associated with coagulase-positive staphylococci. This considerable and well-documented series of observations brings home to us yet again that oxytetracycline, like other broad-spectrum antibiotics, must be prescribed cautiously. Apart from the 2 instances of fatal gastro-enteritis, HAY and MCKENZIE draw attention to other important staphylococcal complications of oxytetracycline therapy: sore throat with a scarlatiniform rash (7 cases); sore throat without a rash (8 cases); balanitis with scarlatina (1 case); and urinary infection (3 cases). The untoward effects in these 21 cases commonly appeared on the fourth or fifth day after the start of treatment. Not all of these 21 patients were examined bacteriologically, but staphylococci were isolated and incriminated as the probable cause in 14 of them. Other side-effects were observed in a further 31 cases: pyrexia (24); urticaria (3); and transient erythema (4). The 24 cases in which pyrexia was the only symptom were not examined bacteriologically, but the time of onset of the pyrexia coincided so precisely with that of the proven staphylococcal cases that there is at least a strong suspicion that the same organism was involved. The reports of the cases of urticaria and erythema read like the usual accounts of skin-sensitisation to antibiotics. Other reports of complications with the broad-spectrum antibiotics, from many sources,¹⁻⁵ combine to give a picture of antibiotic-resistant staphylococci stepping in to colonise the territory from which other bacteria have been eliminated, with rapidly fatal gastro-enterocolitis as a far-from-rare result.

What are we to do about this state of affairs? Clearly we must bring ourselves to understand that oxytetracycline, aureomycin, and the combination of penicillin and streptomycin are potentially lethal. In appropriate cases their use is justified; but we have to become more certain what is an appropriate case. HAY and MCKENZIE reasonably state that broad-spectrum antibiotics should not be used for trivial and minor illnesses. Nor should they be used for routine prophylaxis against infections which are far from inevitable and would be easily controlled if they

appeared. The effects observed by HAY and MCKENZIE, although serious enough to cause misgiving, are by no means as grave as some that have been reported—by TERPLAN et al.,⁵ for example. One reason may have been that HAY and MCKENZIE adopted a relatively moderate scheme of dosage. FINLAND et al.⁶ found, with oxytetracycline, that staphylococcal diarrhoea was about twice as common among patients who received 250 mg. every four hours or 500 mg. every four or six hours as it was among others who received only 250 mg. every six hours. They found also that administration of purgatives during antibiotic therapy tended to precipitate staphylococcal enteritis. In the treatment of urinary infections GOULD et al.⁷ showed that remarkably small doses of antibiotics not only brought about cure but prevented the appearance of resistant organisms. Possibly our attitude to dosage of antibiotics is governed too much by a warlike feeling that we must drive the offending organisms from their hold on the tissues before they can grow accustomed to our weapons and produce a resistant strain; no doubt a right fear of inadequate dosage is partly responsible for the prevailing tendency to give more drug than is either necessary or safe. Our approach possibly lacks subtlety. Bacteria have almost infinite powers of adaptation,⁸ but there is some experimental evidence that by swiftly eliminating all the sensitive organisms from a mixed population we leave the field to the resistant ones. Important recent work by SAZ and EAGLE,⁹ who discuss earlier related experiments,¹⁰⁻¹⁴ now clearly shows that penicillin-resistant staphylococci may be killed if grown on agar along with penicillin-sensitive staphylococci and low concentrations of penicillin. The explanation of this sensitisation phenomenon, which could be demonstrated only in a relatively narrow zone of penicillin concentrations, is not clear; and the results, which were strictly species-specific, were not easy to reproduce with regularity and could not be demonstrated at all in fluid cultures. SAZ and EAGLE wonder whether fractions released from penicillin-sensitive organisms undergoing lysis at low concentrations of penicillin may have been incorporated into the penicillin-resistant members, which were thus transformed to sensitive organisms. This interesting work should at least remind us that bacteria may respond more readily to finesse than to blasting. On every ground we have reasons for trying to find the lowest dose of an antibiotic that will do the job required of it.

Another simple empirical measure perhaps deserves more attention than it has received. MANHEIM¹⁵ gave *Lactobacillus acidophilus* or buttermilk for anorectal complications due to antibiotics, and WILLCOX¹⁶ used yogurt for the same purpose. POLYMERAKOS¹⁷ now reports that the result of giving

6. Finland, M., Grigsby, M. E., Haight, T. H. *Arch. intern. Med.* 1954, 93, 23.
7. Gould, J. C., Bowie, J. H., Cameron, J. D. S. *Lancet*, 1953, i, 361.
8. Adaptation in Micro-organisms: Third Symposium of the Society for General Microbiology. Edited by E. F. Gale and R. Davies. London, 1953.
9. Saz, A. K., Eagle, H. *J. Bact.* 1953, 66, 347.
10. Vourekas, A. *Lancet*, 1948, i, 63; *J. gen. Microbiol.* 1952, 6, 352.
11. Winner, H. I. *Lancet*, 1948, i, 674.
12. George, M., Pandalai, K. M. *Ibid.* 1949, i, 955.
13. Barber, M. *Ibid.* 1948, i, 730.
14. Bennison, W. H., Schwabacher, H. *Ibid.* p. 885.
15. Manheim, S. D. *N.Y. St. J. Med.* 1951, 51, 2759.
16. Willcox, R. R. *Lancet*, 1951, ii, 154.
17. Polymenakos, L. G. *Ibid.* April 3, 1954, p. 732.

1. Kramer, I. R. H. *Lancet*, 1948, ii, 646.

2. Gardner, D. L. *Ibid.* 1953, ii, 1236.

3. See *Ibid.* p. 1245.

4. Golffson, R., Golffson, B. *Pr. med.* 1954, 62, 488.

5. Terplan, K., Paine, J. R., Shaffer, J., Egan, R., Lansky, H. *Gastroenterology*, 1953, 24, 476.

three or four cups daily of yogurt along with broad-spectrum antibiotics is excellent from the point of view of reducing nausea, diarrhoea, and burning in the anorectal region. Lactobacilli are not easily established in numbers within the intestine of normal adults eating a mixed diet, but the situation may be different when antibiotics have removed most of the normal flora of the region and the diet is mostly of milk. If lactobacilli can be established they will certainly make it hard for staphylococci to take charge. Whatever we resolve to do, we dare not continue to ignore a series of therapeutic complications which are not rare and which endanger life.

Salicylates in Rheumatic Fever

THE therapeutic value of cortisone and corticotrophin in rheumatic fever has not yet been fully analysed, but it already seems unlikely that the long-accepted reputation of salicylates will suffer much by comparison. Yet while few would deny the special analgesic and antipyretic properties of salicylates, the case for attributing to them specifically anti-rheumatic action remains unproved—at any rate with regard to carditis and its sequelæ. The recent application to rheumatic fever of hormone therapy, with the full panoply of modern methods of clinical trial, has illuminated some of the shortcomings of previous investigations of salicylates. In 1949, already aware of these inadequacies, Professor ILLINGWORTH and his colleagues initiated at Sheffield a new attempt to assess the value of salicylate treatment, and these workers have now published an interim report.¹

Assessment is difficult in a disease such as this which runs a variable natural course, and the Sheffield group planned their study in a way which provides valid comparisons of accepted simple observations on treated and control groups. In the matter of salicylate dosage, they found real evidence from previous work of the short-term value of high dosage; and they have aimed at blood-levels of 30–40 mg. per 100 ml. The interim findings are based on investigation of 55 children—44 with first attacks and 11 with relapses. Diagnosed on admission by accepted criteria,² these cases were distributed without exclusion between control and salicylate groups, whose treatment was otherwise identical, including continuous antistreptococcal prophylaxis with penicillin or sulphonamides. Professor ILLINGWORTH and his colleagues were determined to let no child suffer if he was allocated to the control group and his progress was subsequently unsatisfactory, and in fact 5 cases were transferred from the control to the salicylate group during the investigation; 2 of these, in which pericarditis was present, were included in the final assessment, thus weighting the salicylate group unfavourably. The strict analysis of results shows that the patients who received large doses of salicylates daily until the erythrocyte-sedimentation rate had fallen to normal and remained so for two weeks—an average period of 65 days—fared better than those not receiving the drug. Analysis under different heads—the effect on arthritis, temperature, sleeping pulse-rate, cardiac murmurs, and erythrocyte-sedimentation rate—showed results

significantly in favour of salicylates only in the effect on the fever and on the sedimentation-rate. After a relapse the speed of fall of the sedimentation-rate in both treated and control groups was distinctly slower than after a first attack; but this rate was still significantly greater in the salicylate-treated cases than in the controls; which, as the authors point out, is at variance with the idea that salicylates are of value only if given early. Other clinical comparisons showed no significant differences; but, despite the adverse weighting against the salicylate group, under each heading such differences as there were favoured salicylates. This was also true of the final clinical assessment of treated and control cases, after periods of observation averaging 31 and 32 months respectively.

This appraisal of the worth of salicylate therapy in rheumatic fever confirms, then, that patients do better with it than without it. The Sheffield study will be a useful yardstick for future clinical trials.

Psychiatric Evidence at Murder Trials

CRIME is social abnormality; and serious crime is often associated also with mental aberration—a defect of will and reason. On a capital charge, it is almost impossible for judge and jury to determine unaided whether or not, at the time when he committed murder, the accused was suffering from a disease of the mind. As soon as any question of this kind arises—and in many cases the very gravity of the offence will raise it—the court will need the advice, if not the guidance, of expert psychiatrists.

The execution of an insane criminal is not merely abhorrent to the community, but is actually itself a crime by the ancient tradition of the common law. Indeed, despite the absurd wording of the verdict "guilty but insane" (which was introduced into our system as late as 1883 on the personal insistence of QUEEN VICTORIA after an attempt had been made on her life), an insane person who has committed murder is not responsible in criminal law, and cannot be punished; he is *not guilty*. How best to collect the necessary data and diagnoses on the issue and present the essential medical evidence to the jury is a problem which has long caused concern, and the situation in English courts is not yet satisfactory. Clear-cut diagnosis of the exact degree and stage of mental disease, and the expression of this diagnosis in terms comprehensible to laymen, is extremely difficult, and the responsibility involved in such a matter of life and death is extremely grave; yet the position of psychiatrists in murder trials is in no way different from that of other expert witnesses in ordinary criminal or even civil proceedings.

These questions were raised (incidentally) during the deliberations of the Royal Commission on Capital Punishment¹; but, though the commission recommended certain minor alterations in the present somewhat haphazard practice, it did not feel justified in making any far-reaching recommendations which would have repercussions beyond the limited field of its inquiry. Fortunately, however, in one of the numerous and valuable appendices to its report, the commission did assemble and publish a considerable amount of up-to-date information about the law

1. Illingworth, R. S., Burke, J., Doxiadis, S. A., Lorben, J., Philpott, M. G., Stone, D. G. H., Scott, J. F. *Quart. J. Med.* 1954, 23, 177.

2. Jones, T. D. *J. Amer. med. Ass.* 1944, 126, 481.

1. See *Lancet*, 1953, ii, 713.

and practice in these matters in foreign countries. This information suggests a definite trend towards a more scientific approach, and should help in formulating the principles that ought to govern psychiatric evidence in murder cases under any modern legal system.

In the United States, and in most Continental countries, the law not only provides for routine psychiatric examination upon arrest of anyone accused of murder, but entrusts this examination to independent psychiatric criminologists appointed either by the court (so-called court experts) or by an autonomous professional body. In France, for instance, experts will be chosen by pricking names on a roll of specialists available at each assize court, and a similar practice obtains under the German code of criminal procedure. In the United States the responsibility of the medical profession in the selection is even more direct. In the State of Massachusetts, for instance, under a law introduced in 1921, the court asks the department of mental health for a report on the mental state of the accused, while in New York State two qualified psychiatrists are usually nominated by the superintendent of a public hospital. The advantages of some such system, which does not rely on prison doctors attached to the remand prisons, are obvious even from comparison of English practice with that in Scotland, where two outside specialists are regularly called in. Psychiatrists thus selected have no connection whatever with the prosecution or the prison authorities—an important point if justice not only is to be done to the accused, but is also to be plainly seen to be done. It is the medical profession itself which, through its organisations, guarantees the independence of judgment and the medical qualifications of the experts. In these circumstances there is greater likelihood that the medical findings will be accepted by both sides, and that conflict of testimony about sanity will be avoided at the eventual hearing in court. Such a development has already been observed in Scotland, but experience in the United States is said to go even further. In Massachusetts, for example, the plea of insanity is rarely raised by the defence where the psychiatric report (obtained in the manner described above) is unambiguously negative, although the defence is fully entitled to appoint its own experts and to call upon their evidence at the trial. Such a result would certainly seem desirable in clear-cut cases. The fact that in English courts insanity is almost always pleaded as a last resort—and often on inadequate grounds—has presumably contributed not a little to the scepticism with which judges and juries nowadays view the psychiatrist.

There are other important points in favour of charging an independent medical body with the appointment of expert psychiatrists for murder trials and with preparation of the necessary report and evidence. Of these the most important perhaps is the possibility thus afforded for long and close observation. Many foreign legal systems seem to work on the assumption that at least two weeks, and possibly as much as two months, of continuous investigation may be required before the necessary case-history can be compiled and a reliable opinion can be formed. Obviously such observation is best

carried out in a mental hospital, and not in an ordinary prison, although some countries, including Holland and France, have established special psychiatric observation clinics attached to certain large prisons. Because of the practical difficulties, the Royal Commission on Capital Punishment rejected for this country the idea that all prisoners charged with murder should be transferred for an initial period of observation to a mental hospital; but we trust that some alternative will eventually be found to the present system whereby examination of the prisoner is normally limited by the facilities (or lack of them) at an ordinary remand prison. Moreover, anyone familiar with the full reports of recent trials on capital charges will be aware that the prosecution often benefits from the fact that the prison doctor has had the accused under continuous observation during the period of remand, whereas outside specialists called for the defence must base their findings on short interviews. This is the more serious in view of the presumption of English law (not known to most foreign systems) that any man is sane unless the contrary is proved to the satisfaction of the jury. It is thus up to the defence to satisfy the jury that the prisoner was so insane as not to be responsible for his actions. In at least one recent murder trial the accused was convicted although the only medical witness who gave evidence at the hearing declared him to be suffering from a serious mental disease.

It is generally felt today that it would be highly undesirable to deprive the judiciary of the final decision on whether or not the accused was so insane at the time of his crime as not to be responsible in the eyes of the law. That this is a legal, not a medical, question is now recognised in all countries. Nevertheless, experience in this country, and the law and practice abroad, should make it possible to devise measures to ensure more reliability—and consequently greater persuasive weight in the courts—for psychiatric reports and evidence. These might be summarised as follows:

- (1) Obligatory and compulsory examination before trial of every prisoner charged with murder, by at least two psychiatrists whose professional qualifications and experience are of a high order.
- (2) Independence of the expert judgments and opinions to be assured by special methods of selection and appointment of the psychiatrists.
- (3) All expert reports and testimony to be based on lengthy and continuous observation and investigation.
- (4) At the trial, strictly scientific, and as far as possible non-controversial, presentation of the evidence on the issue of sanity.

Though there would still be honest differences of expert opinion, testimony of independent psychiatrists, reporting after adequate observation, and freed from some of the less agreeable aspects of hostile cross-examination at the trial, should help to bridge the present gap between the law and medicine on the complex issues involved. True enough, even the present system in this country avoids on the whole the suspicion that insane persons have been, or are likely to be, made to suffer the extreme penalty of the law. It does so by means of the Home Secretary's inquiries, under the Criminal Lunatics Act of 1884, after sentence of death has been passed. But it is not easy to avoid the impression that the very necessity for such a last-minute inquiry

(except in the rare cases where a prisoner has become insane since conviction), and the spectacle of so many death sentences pronounced but never carried into effect, are in themselves a sure sign that all is not well with the law as it stands. It may have something to learn from the practice of other countries.

Annotations

A SURGICAL OCCASION

As we have already announced, the American College of Surgeons is, for the first time, holding one of its sectional meetings in England, and the proceedings which will open at the Royal College of Surgeons on May 17, with Sir Cecil Wakeley in the chair, are likely to be attended by some 400 American and 600 British surgeons. The three-day programme, which promises contributions from some 70 speakers, includes "panel discussions" on intestinal obstruction, on preoperative and postoperative care, on massive haemorrhage from the gastro-intestinal tract, and on hand surgery, together with symposia on gynaecological subjects, on cancer, and on cardiovascular surgery; while official lectures in the Royal College of Surgeons will be given by Prof. Howard C. Naffziger (progressive exophthalmos) and Prof. Walter C. MacKenzie (pancreatitis). Local arrangements made by the English college include visits to London hospitals for operating sessions, special programmes for urologists, ophthalmologists, and otolaryngologists, and an exhibition of surgical instruments. There will be a banquet at the Dorchester Hotel, with the Marquess of Salisbury as the guest of honour, and receptions by the president and council of the Royal College of Surgeons, and by H.M. Government. The new great hall of the college, with a seating capacity of about 700, will be used for the meeting.

After arriving in England next week, many of the American visitors will participate in the meeting of the Association of Surgeons of Great Britain and Ireland which is being held in Leeds from May 13 to 15. The Royal College of Surgeons of Edinburgh, where Prof. Evarts A. Graham is to deliver the Fraser lecture, is holding a reception on May 11; and both before and after the London meetings visits will be paid by groups of individuals to various centres in this country and to further conferences on the Continent.

VIRUS VIRULENCE

THE researches of Burnet and his colleagues^{1,2} in Melbourne and Hirst and Gottlieb³ in New York have clearly shown that when two different strains of influenza virus are grown together, under conditions in which both can infect the same cells, new forms of virus are produced which carry properties from both parents. There is still doubt as to the finer details of how these combined forms of virus are brought into being, but meanwhile Burnet and Lind⁴ have used the genetics of the interaction between two influenza viruses to study the problem of virus virulence.

All strains of influenza virus grow well in the chick embryo, but some kill the chick rapidly by producing haemorrhagic lesions. Again, all strains of influenza virus A grow in the mouse lung; most strains do not produce pneumonia, but by adaptation these strains can be trained to cause fatal pneumonia. Likewise, one or two strains of influenza-A virus have been adapted to produce fatal encephalitis on inoculation into the mouse brain. It is possible therefore to have avirulent influenza strains

and strains which are virulent in one or more of three different situations, and to study the effects of genetic interaction between avirulent and virulent strains. Burnet and Lind⁴ summarise the results of many experiments with the finding that the progeny of crosses of this type generally show many intermediate stages of virulence. This, they point out, accords with the gradual way in which virulence of a virus for a new host is built up by passage, and it suggests that the virulence of a strain is a function of several genes. It is still uncertain how these genes are shared between parents and progeny during the simultaneous multiplication of an avirulent and a virulent strain in the same cell, but Burnet and Lind postulate the existence of virulence genes rather loosely associated with the rest of the "nuclear" apparatus (or genome) of the virus and able to multiply in the host-cell in a rather independent way. Different genomes will have different affinities for these virulence genes, and the two will reassociate at a later stage in virus multiplication.

This type of hypothesis reflects the very rapid progress in the theoretical understanding of the multiplication of these viruses. But the concept of virulence is not an easy one, being inseparable from its counterpart—the susceptibility of the host. Virulence may embody a number of components: the rate of virus multiplication, the amount of virus produced, the possible toxic materials produced, and interference with normal cellular syntheses. Future study will probably be directed to the way in which these and other components are inherited along with the general over-all property of virulence. Meanwhile studies such as those of Burnet and Lind carry wider implications, and should stimulate fresh ideas on the biology of living cells.

THE NEW EPIDEMIOLOGY

BECAUSE of their apparent preoccupation with the work of Snow on cholera, epidemiologists are often accused of having a "Broad Street pump fixation." That charge could not be levelled against Dr. John Gordon, whose views on population problems we noted in a leading article last week. As he said to a meeting of the epidemiology section of the Royal Society of Medicine on April 30, epidemiology is an attitude of mind rather than a body of knowledge, a research discipline now widely applied over the whole field of medicine. Unlike the other basic methods of medical investigation—clinical and laboratory study—it is concerned with groups rather than with individuals, and Gordon believes that it can play a useful and complementary rôle in the study of the aetiology of disease.

Originally, epidemiologists functioned as a fire-brigade, dealing in a patchwork way with dramatic outbreaks of acute infectious illness. Later, by a process of learning while doing (what would now be called operational research), the careful recording and analysis of the sequence of events in a series of outbreaks allowed the generalisation of principles of epidemic behaviour. Even now, the epidemiologist learns his trade by the study of infectious illness. Although still important in the Western world and still dominating all else in many other countries, infections are being supplanted by the degenerative diseases as a cause of death and disability. Some of the old techniques retain their value, but with disorders which evolve slowly, both in the individual and in the community, new ideas are required. The proband method is the only really short cut to a study of the factors which affect the natural history of a disease: essentially, this means the comparison of the past history of known cases of the disease with similar histories for control subjects; the inference is that any differences observed in habit or physical constitution are factors in the causation of disease. Useful as it is in giving clues, this approach has its limitations since we can never be

1. Burnet, F. M., Fraser, K. B., Lind, P. E. *Nature, Lond.* 1953, 171, 163.
2. Burnet, F. M., Lind, P. E. *Symposia on Quantitative Biology, Cold Spring Harbor, New York.* 1953; vol. 18, p. 21.
3. Hirst, G. K., Gottlieb, T. E. *J. exp. Med.* 1953, 98, 41.
4. Burnet, F. M., Lind, P. E. *Nature, Lond.* 1954, 173, 627.

confident that we are indeed observing cause and effect rather than a fortuitous association between habit and disease. Increasingly, therefore, clues given by retrospective studies are being followed up by carefully planned prospective investigations. Thus, retrospective studies on both sides of the Atlantic suggest that smoking is a factor in the aetiology of cancer of the lung, and, to quiet doubts about the possibility of bias in smoking histories, groups of men whose smoking habits have been ascertained are being followed up over a period of years to ascertain the differential incidence of the disease according to smoking habit.

Within communities, the slow evolution of diseases like cancer and diabetes has meant that their natural history has had to be inferred from vital statistics of mortality. Unique clinical observations, like Pott's identification of scrotal cancer with chimney-sweeping, gave way to a systematic search of occupational mortality statistics for the environmental factors which precipitate malignant change. Now, Gordon observes, complete families and communities are under observation and the evolution of disease is studied over long periods of time. In the U.S.A., a survey revealed that 1.7% of a town's population were suffering from diabetes, half of them without knowing it; and when doubtful cases were followed up over the years, frank diabetes was appreciably commoner among them than among the apparently healthy. If anticipation be the first step to prevention, then such studies show one way towards the control of diabetes. Again, long-term studies of uncommon communities, such as nuns in religious orders, may show the modifying effect of a sheltered environment, with restricted stresses and contacts, on the development of degenerative disease.

Geographical pathology is a term with a vintage flavour, but Gordon believes that the subject will justify its resuscitation. Global war and air transport have given it a new lease of life, for we cannot assume that the facts of epidemic behaviour of a disease can be directly translated from temperate to tropical or arctic climates. On the other hand, a comparison of disease behaviour in different climes can give fresh clues about the modifying effects of habits and environment, and lead on to new prospective studies, which Gordon regards as the modern and natural development of the epidemiological method.

BAKER STREET DIAGNOSIS

"My friend took the lady's ungloved hand and examined it with as close an attention and as little sentiment as a scientist would show to a specimen."

"You will excuse me, I am sure. It is my business," said he, as he dropped it. "I nearly fell into the error of supposing that you were typewriting. Of course, it is obvious that it is music. You observe the spatulate finger-end, Watson, which is common to both professions?"

Cardiologists, like Mr. Sherlock Holmes,¹ study hands for clues to the personalities and the diseases with which they have to deal. Silverman and Littman² have listed the manual signs that cardiac patients may show. The moist palm, the coarse finger-tremor, and the cold cyanotic skin of neurocirculatory asthenia contrast with the flushed warm hands of hyperthyroidism. Clubbing and cyanosis indicate chronic cardio-pulmonary inefficiency. Arachnoidactyl or the short coned fingers of mongolism are a hint that a congenital cardiac lesion should be sought.

Subacute bacterial endocarditis produces signs in the hand so specific that they should be woven into the engrams of every examination candidate. Censors do not readily forgive a confusion between Osler's node (first described by Mullen) and the Janeway lesion; the former is a small raised tender red nodule in the

skin of finger or toe, the latter a painless erythematous patch in the palm. The candidate must notice also, as he rapidly inspects the proffered hand of his "short case," the splinter-haemorrhage beneath the nail, the clubbing of the finger-ends (particularly in the forefinger and thumb), and the pallor of the palmar creases.

Diagnosis, like detection, begins with a clue. Spatulate fingers, clubbed fingers, bitten nails, painted nails, nicotine stains, ink-stains, hands firm or fleshy, moist or horny—these are often the first clues from which we construct our mental picture of the disease and of the patient's personality. Flaccid pliant hands are, for example, found in persons who habitually use kinesthetic modes of thought and expression³; they contrast with the stiffer and less expressive hands of visualisers and verbalisers. Yet manual signs seldom justify a spot-diagnosis. Even the great Holmes nearly fell into the error of confusing a pianist's hand with a typist's, until he extended his examination and concluded:

"There is a spirituality about the face, however,—he turned it gently towards the light—'which the typewriter does not generate. This lady is a musician.'

ACUTE OSTEOMYELITIS

PENICILLIN has removed the dread of acute osteomyelitis as a mortal disease; and large series are now published in which there is not a single death. But although most people would agree that the very early infection can be completely cured or aborted by antibiotic therapy alone, the outlook is less cheerful in cases which arrive in hospital about the fourth or fifth day of their illness, as they commonly do; and chronic osteomyelitis remains as serious a problem as ever. We have today little more to offer the patient with chronic bone infection than we had a generation ago; but, on the other hand, we have good opportunities of preventing the development of chronicity.

During the early years of penicillin, there were those who advocated the use of penicillin alone, pus being released or aspirated only when a frank abscess presented. But, largely as a result of the excellent work of Trueta on the likelihood of interference with the blood-supply of the bone, this laissez-faire attitude has largely fallen into the background, and most paediatricians and orthopaedic surgeons would agree that early evacuation of pus is of great importance. The days of open drainage and extensive guttering of the bone are past, but the question remains whether operation and drilling of the bone is best or whether aspiration alone, repeated if necessary, is sufficient. Powerful evidence in favour of operation has been produced by Trueta and his colleagues, who believe that the stripping of the periosteum by oedema fluid, and then by pus, causes ischaemia of the underlying bone and later severe bone changes, occurring after the infection has apparently been controlled. Most of the advocates of aspiration alone have been paediatricians, and their series often contained a preponderance of infants. Hitherto no-one has been able to produce comparable series which would help in deciding the question.

In their article in this issue, Mr. Bremner and his colleagues try to give an impartial answer from the results of their trial, in which some cases were treated by aspiration and others by operation. As far as possible, they have adopted strict criteria in selecting comparable groups of cases, and this strictness means that they have been limited to the relatively small total of 23 cases. They set out to decide whether, when, and how to remove any pus present. They are in no doubt that it should be removed and the earlier the better; they found little to choose between the results of repeated aspiration and of incision, drilling, and suture. They

1. Conan Doyle, A. The Complete Short Stories of Sherlock Holmes. London, 1928; p. 340.

2. Silverman, J. J., Littman, D. S. *New Engl. J. Med.* 1953, 249, 839.

3. Short, P. L., Walter, W. G. *Electroenceph. clin. Neuro-physiol.* 1954, 6, 29.

prefer aspiration for various reasons, but its successful application "demands a high standard of clinical judgment, with daily reassessment, and may not be achieved consistently except in centres where many cases are seen."

Trueta and Morgan¹ have just published the late results of the first hundred cases treated by Trueta's method, and it is interesting to see how very similar their findings are. Trueta advises larger doses of penicillin (1,000,000 units per twenty-four hours), but in both series penicillin is given for an average period of thirty days and recovery takes sixty to eighty days. It is good to note the low proportion of penicillin-resistant staphylococci both in Newcastle and Oxford at the time of these trials, but perhaps resistant strains are now more troublesome. Trueta gives a very clear-cut plan of treatment; operation is undertaken unless the second examination, twenty-four hours after admission, shows clear evidence that the condition is improving. It seems that this twenty-four-hour rule was followed irrespective of the physical signs on admission, but that operation was, in fact, undertaken in nearly every case. Although the two groups are not strictly comparable, it seems likely that radiologically the Oxford patients have suffered rather less bone damage than the Newcastle group, but the latter perhaps had more severe infections. Even though they are described as "late results," the Oxford cases are of less than ten years' duration, and, alas, osteomyelitis can flare after many decades of dormancy.

Even though the question of detail remains uncertain, these two pieces of evidence agree in principle. For the surgeon without wide experience of this condition, Trueta's open evacuation of pus and limited drilling of the bone will be simpler in application and it will probably produce less anxiety and less unwanted bone. But neither side can yet be said to have won the day.

ORIGIN OF LIFE

Is life universal, or confined to our planet? Was there a single Creation in time past, or must we try to conceive of life as a regular by-product of matter, perpetually renewed somewhere in the universe—just as, according to the theories of Fred Hoyle and others, matter itself is continually created out of void? It is less than a hundred years since Pasteur gave the coup-de-grâce to belief in spontaneous generation as an everyday process on earth, and knowledge of what goes on elsewhere awaits the explorations of the astronauts. Will they really meet intelligent sentient beings straight from the pages of science fiction? Many new facts and interpretations in astronomy, geophysics, and biochemistry throw light on these problems. More important, as the four contributors to a popular symposium² make plain, there has recently been something of a philosophical reorientation in scientific thinking on the subject.

Partly this is the recognition that the term "living" must be applied to practically anything which can catalyse the production of more of itself from raw materials in its surroundings. To think only in terms of green plants and legged beasts is too restrictive; these are the forms of living things shaped by purely terrestrial conditions, but elsewhere evolution might take a totally different and unimaginable path. On Jupiter, for instance, liquid ammonia has the prevalence of water on earth: are there races of self-reproducing units in those cold nitrogenous seas? Haldane goes so far as to imagine that there might be a new form of life in the interior of the earth—organisms made of molten silicates, drawing the energy for their growth from the slow oxidation of the metals in the core. It is clear that "life" no longer implies necessarily the protein-carbo-

hydrate biochemistry to which we are accustomed. Those who study meteorites, embark on interplanetary voyages, or still look to discover spontaneous generation on earth must seek with innocent eyes, with minds cleared of all old preconceptions, if they are to see the alien forms that life may take.

Even simple terrestrial organisms such as amoebae or bacteria are extremely complex biochemically, and cannot possibly represent starting-points of the evolution of the animals and plants we know. Their spontaneous generation in the dilute soup which the seas may have been a thousand million years ago is as unlikely as it would be in broth under modern laboratory conditions. Biologists therefore recognise that the evolutionary line must be prolonged backwards through much simpler chemical systems to the simplest of all—the self-reproducing molecule. Perhaps there were many of these molecules of different kinds competing against one another for millions of years. Perhaps they had a tendency to fuse or aggregate. Perhaps once in a hundred thousand years the fusion of two dissimilar self-reproducing molecules led, not to the extinction of one or both partners, but to a viable product with enhanced powers of replica synthesis. Such subvital units of many kinds may have been the true raw material of evolution, and the creation of such units is the proper goal in any future work on spontaneous generation, or biopoiesis.

This leads to a third theoretical development, which indicates the kind of subvital units to expect at the dawn of terrestrial life. It has often been pointed out how admirably the earth's physicochemical nature fits it for the maintenance of life. This is so, says Bernal, because it is the chemical and physical properties at the earth's surface that have directed primitive evolution. Chemical processes which occur in almost all organisms are likely to be the most primitive and to most resemble the changes in ancient rocks—the oxidation and reduction of iron and sulphur, and the polymerisation and break-up of phosphates. The fact that proteins are strongly adsorbed by clays suggests some kind of spatial resemblance between clay and protein, which might have resulted if the first subvital protein-like units arose in the interstices of a clay "soil" rather than in the open sea. Living things, unlike even the primitive sea, contain much potassium: clays also adsorb this element strongly. On the other hand, clays are aluminium compounds and if life evolved under their influence it is surprising that aluminium has no metabolic rôle in the organisms of today. This objection of Pringle's however, leaves the principle of the method unassailed.

Meanwhile, the geochemists continue to delineate the setting for the play of life on earth. The earth arose by dust condensation perhaps 4000×10^6 years ago, and has never been very hot—perhaps no hotter than boiling water on the surface. Its early atmosphere may have been chiefly of methane and ammonia, with some water and hydrogen: lightning striking through such a gas mixture produces traces of amino-acids, such as glycine and alanine. Study of the relative abundance of the two isotopes of sulphur—S³² and S³⁴—in rocks of various ages indicates that the first photosynthetic sulphur bacteria (which use one isotope preferentially) began their existence about 800×10^6 years ago. Biochemists are unravelling the universal chains of living tissues—the polypeptides, polysaccharides, and polynucleotides—and describing in a few organisms, such as tunicates and beetles, the bizarre chemistry which may represent vestiges of the biochemical past. Even if the creation of life in the laboratories remains an unattainable ideal, the new ideas are going to stimulate valuable research.

Prof. F. L. Hopwood, D.Sc., consulting physicist to St. Bartholomew's Hospital, London, and hon. secretary to the British Empire Cancer Campaign, died on May 2 at the age of 70.

1. Trueta, J., Morgan, J. D. *Brit. J. Surg.* 1954, 41, 449.

2. Haldane, J. B. S., Bernal, J. D., Pirie, N. W., Pringle, J. W. S. *New Biology*, no. 16. Harmondsworth: Penguin Books. 1954. Pp. 135. 2s.

Special Articles

TUBERCULOUS DIABETICS

The Birmingham Regional Service

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THE Central Health Services Council¹ has suggested that, as tuberculous diabetics require special arrangements for their treatment, they should be concentrated in sanatoria where they can have expert advice and where there are facilities for laboratory investigation and supervision. The Ministry of Health² recommends that diabetic services should be planned on a regional basis, with provision for special groups of patients such as the tuberculous, the pregnant, and the aged. Tuberculous diabetics in the region should, where practicable, be concentrated in a single sanatorium closely linked with a diabetic clinic, and in Birmingham for the past two years we have provided a coöordinated service for these.

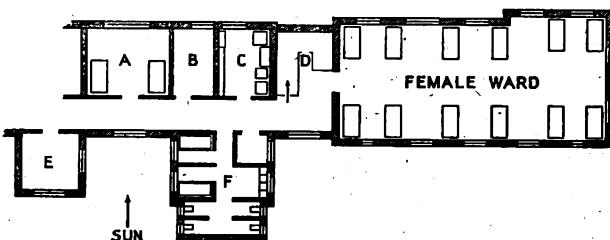
It is estimated that there are 3 diabetics per 1000 of the population, and that 3 out of every 100 diabetics show radiological signs of pulmonary tuberculosis. On this estimate there are 3900 tuberculous diabetics in England and Wales. All need careful supervision, and probably a quarter or more have active tuberculosis.

DOUBLE NEEDS

The diabetic with a complicating tuberculous infection is unsuitable for domiciliary treatment. The detailed attention required for careful management of these two diseases cannot be given except in a special hospital unit with adequate laboratory facilities; and, moreover, there should be no delay in providing inpatient treatment for the newly diagnosed case, which is a medical emergency. It is all too common to find that diabetics who are admitted to a sanatorium for the treatment of a complicating tuberculous infection have their diabetes inadequately treated, with serious consequences. These patients need the close supervision of a physician experienced in the management of both diseases and they also need specialised nursing care. A dietitian or a sister trained in dietetics is essential, and a visiting chiropodist

is also required, since the care of the feet is important in the management and follow-up of diabetics.

Until recent years the combination of these diseases had carried a poor prognosis, but this was due to insufficient and haphazard treatment of either or both conditions. The modern treatments for both diseases have changed the outlook. Chemotherapy and the better application of collapse therapy and resection have greatly improved the control of pulmonary tuberculosis, while the newer insulins and the modern dietetic methods which these have permitted have revolutionised the care of diabetes. When both diseases are effectively treated the prognosis of tuberculosis in the diabetic today is comparable to that in the non-diabetic. But regional units are needed to achieve these modern standards of treatment for both diseases.



Plan of kitchen, &c., and female ward.

A, emergency and/or observation ward. B, duty room. C, diet kitchen. D, staircase leading down to male ward. E, laboratory. F, bathroom and lavatories.

THE BIRMINGHAM SERVICE

The scheme for the management of tuberculous diabetics in Birmingham was started in September, 1951. It includes:

1. The inpatient hospital unit.
2. The outpatient consultative clinic.
3. The domiciliary service.

All three are essential, since they ensure continuity of supervision and treatment both of inpatients and outpatients by the same skilled staff.

The inpatient unit at Romsley Hill Hospital has 25 beds. It consists of two 12-bed wards (one male and one female), with a single side-ward for observation or for emergencies. The unit has its own dietetic kitchen close enough to the wards to be supervised by the dietetically trained sister-in-charge. Special cooking and elaborate dietetics are not necessary, but accurate weighing or measuring of foods is; and all meals are served from this kitchen by an individual tray service for each patient. There is also a small laboratory with facilities for examination of urines, estimation of blood-sugar levels, and other essential investigations. A dietitian is attached to the unit and helps in the education of patients in hospital and in the provision of a varied diet.

The outpatient consultative clinic is held fortnightly at the Birmingham Chest Clinic. Here all tuberculous diabetics under outpatient supervision are seen by the physician-in-charge, and patients discharged from the inpatient unit are followed up. The dietitian also attends this clinic.

The domiciliary service has the lively interest and support of both the local health authority and the general practitioners. Health visitors, district nurses, home helps, the therapeutic dietitian, and the physician coöperate in this. When necessary the physician visits patients at

1. Annual report for the Central Health Services Council, 1952.

2. H.M.C.(53)82.



Diet kitchen.

home, usually at the request of a general practitioner, or after discussion with a health visitor or the dietitian. The dietitian pays home visits once a month, in much the same way as health visitors do for other tuberculous patients, and helps in the day-to-day problems of the diabetic who is taking insulin. Advice is given on diet and the preparation of meals, insulin dosage and injections, and urine-testing.

This integrated scheme provides close liaison between inpatient treatment, outpatient supervision, and domiciliary care. The best results for both diseases can be obtained only under such a comprehensive service of long-term management.

The unit for the treatment of patients with pulmonary tuberculosis and diabetes was established on the recommendation of the tuberculosis advisory committee of the Birmingham Regional Hospital Board. It is a pleasure to acknowledge the interest of Dr. S. J. Scurlock, the senior administrative medical officer, in all the complex problems of the treatment of the tuberculous diabetic.

CLINICAL PATHOLOGY

MANY people believed that if the services of the hospital pathological laboratory were made available to general practitioners, the extra burden of work would be more than the laboratory could manage. But this fear has proved unfounded : in 1952, 55% of all hospital pathological laboratories dealt directly with G.P.s' requests, and these requests accounted for less than 5% of the work in these laboratories.¹ So there is good reason to encourage more laboratories to offer this service and to extend what Dr. W. N. PICKLES, president of the College of General Practitioners, has called "the happy alliance between the general practitioner and the laboratory." Dr. Pickles was speaking at the 52nd general meeting of the Association of Clinical Pathologists, held in Harrogate from April 8 to 10, and he drew examples from his long experience to demonstrate the increasing help which laboratory investigation has given to the practitioners' work.

The following are summaries of some of the papers read at the meeting :

Ulcerative Colitis and Cancer

Discussing the pathology of ulcerative colitis, Dr. CUTHBERT DUKES (London) observed that almost all those who, during recent years, had inquired into the relation between ulcerative colitis and carcinoma had reached the conclusion that colitis predisposed to cancer and that the extent of this predisposition had been underestimated in the past because of difficulties in diagnosis, both clinical and pathological. Dr. Dukes's experience was based chiefly on the examination of colons removed by colectomy from severe cases of ulcerative colitis. In a consecutive series of 120 cases of severe colitis, carcinoma was found in 7 (5.8%). The average duration of symptoms of ulcerative colitis before the onset of cancer was fifteen years. The answer to the question "How often does cancer follow ulcerative colitis?" depended on the severity of the disease and on the duration of symptoms ; any patient who had had severe ulcerative colitis for ten to fifteen years was exposed to a serious risk of cancer.

Miliary Tubercles in Bone-marrow

Dr. J. L. EMERY and Dr. N. M. GRIBBS (Sheffield) reported the results of examination of the bone-marrow in cases of miliary tuberculosis. The present methods of diagnosis depended largely on the radiological appearance of the lungs and examination of the eye for tubercles, and by these means alone it was impossible to establish the diagnosis in more than half of the cases. A study of 0.1 ml. of bone-marrow from 44 children who had died with generalised miliary tuberculosis had revealed miliary tubercles in 23 cases. In these 44 children a

clinical diagnosis of miliary tuberculosis had been made by radiography of the chest in 13 and examination of the eye in 14 cases. These two methods in conjunction produced the diagnosis in 18 cases. Marrow biopsy would theoretically have enabled the clinical diagnosis to be made in a further 5 cases.

Nephrocalcinosis and Hypercalcæmia in Infancy

Dr. I. M. P. DAWSON and Dr. W. S. CRAIG (Leeds) discussed the case of a male child who, at the age of five months, had anorexia, vomiting, constipation, and hypotonia. The condition persisted, with periods of irregular fever, till he died six months later. Investigations showed raised serum-calcium and blood cholesterol and urea nitrogen. Other biochemical findings, including plasma bicarbonate, alkaline phosphatase, and chloride, were normal. The urine was acid and contained pus cells. X-ray examination showed increased density of the skull and long bones. Necropsy revealed bronchopneumonia, without parathyroid hyperplasia or gross changes in other organs. Microscopically, the lungs showed unresolved pneumonia. In the kidneys there was patchy hyaline change in some glomeruli, and both calcium-containing and eosinophilic casts in the distal and collecting tubules, with some calcium deposition in surrounding tissue. The proximal tubules showed vacuolation and degeneration with calcium deposits in degenerate areas. This case was thought to be similar to those described by Lightwood² as idiopathic hypercalcæmia. The pathological changes are those of a nephron nephrosis of unknown aetiology, and the biochemical disturbances are probably secondary to primary renal damage.

Hæmoglobin S and Hæmoglobin C

Dr. H. LEHMANN (London) and Dr. G. M. EDINGTON (Accra) reported a case of sickle-cell-hæmoglobin-C disease from the Gold Coast. Six human hæmoglobins are now known. Five seem to be alleles genetically : normal-adult (A), sickle (S), C, D, and E. Foetal hæmoglobin (F) is not usually found after the first year of life, but it can accompany certain hereditary anaemias and other anaemias acquired before the physiological hæmoglobin-F formation came to an end ; hæmoglobin F is resistant to alkali-denaturation. A, S, and C hæmoglobins differ in their behaviour on paper electrophoresis, and a further feature of S is its tendency to gel at reduced oxygen tension. At pH 8.6, A migrates fastest, S more slowly, and C is slower than A or S. D has the same electrophoretic properties as S but does not gel at reduced oxygen tension. E migrates at alkaline pH at the same rate as A, but differs from A at acid pH. D and E have so far been found in one family each, but S and C seem to be widely distributed, and their incidence pattern is of anthropological interest. The present case is the first to be reported from outside the U.S.A. A systematic survey of C incidence in West Africa is now in progress.

A Calcium-tolerance Test

Dr. B. E. C. NORDIN (London) described an intravenous calcium-tolerance test which might assist in the diagnosis of certain types of metabolic bone disease. Calcium gluconate (15 mg. of calcium per kg. body-weight) was given intravenously in normal saline over a four-hour period after the subject had been on a low calcium diet (100 mg.) for three days. In 9 normal subjects, the mean urinary calcium excretion during the twelve hours after the infusion began was 50.7% of the administered dose : the normal range was 38–62%. In 7 cases of proven osteomalacia the excretion was always less than 25%. In 9 cases of osteoporosis the excretion was well above the normal range in 8 (all young adults) but within the normal range in 1 (all postmenopausal osteoporosis). An interesting aspect of the test was the fall in urinary phosphate clearance which followed the infusion and which was greatest in the patients with osteomalacia. It seemed possible that this was the result of suppression of parathyroid activity.

Pasteurella Septica in Bronchiectasis

Dr. J. M. TALBOT (London) said that most examples of *Pasteurella septica* infections in man were wounds

1. See *Lancet*, 1953, ii, 559.

2. Lightwood, R. *Arch. Dis. Childh.* 1952, 27, 306.

inflicted by animals, but there were some cases in which no direct animal contact was known. The organism seemed to live as a symbiont in the respiratory tract of patients with disease of the bronchi, lungs, or nasal sinuses, especially those with bronchiectasis. He described a case in which this organism was persistently present in the sputum—a finding not previously reported in this country. More examples of this condition might be found if a careful watch was kept.

Epidemiology of Proteus Infections

Dr. A. C. CUNLIFFE (London) described work on the serological classification of *Proteus vulgaris*. This had provided an accurate method of subdividing the species, and the epidemiology of proteus infections in a number of populations has been elucidated. The typing of strains isolated at a general hospital and from patients in a burns unit suggested that infection with *P. vulgaris* occurs in two ways—by self-infection from the gut and by cross-infection.

Haematological Control of Risks from Irradiation

Dr. R. H. MOLE (Harwell) said that in human cases of serious anaemia due to radiation little if any warning of the illness was given by the white-cell count. Changes in the blood-count were unlikely unless exposure to radiation was many times the maximum permissible dose. Damage to the gonads occurred with smaller dose-rates. Physical measures of control seemed preferable to haematological ones.

SMALL-LIST DOCTORS

At the request of the Ministry of Health and of the General Medical Services Committee the Working Party on the remuneration of general practitioners have been considering whether the new arrangements for the payment of general practitioners introduced in April, 1953, have caused hardship to single-handed doctors with National Health lists of fewer than 1200 patients. Their report to the G.M.S. Committee¹ shows that a small group of doctors starting in practice and a larger group of elderly doctors—some 500 to 600 in all—have been placed at a disadvantage.

To help these two groups the Working Party recommend that a basic payment of £250 per annum should be made to single-handed doctors, who are starting in practice or are over 60 years of age, with lists of between 300 and 1200 patients, and that a fee of 10s. should be paid, in addition to the normal capitation fee, for each patient on their lists between 300 and 500. No loadings under the usual arrangement would be payable to them.

The Working Party propose that doctors starting in practice would be eligible for these supplementary payments only for five years during which they should have an increasing list. Payment would be withdrawn where a list decreased over four consecutive quarters by more than 10%.

To come under the scheme a doctor over 60 should have been in single-handed practice in the area where he is now practising for at least ten years. Payments would cease if his list dropped below 300 and remained below 300 for four consecutive quarters. Payments would be reviewed when the doctor reached the age of 70.

The Working Party estimate that the scheme will cost £120,000 a year, which would be met from the pool already set aside to meet any hardship arising out of the new rates of remuneration. They propose that payments should be made without regard to the doctor's total professional income and only with regard to the size of his list. They should be retrospective to April 1, 1953.

The G.M.S. Committee have accepted the recommendations and will present them to the annual conference of representatives of local medical committees.

¹ Brit. med. J. May 1, 1954, suppl. p. 206.

Public Health

MATERNAL RUBELLA AND CONGENITAL DEFECTS

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The original work of Gregg (1941) on rubella and congenital defects stimulated much interest and further research. In this country the subject was systematically pursued by Clayton-Jones (1947). *The Lancet* (1946) said:

"For though german measles is the commonest exanthem in adults the chances of a mother catching the disease early in pregnancy are very small indeed—a rough estimate could no doubt be made on the figures from Manchester, one of the few places where rubella has been notifiable."

Rubella has been notifiable in the City of Manchester since 1916 in relation to first cases in a household, and since 1920 for all cases. For some years we have been making an investigation based on the Manchester notifications, which in recent years have been as follows:

Year	Notifications	Year	Notifications
1938	375	1946	351
1939	739	1947	1247
1940	3543	1948	2022
1941	2777	1949	386
1942	2624	1950	375
1943	910	1951	976
1944	3706	1952	8010
1945	358	1953	573

The population of Manchester was 732,900 in 1938 and 701,800 in 1953.

METHODS OF INVESTIGATION

There appeared to be two methods of determining the relationship or otherwise between rubella and congenital defect. One method is to investigate the antenatal history of the mother if congenital defect in the infant has been discovered. The other method is to note the occurrence of rubella in the mother and to observe the pregnancy and its outcome as regards mother and child.

The first method was followed in Manchester in 1946, when Dr. G. Stewart Smith, then director of pathological services in the City of Manchester, surveyed the results of necropsy of 35 infants who had died in hospitals and had congenital malformations. Investigation of the history of the pregnancy of each mother was next undertaken to ascertain whether or not she had had rubella during pregnancy. No history of rubella was found in these cases.

In 1952 we analysed in retrospect the health department records of (1) rubella notifications in 1936–51 for females aged 15 or more; (2) notifications of birth in corresponding years related to these rubella notifications; and (3) congenital malformations in the children.

RESULTS

The results were as follows:

Year	Notifications	Pregnancies	Congenital abnormalities
1936	43	—	—
1937	32	—	—
1938	15	—	—
1939	53	—	—
1940	725	6	—
1941	197	1	—
1942	199	4	—
1943	72	—	—
1944	514	3	—
1945	26	—	—
1946	12	—	—
1947	101	1	—
1948	101	—	—
1949	16	—	—
1950	9	2	—
1951	41	2	—

These figures are of interest, but the results are negative. This is not surprising in view of the fact that most of the records were old, and no examination of the children was conducted for this purpose after the age of 5 years. It appears to be sounder to ascertain first the incidence of rubella during pregnancy and then to seek for congenital abnormalities. This method was used in 1952, when the level of rubella notifications reached unprecedented heights and therefore presented an unusual opportunity of dealing with large numbers.

In 1952 rubella notifications in females aged 15 or more numbered 468. We have traced 28 cases in which the women were pregnant at the time of rubella infection. Data on these 28 cases are given in the accompanying table. The defects specified are gross, and observation is being continued to ascertain the appearance of latent defects, if any, when the children are older.

Of the 28 cases of rubella in pregnancy, 21 were ascertained as a result of formal notification and 6 as a result of a concurrent and wider investigation which was made by the Ministry of Health in conjunction with the Manchester and many other local health departments and is continuing. The remaining case was found by one of us (B. J. N.). It follows that only 21 of the 28 pregnancies are included in the 468 notifications, but all of the 28 mothers had rubella at some time during their pregnancies.

There were 5 cases of gross congenital abnormality in the children. The case of missed abortion is not included as congenital abnormality, although it is possible that the foetus died from rubella.

5 cases of congenital abnormality from 28 cases of rubella in pregnancy is 17.9%. In 1952, 245 cases of congenital abnormality were ascertained in the 12,367 live babies born in Manchester—i.e., 2.0%. In 13 of the 28 pregnancies, rubella occurred before the thirteenth week of pregnancy, and among these 13 cases the infants had congenital abnormalities in 4 (30.8%) instances.

This report is provisional only, and the final assessment of the Manchester figures cannot be made until observations over some years have been completed. If the figures had been much larger and equally representative, the difference between 17.9% and 2.0% would have provided

CONGENITAL ABNORMALITIES IN OFFSPRING OF WOMEN WHO HAD RUBELLA DURING PREGNANCY IN 1952

Mother's age (yr.)	Parity	Week of pregnancy in which rubella occurred	Congenital abnormalities
21	1	22	..
18	1	26	..
26	5	12	Infant died at 3 days; congenital cardiac lesions
25	2	12	..
28	4	39	Bilateral cataract and micro-phtalmos; thrombocytopenic purpura
28	3	1	..
27	3	At time of last menstruation	..
28	4	27	Stillbirth; congenital cardiac lesion
26	1	4	..
29	2	11	..
31	1	16	..
38	3	15	..
26	2	1	..
22	2	12	Missed abortion; foetus died shortly after rubella infection
29	4	10	Family lost sight of
27	2	13	..
21	1	32	..
25	1	6	..
33	2	33	..
27	1	8	..
20	1	5	..
22	2	24	..
21	1	7	..
23	3	14	..
26	3	30	..
32	8	22	..
24	1	21	Stillbirth, anencephalus
35	1	1	Cataract of right eye

* Ectopic gestation, abortion of tubal pregnancy; insufficient evidence of congenital abnormality.

good evidence of the effect of rubella in the causation of congenital abnormalities. Some significance may perhaps be attached to the high proportion of cases of congenital abnormality following rubella in early pregnancy. The smallness of the figures limits their value.

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Illnesses Treated in Hospitals

The Registrar-General's supplement¹ on hospital inpatient statistics for 1949, published this week, forms part of the study of morbidity statistics that is being undertaken in the General Register Office, and it is a companion volume to the 1949 supplement on general morbidity, cancer, and mental health.² Some preliminary figures based on the first six months of the inquiry were published³ in 1951, and the tables now published relate only to the full year 1949. The figures cover the majority of teaching hospitals and 24 hospitals under regional boards.

The final diagnoses of principal conditions treated or investigated are classified according to the International Classification of Diseases and Injuries. The main table reproduces this classification, with minor exceptions, in its entirety; and the number of men and women at different ages discharged during the year, together with the number of deaths in hospital at all ages, are shown for over 1200 diseases or injuries. The detail in which the main diagnoses are shown makes it possible to rearrange them, within the limits of the classification, to form other clinical disease-groupings. There are some interesting variations in the sex-ratios for certain diseases; for example, there were nearly twice as many boys as girls admitted for appendicitis at ages 1-4 in the teaching hospitals, but nearly twice as many young women as young men at ages 15-24. Other tables show the variation in average duration of stay for selected diseases and disease groups according to age in the London teaching, provincial teaching, and regional board hospitals. There were often appreciable differences in the average duration of stay for the same disease between the teaching hospitals in London and in the rest of England and Wales. In most cases, the stay in hospital was shorter for the provincial teaching hospitals, and this is reflected in the average stay, over all conditions, of 16 days for men and 14 days for women, compared with averages of 21 and 20 for the London teaching hospitals. In the relatively few hospitals under regional boards which were included in the inquiry the averages for males and females were 23 and 19 days respectively, but these figures were much influenced by the higher proportions of old patients and patients with chronic diseases who have relatively longer durations of stay.

The new supplement adds useful information to what has already been collected about the hospital service, and it will be a help both in the administration of the service and in medical research.

A Smokeless Zone in Bolton

Last December the town council of the county borough of Bolton designated an area of approximately 86 acres in the town centre as a smokeless zone, and the Minister of Housing and Local Government has now confirmed the order bringing this into effect as from Nov. 1, 1954. In his report to the health committee, the medical officer of health, Dr. R. W. Elliott, says that occupiers of premises in the zone will be given instructions, and a sanitary officer specially trained in smoke abatement will be available to advise them. There are 1050 premises in the zone—residential, business, and manufacturing, including a brass foundry, two engineering works, a paint factory, and a tannery.

1. The Registrar-General's Statistical Review of England and Wales, 1949: Supplement on Hospital In-patient Statistics. H.M. Stationery Office. Pp. 485. 15s.

2. See *Lancet*, Jan. 9, 1954, p. 110.

3. Studies on Medical and Population Subjects no. 4 Hospital Morbidity Statistics. H.M. Stationery Office, 1951.

In England Now

A Running Commentary by Peripatetic Correspondents

I HAVE just been looking at the children in the Academy Summer Exhibition. I always look at the children because I may not know much about Art (as they say) but I do know what children look like, as I sit diagnostically in front of the little horrors for most of my working day. As usual, this year I was incredulous of all those clean faces. Some, at least, had untidy hair. Prosper Devas did, and he looked as if he were anxious to get away. He was painted by Anthony Devas, perhaps his father who knows him well. Master Clive Forster-Cooper was sitting very still. From his expression I doubt if he could keep it up for long.

One trouble is that children seldom look at you for long if you are looking at them, and when I look at a picture in which the child is looking at me it seems all wrong. I feel as if I am intruding. Perhaps that is why I prefer sculpture, because you can walk round it and study it unobtrusively, just like a real child. Not that the Infant Imogen would have minded being looked at, because she is too young. I thought she would have to have her nose wiped quite soon and that seemed homely. I was a bit worried about Francesca's flush, but Paul seemed lively enough. I think he might be a bad lad: I hope so. But talking of bad lads, what is John Walter Wolseley doing with that whip? Best of all I liked Ismond Rosen's Honey. She looks best from a three-quarter front view, her expression is quite different when she sees you looking at her, which is just what I said.

* * *

While in a peripatetic state of mind at a lecture on pharmacology the other day, it occurred to me that sometimes the Fates must be rather cold. "Why?" you ask. Well, they have atropin, lachesin, but no clothin. Moreover it often gets a bit parce.

* * *

The *Rosemary Ann* is lying on the mud-flats with her side stove in. News of the disaster came from two local fishermen called Dick Rag and Bill Grimes who sent me a letter, distasteful in tone and unmentionable in syntax, to say they had salvaged my sailing dinghy in the recent gales, floating bottom-up with all the tackle gone. They suggested I paid them compensation amounting to a third of her value or they would put the matter into the hands of the Receiver of Wrecks. I grabbed the phone.

"What's all this damn nonsense about my boat and the Receiver of Wrecks?" It was a bad start but I was in no mood for the conventional approach.

"No nonsense about it," said a voice which I later identified as Grimes's. "If you don't pay up, me an' Rag will report it to the Receiver, and then you're in for a packet . . . and they'll impound your boat."

I got in touch with H.M. Customs and found to my dismay that their claim was justified. Accordingly I phoned Grimes again and told him I would meet him on the shore to talk business. I found him and Rag sitting on my upturned boat smoking their pipes.

"Well, gentlemen, I believe you were good enough to save my boat—a very seamanlike action. I am grateful to you. . . ." Such an opening ought to have shrivelled them into powder but as far as I could see they were unmoved.

"Grand evening," said Grimes, knocking out his pipe against the keel.

"Tidy weather," said Rag.

I began to feel hot. "Shall we get down to business? If you feel entitled to a little compensation—some small token reward for your trouble—I am not the person to be unmindful of a good turn. That, after all, is why we are all here—to do one another good turns."

"Wind's veering," said Grimes.

"Blowing southerly," said Rag.

I had an ungovernable impulse to break the tiller of my boat over their heads. Unfortunately it had been lost with the rest of the tackle. "How much do you want?" I said.

Rag stared fixedly at a starfish near his feet. Grimes spat with precision into a small rusty tin two yards away. The curlews engraved their swift beauty into the evening sky and the tall herons stood motionless in the shallows of the tide listening for the fall of night.

"What is it worth to buy?" asked Grimes, looking out to sea.

This was a cunning question. If they really wanted to buy it, I ought to put the price up. If they were fishing for a valuation on which to base their salvage claim, I ought to keep it low. I looked at Rag for a clue. He was still looking at the starfish with a face more full of emptiness than I thought permissible to the human race. Grimes pulled steadily at his pipe and looked as open and ingenuous as the tomb of Tutankhamen. An idea of delicate and refined subtlety side-slipped my conscience and crept into my mind.

"I would never sell her."

Rag lifted his eyes from the starfish and fastened them on a worm cast. Grimes stopped puffing and a thin wisp of smoke climbed up from his pipe like a tenuous question-mark.

"Why not?" he asked.

"Before I brought her to these parts the previous owner set out in her one morning on the ebb for a day on the cockle beds. At sunset she came back on a strong flood tide, sheet lashed to the tiller and running with the wind—alone. He was never found. No, gentlemen, she is a boat to be reckoned with and knows how to take her revenge."

They remained rigidly attentive during my story, and I suspected they had seen, with alerted imaginations, the sudden squall, the massive and voracious sea, the shroud in the folding wave.

Grimes spat once again at the tin . . . and missed. Rag pulled his jerkin more closely about him.

"Getting a pit parky," he said.

"Aye, getting a bit thin," said Grimes.

They moved off slowly over the ribbed sand to their nets by the shore. And I was left alone with the *Rosemary Ann*.

* * *

My window-cleaner just home from the sanatorium was anxious to return to work. He was not impressed by my slight concern about the strain of climbing ladders and carrying heavy buckets. "You see, sir," he explained, "I am the boss. I only washes bottoms."

* * *

They B.B.C. chaps' wanting to build their T.V. station on Hessary Tor is bothering us folks down Widdicombe way, for my old grandad swears we've ancient common rights to that part of Dartmoor. Gaffer says that if he remembers rightly we used that land way back in Saxon times; but anyway, even if we didn't, we certainly got it again as a grant from they Norman furriners who came down here not so long ago and called themselves lords of the manor or some such fancy name. Us villagers didn't hold with your Statutes of Merton and Westminster, we weren't frightened off by your Black Death, we weren't pushed out by your Tudor wool trade or your Inclosure Acts, and we don't see why us Devon men should have to suffer all that there T.V. nonsense on our moor.

You can't teach our Gaffer anything about his common rights of pasture, piscary, turbary, and estovers; we know what's ours and what we can take for nothing from the Moor. Now if they B.B.C. chaps was to buy old Betsy's cottage next the smithy they would be commoners along of us, but Gaffer's not too happy about what they lawyers call profits à prendre; for as he says they be taking nothing from the moor, they wants to put it in. But then, he says, look at all they other folk in Exeter and Plymouth who will be pinching our T.V. waves; that'd be carrying common rights too far to his way of reckoning.

* * *

Patient: "I think I've got a herbaceous cyst, doctor." I forgot to see whether she had green fingers.

Letters to the Editor

THE BOMBS

SIR.—I think Dr. Stafford-Clark's reply last week to my letter of April 24 may be based on a misunderstanding of what I said. To determine which of two cultures in conflict constitutes the greater danger to this country we should require a political and economic analysis too extensive for your pages and more related to personal opinion than to sociology. What I said was that, in the context of the hydrogen bomb, the present attitude-patterns of American society seemed to me more dangerous than those of Communist society, and what I implied was that the risk of a "deliberate mistake" by the military and political authorities of the United States is a danger to be reckoned with on psychological grounds.

I do not base this view upon political preferences, but on the opinion of a number of American sociologists, who regard the present developments with grave concern. Lewis Mumford, for example, recently wrote¹: "If as a nation we have become mad, it is time for the world to take note of that madness. If we are still humane and sane, then it is time for the powerful voice of sanity to be heard once more in our land." There might well be Russian sociologists who would express themselves equally forcibly about aspects of the Russian attitude (if they were allowed to), but the evils they denounced would not be the same. A criminologist would say that the "modus operandi" of this particular form of delinquent behaviour, which bears a very close resemblance, I think, to the psychology of individual suicide, is not characteristic of the Communist societies, though they have plenty of others of their own. As Mumford points out, we are clearly entering the field of aberration when a people, or a section of that people, becomes convinced that the destruction of organised civilisation is a preferable alternative to the success of an opposing political system.

The development of atomic weapons is itself largely responsible, in the view of many American psychologists, for the development of these attitudes. In the words of Mumford once more, "Our need for secrecy . . . has produced pathological symptoms in the whole body politic—fear, suspicion, non-co-operation, hostility to critical judgment, above all delusions of power based on fantasies of unlimited extermination." The butt of the atomic weapon is considerably more dangerous to any society whose standards, like those of the vast majority of Americans, are humane and liberal, than is the muzzle. Any community which violates its own mores is liable to demoralisation, and the degree to which it is demoralised will be predictably greater in proportion to the sense of guilt which this departure engenders. It is upon these grounds, as well as upon the testimony of psychological observers whose opinions we dare not ignore, that I consider that there is in official America today a pressure towards self-destruction as an emotional release, which is probably absent from the Communist societies, and is certainly an acute danger to Western survival. To assert my independence from the propaganda of both camps in making this judgment ought, perhaps, not to be necessary. It is hard to see how, in the Cold War, a medical sociologist could be other than a neutral.

Loughton, Essex.

ALEX COMFORT.

SIR.—Dr. Stafford-Clark states that "it is a matter of historical fact that it was the United States who proposed, and still propose, international control of the production and development of atomic weapons, while the Soviet Union have consistently refused to accept such

1. *New York Times*, March 28, 1954.

control." Since the beginning of the Cold War, it has been an effective line of propaganda to disseminate the idea that the Soviet Union has put obstacles in the way of the banning of atomic and similar weapons of mass destruction. This propaganda has succeeded in misleading many people and increasing international tensions.

In order to remove misconceptions on this important subject, Science for Peace has just issued a pamphlet¹ giving a tabulated analysis of the U.S.A. and U.S.S.R. proposals made at the U.N. Atomic Energy Commission, and of their respective objections to each other's proposals. Russia objects that the U.S.A. plan does not prohibit manufacture. But it will be seen that the differences separating agreement are less than many of us have supposed. Given the will, these differences can be surmounted, thus paving the way to the accommodation between nations that you, Sir, and your correspondents have urged.

London, N.W.3.

P. D'ARCY HART.

SIR.—It is difficult for those of us engaged in the daily practice of medicine to know how most effectively to add our small voices to what should become a gigantic outcry against not only the atom, hydrogen, and cobalt bombs, but against the whole silly but iniquitous and monstrously tragic business of war.

There are, however, approaches open to us. First we can attempt to influence our profession, public opinion, and eventually our leaders by every channel open to us; and I include in such channels conversations with colleagues over the lunch table, association with anyone (be they conservative, liberal, socialist, or even communist) who is willing to sit down and discuss the problem of preventing war, as well as letters to the lay and medical press. I welcome therefore your thoughtful and impressive leader of April 17, and hope you will keep your column open for what should be a spate of letters about "the bombs."

Professor Haddow, in his letter to the *Times* to which you referred, suggests a *concilium* of world science, representative especially of physics, chemistry, biology, and medicine, which would have "an unimpeachable primary loyalty to humanity as a whole." There could, incidentally, be no more appropriate phrase to guide what is, or should be, the attitude of our profession in all countries to the bombs, and to war generally. As a second effective step we can, by our meetings and conferences, foster within our own profession the kind of international atmosphere in which such a *concilium* could thrive. I doubt whether parties on officially sponsored visits of good will have much further value. But we could meet our colleagues from eastern Europe and Russia in the same spirit as we do those from western Europe and the Americas; not so much, perhaps, at big international conferences, which often breed international rivalry, as at smaller, more intimate meetings in branch subjects of medicine like paediatrics, public health, midwifery, and so forth. As a by-product of quietly pursuing our own business, there can arise at such meetings a flow of friendly feeling which, in terms of international scientific relations, is worth any number of planned welcomes and visits of good will.

You rightly stressed that, as a first step to a return of human relations, the east and west should call a halt to aggressive propaganda. I submit that this term includes the letting off of bombs at tactical moments, to say nothing of threats, overt or thinly veiled, to use them in earnest; and we have a right as well as a duty to ask that all such posturings, however defensive, should be indefinitely abandoned by both sides.

London Hospital, E.1.

RICHARD H. DOBBS.

1. The Control of Atomic Energy. Issued by Science for Peace, 16, Ulster Place, N.W.1, London. 4d.

GLUCAGON-FREE INSULIN FOR INSULIN-SENSITIVITY TESTS

SIR.—The work of Himsworth¹ on insulin sensitivity has often been considered as a means of classifying diabetics. Somogyi² has pointed out that the usual insulin-tolerance tests do not adequately measure sensitivity, since a fall in blood-glucose below the fasting level rapidly sets in action mechanisms that mask the response to insulin. Moreover, in crystalline insulin now available in the U.S.A. and Canada, the uncertain persistence of the hyperglycæmic-glycogenolytic factor (glucagon) makes it impossible to estimate the initial effect of the beta-cell hormone, for it delays the onset of the fall in blood-glucose level (the "latent period" of Himsworth) and affects the subsequent rate and regularity of fall. Probably the interfering glucagon has prevented workers in this hemisphere from finding a practical application for Himsworth's work.

With glucagon-free insulin intravenously in small doses (1-3 units), it is possible to show the immediate effect of insulin before the fall in blood-glucose can excite counter-measures. This beta-cell effect is shown by blood-glucose readings at 2, 4, and 6 minute intervals after insulin has been given. Thereafter, the glucose curve levels out towards its nadir, which usually occurs within 30 minutes of the insulin injection; thus, it is the response to hypoglycæmia rather than to the beta-cell hormone that is recorded in the 30-minute test. During the first 6 minutes after the insulin, only those factors actually operating in the body at that particular time can prevent or delay the onset of hypoglycæmia or reduce the rate of fall of blood-glucose.

Our findings in 100 unselected diabetic patients support the prevailing view that there are factors which counteract the effect of insulin and create a relative deficiency of insulin, and so produce diabetes. In insulin-sensitivity tests, every effort is made to minimise any suprarenal effects, so it is likely that other anti-insulin factors are responsible for keeping up the blood-glucose.

In a group of non-obese, non-diabetic medical students and nurses there was a prompt fall in blood-glucose to 6-25% of the fasting level within 6 minutes of giving glucagon-free insulin. In the obese adult diabetic, before the start of clinical treatment, there was usually little or no fall, or even a pronounced rise in blood-glucose after insulin. The juvenile diabetic at any age showed a prompt fall of blood-glucose level to within the normal range or lower, and the rate of fall was greater than normal. A third pattern was seen in the labile or so-called "brittle" type of diabetes in which the initial fall was extremely great and sudden, and was followed by a prompt rebound, often to well above the fasting level.

With effective dietary treatment and loss of weight, the poorly sensitive individual can often be made normally sensitive to insulin. In the juvenile type of diabetic, excessive weight, or a rapid gain in weight, often goes with the declining response to insulin.

Several applications of the 6-minute insulin-sensitivity test are possible. It can usually differentiate clinical types of diabetes and so help in treatment: the poorly sensitive obese adult diabetic can often be made sensitive to insulin by reducing his weight (with or without insulin). The test can determine whether the normal blood-glucose levels produced by treatment are merely an artificial improvement resulting from a forced stoichiometric mass effect of extrinsic insulin on blood-glucose, or a real improvement in the patient's ability to respond to insulin from within or without. It gives us a simple clinical laboratory method of making this distinction. Research is in progress to verify the suggestion that excessive doses of extrinsic insulin may decrease sensitivity to insulin.³

1. Himsworth, H. P. *J. Physiol.* 1934, 81, 29; *Clin. Sci.* 1935, 2, 67.

2. Somogyi, M. *J. Biol. Chem.* 1949, 179, 217.

3. Evans, M. A., Halst, R. E. *Amer. J. Physiol.* 1951, 167, 176.

Obese adults in a diabetic family may show normal fasting blood-glucose levels and normal glucose tolerance but poor sensitivity to extrinsic insulin. In these so-called "normals" the 6-minute sensitivity test will provide a more delicate index of impending clinical diabetes than does the usual glucose-tolerance test or the postprandial blood-glucose level. The latter tests show abnormal results only after some reduction in carbohydrate tolerance has already taken place.

I suggest that the 6-minute sensitivity test may be a useful tool in exploring the problem by identifying potential diabetes.

State University of
New York College of Medicine,
New York City.

GEORGE E. ANDERSON.

THE PLIGHT OF SENIOR REGISTRARS

SIR.—Much has been said and written about the plight of senior registrars. To Officialdom they must appear as pawns, to be dealt with as quietly as possible. There also seems to be a united psychological approach to them—by agreeing with all they have to say!

What seems to be forgotten is that they are human beings with a responsibility to their families. As wives, we have stood by whilst they have taken higher qualifications when the competition has never been so great nor the standard so high. We claim no reward for this, although it has not been easy for us; but now we are led to believe that years of responsibility and experience, together with these once prized qualifications, are valueless.

Our standards of life have been such that a lay person recently asked me if my husband would soon be qualified, and was somewhat taken aback to learn that this had happened over thirteen years ago.

We are educating our children as best we can, and a poor best it is compared with our own education; but the price of education has doubled since we were at school. Their future is also staked in this mad world.

Many wives have delayed having children until they could have some settled future and not have to be char-women, cooks, laundrymaids, and kitchenmaids rolled into one; but in a few years they will be too old.

Worst of all to bear is the hopelessness and the strain, and one wonders how long these men and women can keep going before they break.

Surely these men are worth more than makeshift jobs in a country that is crying out for clinical skill? Has the medical world lost its conscience and sense of responsibility towards its brothers?

SENIOR REGISTRAR'S WIFE.

REMUNERATION OF HOSPITAL MEDICAL STAFF

SIR.—Much is being said and written about the importance of the battle against tuberculosis. Under the World Health Organisation, millions of children are being vaccinated against this disease. Important memoranda urging review of the campaign against tuberculosis are being issued by the Ministry of Health. The propaganda of the National Association for Prevention of Tuberculosis carries the fight to the remote corners of the Commonwealth. In England surely one will see every available weapon brought to bear by men of high skill and rare endeavour. But no! In England much of the anti-tuberculosis work is done by disgruntled senior hospital medical officers, whose status has been further lowered by the recent salary increases for hospital staffs. What is the reason for this inconsistency?

Hampshire.

H. S. FRASER.

SIR.—Dr. Gray, in his letter of April 24, states that he is pleased with the recent award to hospital medical staff, though so many of his colleagues feel that it is not enough.

In referring to his income of £600–800 per annum as a tuberculosis officer in 1941, and contrasting this with his present rate of remuneration of £1500–1950 per annum as a senior hospital medical officer, he makes the remarkable statement that this constitutes "a betterment factor of 150%." Dr Gray presumably regards this as a satisfactory state of affairs, but I would ask him to consider, by the same token, the position if, in 1941, he had been in receipt of a slightly higher rate of salary—say £840–1240 per annum. Applying the betterment factor of 150% the rate of remuneration would today amount to £2100–3100—the salary of a consultant without a merit award.

Casting our minds back a little over six years to May, 1948, the Spens report defined the salary of a consultant as £1500–2500 per annum in terms of the 1939 value of money. Let us, however, ignore any increase in the cost of living or depreciation in the purchasing power of the pound between 1939 and 1941, and apply to the Spens scale the betterment factor which Dr. Gray considers to have been applied in his case. The 1954 scale for whole-time consultants becomes £3750–6250 per annum. If this were the case, no doubt Dr. Gray would find that his colleagues shared his enthusiasm over the recent award. In fact, those who were in receipt of a salary of £375–625 per annum in 1941 would possibly feel sympathetically disposed to the S.H.M.O. with a betterment factor of only 150%, compared with 1000% for his consultant colleagues.

The Chancellor of the Exchequer was asked in the House of Commons on April 6 what would be the pre-war equivalent purchasing power of a married man with two children now earning an income of £5000 per annum. The answer given was £1090 per annum. Dr. Gray's present income has therefore the 1941 equivalent of £500–625 per annum, so that after thirteen years' further service he is in fact rather worse off financially.

Plastic and Jaw Unit,
Basingstoke,
Hampshire.

N. L. ROWE.

RADIOACTIVITY OF TOBACCO AND LUNG CANCER

SIR.—I was very interested to read the letter¹ from Professor Spiers and Professor Passey. They believe that there is little or no radioactivity in cigarette-smoke, though their findings for tobacco ash are roughly comparable to my own. I have recently tackled the problem from another angle: instead of testing the cigarette-smoke with a Geiger counter, I have estimated its potassium content; as there are 11 parts of radioactive potassium in 100,000, the results can be compared.

The smoke was sucked through a series of tubes containing 0.01 N HCl, and the resulting solutions were tested for potassium. A control test on the laboratory air was made on another day. Analysis of the solution showed that there was 300 µg. of potassium in the smoke of 20 cigarettes, or 15 µg. per cigarette, compared to 150 µg. in the laboratory air. These estimations were made by means of a flame photometer, and, as the margin of error could only be very slight, it is a reasonable assumption that they show an appreciable amount of potassium in cigarette-smoke.

The amount of cigarette-smoking that some authorities consider necessary to produce a neoplasm is 20 cigarettes daily for 20 years; in other words, a daily intake into the bronchial tree of 300 µg. of potassium. The dosage is, of course, extremely minute, but it is a surface dosage additional to that mentioned by Professor Spiers and Professor Passey—namely, the dosage received by the tissues from their normal potassium content.

Very little appears to be known of the effects of long-continued radiation of very low intensity. Many support the view that it is possible for a neoplasm to be initiated by low-intensity radiation spread over a very long period

of time. The possible effect of potassium cannot be ignored, for it is the only naturally occurring radioactive element that gains entrance not merely to the cytoplasm of a cell but to its very nucleus, at which site, most observers believe, malignant changes begin.

Could not the active beta-radiation of K⁴⁰ in a cell undergoing abnormal mitosis—e.g., in areas of chronic irritation or in involuting glands—be a factor in the initiation of a cancer? The storage of potassium in the body is almost completely intracellular, and it may be, therefore, that, in people who are on a high-potassium diet during their whole life, the intracellular content of potassium is greater than normal. This hypothesis is supported by the fact that, if large doses of potassium are administered, it is some two or three days before the excess is fully excreted. Also, the ratio of K⁴⁰ to K³⁹ and K⁴¹ in human potassium is not necessarily constant. Variations have been reported, and it can be envisaged that factors at present unknown might result in an increased concentration of K⁴⁰ in the cell cytoplasm. It is well known that a tumour grows much more rapidly in the presence of abundant potassium; indeed, the potassium content of a tumour is higher than that of normal tissue.

London, W.1.

D. K. MULVANY.

TREATMENT OF DEAFNESS

SIR.—I was interested to read, in your issue of April 24, the letter by Mrs. Chadwick, a member of the Ardent Audiotherapy Unit. I must have worded my own letter badly if I conveyed the impression that I did not realise the tremendous value of auditory training. It is universally recognised that this is essential for all persons issued with a hearing-aid; it is given in many centres and also by several well-known hearing-aid firms as a part of their after-sales service. My motive in writing was to raise certain points.

Auditory training *without* hearing-aids, though it may be very useful in children learning speech and vocabulary (and should always be used for them), is not yet proved to be of value in adults by improving hearing for any reasonable length of time, other than through a physical ability to hear better.

In spite of Mrs. Chadwick's assertions, I consider that most authorities are not yet satisfied that true organic "cortical or central" deafness does occur. Abnormal auditory imperception needs fuller investigation before it can be established that this is not a lack of listening or concentration ability. (I am not considering here "word-deafness.") It is a well-known fact that psychological improvement can and does occur, either with training or as a result of such events as a fenestration operation, often to a remarkable degree; I agree with Mrs. Chadwick that the "social adequacy index" is useful to assess this improvement.

Hearing-aid firms, whether actual manufacturers or subsidiary vendors, are not necessarily correct in advocating re-education methods for those not deaf enough to need hearing-aids. Aural surgeons will be pleased, even thrilled, with any type of help that the hard-of-hearing can derive from any form of treatment or training; but a psychological, as opposed to a physical, improvement is one so easily gained by many anxious, handicapped persons that "commercialised" training seems open to question.

It is this point that I wish to stress; that further investigations are needed before this aspect of auditory training is accepted. The claim that all types and degrees of deafness improve almost equally must surely be open to investigation also.

It seems a pity that the American otologist working with and for a hearing-aid firm has declined an offer to attend a meeting of British otologists to describe the system advocated in his book and practised by the firm's "re-education unit."

London, W.1.

IAN G. ROBIN.

1. *Lancet*, 1953, ii, 1259.

ADMINISTRATION OF PENICILLIN

SIR.—The comment in your annotation of April 24, that "repeated injections . . . in children should be avoided if possible," prompts me to say that for the last six years I have ordered all injections of penicillin to be given subcutaneously rather than intramuscularly. I started this method after an interchange of letters with Sir Alexander Fleming, and those who will adopt it will find that it is relatively painless to all patients. In this way, penicillin can be administered by any intelligent person—for example, a school matron. The method is particularly suitable for children, who will more readily accept three or four subcutaneous injections a day by a small needle. Moreover, by this route the penicillin is more slowly absorbed, and I have never seen an anaphylactic reaction.

Broadstairs, Kent.

MARTIN O. RAVEN.

HÄMOLYSIS AND ECLAMPSIA

SIR.—In your annotation of April 17 you examine the data of 3 unusual cases of eclampsia,¹ complicated by haemolysis and by a derangement of normal haemostasis. In the absence of any ascertainable cause, an immunological reaction was thought to be responsible for both abnormalities.

The fact that 2 out of the 3 patients died suggests either a very severe toxæmia or a complicating factor. The authors of the paper discussed both thrombocytopenic purpura and lupus erythematosus in this connection, and could not exclude the latter satisfactorily.

You emphasise the significance of haemolysis in the aetiology of eclampsia, especially from the evidence provided by these 3 cases. For, if your second paragraph is germane to the argument, you must be held to imply that pigment casts in the collecting tubules of the kidney are the products of haemolysis alone and that their presence in fatal eclampsia, fatal accidental haemorrhage, or fatal obstetric injuries cannot otherwise be explained. But such pigment casts can be experimentally produced when intermittent and frequent electrical stimulation of the renal nerve evokes cortical ischaemia.²

In discussing the failure of haemostasis in these cases, you cite certain experiments in which trauma of the placenta led to fibrinogenopenia, which has also been demonstrated in patients with eclampsia or with retro-placental haematomas. In the same context and notwithstanding the fact that fibrinogenopenia was not evident in these 3 cases, you suggest that placental damage could have been the cause. Others, besides myself, must reject this inference as unproven from the facts.

There are certain possible explanations for haemolysis, other than those you suggest.

A mild haemolysis is often found in the puerperium, and an exacerbation of this apparently normal happening may have occurred coincidental with the mounting toxæmia. It should be noted that, in 2 of the cases described by Pritchard et al.,¹ there was "a slightly increased erythrocyte osmotic fragility."

Employing purely physical methods for effecting the transfer of water, Hamburger has provoked a visible increase in the hydration of cells.³ In the intact animal, equivalent methods have resulted in an electroencephalogram similar to that found during epileptic convulsions⁴ and presumably due to increase in the water-content of the brain cells. Cellular overhydration could be a possible cause leading to haemolysis in pregnancy and to the onset of eclampsia. Loss of fluid from the plasma could prove a sequel, explaining haemo-concentration⁵ in severe toxæmia.

1. Pritchard, J. A., Weissman, R., Ratnoff, O. D., Vosburgh, G. J. *New Engl. J. Med.* 1954, **250**, 89.
2. Sophian, J. *Toxæmias of Pregnancy*. London, 1953; p. 123.
3. Hamburger, J., Mathé, G. *Métabolisme de l'eau*. Paris, 1952 p. 83.
4. *Ibid.* p. 305.
5. Dieckmann, W. J. *Toxæmias of Pregnancy*. St. Louis, 1952.

So far, in toxæmia, an increased electrolyte concentration in the cell (e.g., the red blood corpuscles) compared to the extracellular fluid (e.g., the plasma) has not been shown to exist, and the cause for a possible overhydration of the cell must be sought elsewhere. Recently Lambotte-Escoffier et al.⁶ produced "data to suggest that pre-eclampsia and possibly other abnormal pregnancies are characterised by increased intracellular penetration of sodium and water." They have made reference to the work of Gaudino and Levitt⁷ to explain the redistribution of water and sodium from extracellular to intracellular space under the influence of cortisone, corticotrophin, and deoxycortone acetate. I have discussed⁸ certain difficulties in correlating their findings. Transfer of electrolyte and water from cell to extracellular fluid and in the reverse direction could occur during cation-exchange-resin treatment in resistant toxæmia and its repetition could damage the red blood corpuscles and explain the haemolysis in the case described by Baker et al.⁹

The rarity of haemolysis and disordered haemostasis in eclampsia is against their being of primary aetiological significance. They appear to be incidents grafted on the central and essential problem of water retention.

London, W.1.

JOHN SOPHIAN.

ESTIMATION OF DINITRO-ORTHO-CRESOL IN BLOOD

SIR.—The measurement of dinitro-ortho-cresol (D.N.O.C.) in the blood is a very important procedure for the prevention of D.N.O.C. poisoning in farm-workers or, more especially, contract-spraying operators using this poisonous spray chemical. By this means, it is possible to demonstrate whether, at the time of sampling, the worker's absorption of the chemical was trivial (1–10 µg. D.N.O.C. per ml. whole blood), appreciable (10–20 µg. per ml.), unsafe (20–30 µg. per ml.), likely to cause some toxic effects (30–40 µg. per ml.), dangerously high (40–50 µg. per ml.), or critically dangerous (over 50 µg. per ml.). Only by knowing the blood D.N.O.C. level is it possible to keep occupational exposures within safe limits, to study the safety of different working methods, or to confirm or refute the diagnosis of suspected D.N.O.C. poisoning in a sick spray operator.

The analytical technique of Parker¹⁰ and its modification to a micromethod by Harvey¹¹ both involve the use of a photo-electric colorimeter and calibration curve. The standard of accuracy thus sought, although of value for special investigations, is not really necessary either for routine or emergency analyses. An inaccuracy of perhaps 5 µg. per ml. is acceptable in a method which offers simplicity, speed, and ready availability outside the clinical laboratory. With this in mind, a more simple procedure has been developed.

1 ml. of the blood sample is added to 5 ml. of methyl ethyl ketone and, after adding about 1 g. of a mixture of 9 parts sodium chloride/1 part anhydrous sodium carbonate, is vigorously shaken for thirty seconds. (The solvent extracts the D.N.O.C. from the blood almost completely, and at blood D.N.O.C. levels over 10 µg. per ml. will be visibly yellow.) The solvent extract is now filtered free from blood coagulum and particles, and compared in a standard comparator with a series of nine permanent standards ranging from 5–45 µg. D.N.O.C. per ml. whole blood, either in good daylight or in reflected white light. The blood D.N.O.C. content can then be "read off" to the nearest matching disc, in terms of µg. D.N.O.C. per ml. whole blood.

The results obtained by this method are within 4–5 µg. per ml. of the blood D.N.O.C. levels as determined by the absorptiometric techniques, which usually give the higher result. The whole procedure of venepuncture and D.N.O.C. estimation can by this method be carried out

6. Lambotte-Escoffier, C., Moore, D. B., Taylor, Howard C. jun. *Amer. J. Obstet. Gynec.* 1953, **66**, 18.
7. Gaudino, M., Levitt, M. F. *J. clin. Invest.* 1949, **28**, 1487.
8. Sophian, J. *Amer. J. Obstet. Gynec.* 1953, **66**, 1369.
9. Baker, W. S. jun., Baker, J. P., Lussy, W. J., Bancroft, C. E., Clairbone, H. A., Lehman, J. J. *Ibid.* p. 842.
10. Parker, V. H. *Analyst*, 1949, **74**, 885.
11. Harvey, D. G. *Lancet*, 1952, **1**, 796.

within a very few minutes, with an accuracy which is quite satisfactory for most purposes. The extraction and estimation techniques serve equally well for the measurement of dinitro-butylphenol, another toxic chemical used for controlling weeds in peas, beans, and other legumes. If, for any reason, plasma or serum is used instead of whole blood, the measurements will be approximately twice as high as the whole-blood levels, since the vast majority of the chemical is held in the plasma, with little in the cells.

The comparator and special 'D.N.O.C.' disc are available from Messrs. Tintometer Ltd., Waterloo Road, Salisbury.

Pest Control Ltd.,
Cambridge.

E. F. EDSON
Medical officer.

HOSPITAL, DOCTOR, AND PATIENT

SIR.—May I crave a little more of your valuable space to enter the arena again?

Mr. King (April 17) is acting with admirable intention and no doubt in his hospital it works. But may I ask what steps he, or the management committee, take to inform the parents of his availability for interview? Is it printed on the admission note?

Patients have a great fear of authority, and particularly when it is shrouded in the grand mystery of imposing hospital buildings. I am sure a parent would not ask a sister for this privilege (if privilege it is) unless directly guided to do so.

Secondly, is the sister always on duty at visiting-time? During my recent stay as a patient in hospital, visiting-hours were often manned by junior staff. Are they allowed to conduct a policy other than that of "sealed lips"?

Thirdly, how many of us take up an opportunity for an interview, or write about our queries? This universal lassitude, or desire not to give trouble, is, I think, a national characteristic and may account for the fact that many ill-conducted dirty surgeries (do not think I condone them) are still beloved by the patients, because there they can always find their doctor without appointment and can talk to him without prior notice of their queries.

Yours,

F. CHARLOTTE NAISH.

MEDICAL TERMS

SIR.—In your review last week you seem to have completely misunderstood the purpose of this book. Owing to the accidental omission of a "t" in "ballottement" and other "small errors" the reader is warned "that he is being addressed by a fellow doctor rather than a professional philologist." If this warning is intended to convey that the reader must not expect philological perfection I am grateful, though I have yet to learn that works by professional philologists are invariably free from minor errors. But since you evidently imply that a "fellow doctor" is unqualified to write on the subject I must beg to differ. It is just because no professional philologist has attempted the task that I have stepped in, though fully conscious of my limitations, where angels have been too superior to tread.

You sneer at the book because it is "designed on an elementary level." Perhaps you will condescend to tell me from your Olympian heights on what other level it should have been designed? Recollection of my student days and a lifetime's experience of students, nurses, and auxiliaries have forcibly impressed upon me the confusion and difficulties arising from their ignorance of the meaning of words. One student, at his Final Examination at one of our older universities, had no idea why the lingual artery was so called. Nor are some of their instructors in better case. One of them, a consultant of high standing, was astonished to learn how "cyanosis" was constructed.

It is to such as these—the common people if I may be allowed without offence to call them—that the book is addressed by one of their number. I do not claim to be anything better than a verbal social worker or missioner in the linguistic slums in which I was myself reared, and which have been created not by any fault of the inhabitants but by the over-population of scientific terms. Those precious and delicate minds who have "any considerable knowledge of words" and who are "sensitive to inaccuracy" (even to trifling misprints) should shun the book like the plague. I have certainly no wish to cause them pain. But Heaven help us from clever people!

My derivation of "anaphylaxis" is linguistically correct. If Richet coined the word for the sake of euphony (which you seem to approve) all I can say is that were this example to be generally followed the language of medicine would soon degenerate into the nomenclature of modern drugs and detergents in which a higher commercial value naturally attaches to euphony than to sense. You would no doubt be delighted at such an outcome; I should regard it with dismay. If my modest contribution to the subject does something to prevent such a consummation I shall feel that I have not written it in vain.

Chesham, Bucks.

FFRANGCON ROBERTS.

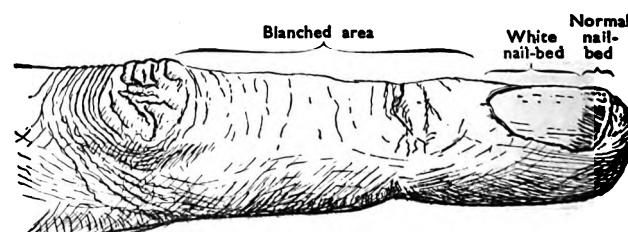
WHITE NAILS

SIR.—Dr. Terry's extremely accurate and detailed description (April 10) of white nails in hepatic cirrhosis is of particular interest to me, because I have been closely observing what I assume to be a similar phenomenon in a man of 79 with a grossly dilated heart, angina, and cardiac failure, following myocardial infarction in 1938.

I had been treating him for severe and intractable angina at rest (though there was no electrocardiographic sign of recent infarction) and early cardiac decompensation (there was little indication of it but fine râles at the bases) since last September, when I was horrified to notice, on Feb. 15, the deathly pallor of all but the terminal 3-4 mm. of his fingernails (see accompanying sketch). There was also striking blanching of the skin on the dorsum of the fingers distal to the proximal interphalangeal joints, and several scars on the forearms stood out startlingly white against the rather dusky surrounding skin. It may have been the gas-light that emphasised these features. Despite their appearance, his fingers were perfectly warm, and his conjunctivæ belied their suggestion of anaemia. His pulse volume was fairly good, and his haemoglobin I found next day to be 13.2 g. per 100 ml.

Now that he is no longer in failure, the nail-beds remain as white as they were, though the skin has resumed its normal hue, and, as far as I can make out in the presence of onychauxis, his toe-nails are similarly affected. There is no abnormal ridging of the nails; and, although his liver was admittedly tender and slightly enlarged at the height of his decompensation, there is no clinical evidence of liver damage now.

If this is the condition described by Dr. Terry, as I feel it must be, I cannot offer any hypothesis as to its cause, but I had assumed the condition to be a vascular one. It seemed to me that the arterioles, if not dilated, were certainly not constricted as in Raynaud's phenomenon, because the fingers were warm; similarly the



capillary bed appeared to be functioning normally except on the dorsum of the fingers. Can it be that the capillary bed in the proximal part of the nails (and perhaps in scar tissue) is unusually thin and that this area is pale because the deeper, reticular layer of the corium is abnormally pale? One can perceive, even in normal nails, a slight difference in depth of colour between the distal 3 mm. and the rest of the nail. And could it not be that the latter, being less well protected by a vascular coat, is the seat of that intolerable ache that occurs when one's fingers are thawing out? I advance this theory with great hesitancy, in the hope that, if it be foolish, it may enable someone else to get nearer the truth.

Kingston-on-Thames,
Surrey.

CHARLES STEER.

GRADUATE WIVES

SIR.—I have read with interest your annotation last week, and I would like to utter a few complaints about the way married women doctors are treated by the medical profession.

The fact is that part-time women doctors are just not wanted. I have tried unsuccessfully (as I know have many of my colleagues), in between bringing up a family, to obtain part-time employment in infant-welfare clinics—work for which I should have thought married women doctors were particularly well suited, having not only a medical qualification, but also personal experience in bringing up children. It seems, however, that the market is full to overflowing with full-time and part-time workers; and additional letters after one's name count for more than personal experience. To obtain additional qualifications, it is usually necessary to hold a resident post, which is an impossibility with a husband and family, who must come first, to care for.

I imagine the position is particularly difficult in the London area, owing to the larger proportion of graduate wives compared to other parts of the country. Another cause, I feel, is the large fees offered for sessional work; local authorities find it cheaper to maintain a full-time staff. Most married women doctors would be content to have a little pocket-money in hand after deduction of income-tax and after any additional domestic help had been paid for. So we might save the National Health Service a little of its vast expenditure.

London, S.W.15.

MARY E. LENNOX.

REPAIR OF LARGE HERNIA WITH NYLON MESH

SIR.—I would like to add my appreciation of Professor Stock's article of Feb. 20. One or two details of technique may be of interest.

I first started using nylon when I was senior registrar to Mr. S. V. Unsworth in 1951, when pre-cut nylon material was being implanted. At my suggestion we used nylon tricot—the light self-locking material which is used for ladies' underwear. This is very much lighter than the nylon mesh used in shoes and is quite strong enough, as experience has proved. It is easily obtained from any fashion store; I am using pink tricot material now but the colour comes out with boiling for sterilisation. By using tricot, the graft can be cut to shape *in situ*. The approximate size is cut and one side anchored to the inguinal ligament; I myself use continuous braided nylon thread, the most important stitch being the one bringing the graft down to the pubic bone. The upper edge is stitched with the graft laid in place, and an estimate can be made of the required tension, then the excess of material is cut away, the graft being thus tailor-made.

In regard to the ring, I make a slit in the nylon from the outer edge, which enables me to sleeve the cord,

instead of having sharp edges as may occur with Professor Stock's method. I have used this technique in Fiji with all large herniae and have had no sepsis. At first I gave 1.5 mega units of procaine penicillin but I have found this unnecessary. I agree that it is ideal material for incisional herniae, and I feel sure that it would be excellent for closing a diaphragmatic hiatus.

At this distance, I am not able to confer with Mr. Unsworth, of the Royal Liverpool United Hospital, but I would like to thank him for his very large part in the development of this method while I was his senior registrar.

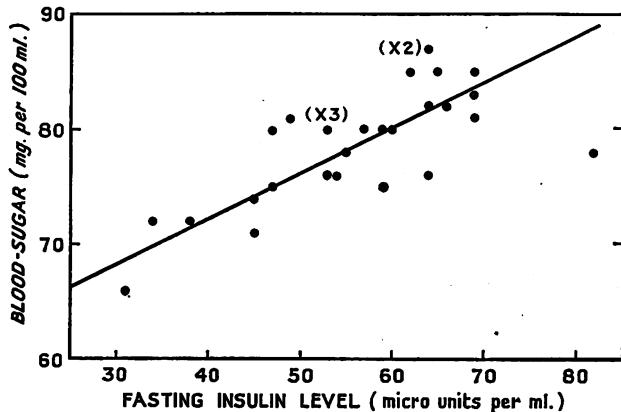
Colonial War Memorial Hospital,
Suva, Fiji.

ROBERT I. COHEN.

ESTIMATION OF PLASMA-INSULIN

SIR.—We should like to thank Dr. Edwards for his critical letter (Feb. 6) on our paper which appeared in your issue of Jan. 9.

Our data have now been reconsidered and further work has led to changes in the method of calculating the results, without, however, altering our general conclusions. While a full account of the revised method



Insulin levels in normal fasting subjects (recalculated) indicating the apparent relation between these values and their corresponding blood-sugar levels.

will be published elsewhere, we wish to make the following comments.

We did not make it clear in our paper that the values were calculated on linear scales between 10^{-5} and 10^{-4} and between 10^{-4} and 10^{-3} units per ml. of insulin. It has now been found by taking intermediate values that the graph of glucose uptake against the insulin concentration is curvilinear at the above concentrations. There was still an apparent curvature when the insulin values were plotted logarithmically. It now appears that a better approximation to a straight-line relationship over the required range, 10^{-5} to 10^{-3} units per ml. of insulin, is obtained by plotting glucose uptake against the cube root of the insulin concentration.¹ We have recalculated our results and find that the fasting insulin values fall between 31 and 82 micro-units per ml.; there still appears to be a direct relationship to their corresponding blood-sugar levels as previously suggested (see accompanying figure). The standard error of the deviation about the line was 14%. In recovery estimations, when known amounts of insulin are being estimated, the standard error of the percentage discrepancy was 21%. But we are here dealing with the difference of two estimations, each of which is subject to variation and the standard error of the difference would be expected to be greater than the standard error of either estimation separately.

To reply to the criticism that insulin was not being measured in the fasting state, we have carried out the following experiment.

Blood was taken from a fasting male subject, who was then given soluble insulin intravenously (0.1 units per kg. body-

1. Finney, D. J. Statistical Methods in Biological Assay. London, 1952.

weight); a further sample of blood was removed twenty minutes later, by which time the subject felt hungry and was perspiring. The blood-sugar and the plasma-insulin levels were estimated in each sample. In the fasting state the blood-sugar was 84 mg. per 100 ml. and the plasma-insulin 64 micro-units per ml.; twenty minutes after intravenous insulin, the blood-sugar had fallen to 30 mg. per 100 ml., whereas the plasma-insulin had risen to 400 micro-units per ml.

This experiment, together with the previously reported inhibition of the insulin effect by cysteine and glutathione, strongly suggests that what is being estimated in the fasting state is the effective plasma-insulin concentration.

J. VALLANCE-OWEN
BARBARA HURLOCK
N. W. PLEASE.

Postgraduate Medical School
of London, London, W.12.

TREATMENT OF CONVULSIONS IN CHILDHOOD

SIR.—Because of its efficiency and comparative safety, intramuscular paraldehyde is being widely used in hospital practice in the emergency treatment of continuous convulsions in children. When, however, a small quantity of hyaluronidase solution is thoroughly mixed with the paraldehyde just prior to injection, it will be found that the beneficial effect is extremely rapid in onset and that only a comparatively small dose of paraldehyde is usually required.

Hillingdon Hospital,
Uxbridge, Middlesex.

HARRY V. L. FINLAY.

TEXTBOOK ILLUSTRATIONS

SIR.—The standard of illustration in the new edition of a well-known textbook has led me to write this letter.

For a number of years the photographic departments of almost all medical schools and teaching hospitals have accumulated a considerable amount of clinical material. The black-and-white and colour photographs are filed and cross-indexed according to the names of diseases. While the records of any one department may cover only a limited number of conditions, each will have established comprehensive collections of the subjects which are of special interest to its hospital or institution. By courtesy of the consultants, these pictures are being made available to the medical staff of other hospitals. Authors and lecturers can thus, by consultation with their photographic department, obtain the best existing examples of the disease in which they are interested.

The search for the most suitable illustration would be facilitated by the formation of national or regional collections. Such libraries would receive 35 mm. lantern slides in colour or in black and white from their affiliated hospitals. This is the least expensive method of securing file copies, as most of the 35 mm. reversal black-and-white and colour films are bought at a price which includes the cost of processing. After exposure the cassettes are sent to the appropriate laboratories which return the finished transparent pictures.¹ The use of 35 mm. reversal film would therefore reduce the cost of preparing duplicates and require very little space for filing. The prospective author or lecturer would see all the available material in one central place. Once his choice were made he would be referred to the hospital which owns the original illustration. Such a collection should eventually include copies of diagrams, paintings, and radiographs, as well as photographs.

Until these libraries are established, reference to the nearest photographic department will help in the selection of the most suitable material for the illustration of lectures and textbooks.

Guy's Hospital Medical School,
London, S.E.1.

C. E. ENGEL.

1. Engel, C. E. *Med. biol. Ill.* 1954, 4, 1.

PREVENTION OF AIRBORNE INFECTION

SIR.—I was a little surprised to read the letter by Dr. Williams and Dr. Lidwell in your issue of April 10. The details of their tests are known to me but the reasons for the failure are at present inexplicable. Your readers may be left with the impression that these results are a scientific refutation of an unsubstantiated claim—which is far from the truth. Dr. Williams and Dr. Lidwell do not mention the results of other workers.

Several thousand tests on hexylresorcinol aerosols have been carried out in these laboratories in the past fifteen years, using saliva and 17 species of laboratory cultures as test organisms. Naturally the results varied from one type to another, but with standardised conditions worthwhile kills were always obtained. Mackay's experiments,² carried out in a 16,500 c. ft. chamber, completely confirmed our findings and on a scale comparable with the size of rooms used in Dr. Williams's tests; admittedly, the test organism was not the same in the two cases. In the Medical Research Council's own report³ resorcinol and alkyl resorcinols are listed among "... air disinfectants known at present and [which] appear outstanding" (p. 314); and "For the dispersal of disinfectant, vaporisers are usually most convenient ..." While the above examples may be regarded as referring simply to laboratory tests on a small or large scale, they cannot be ignored. On the other hand, success under operational conditions cannot be claimed on these grounds alone. My letter of March 6 suggested that continuous-flow aerosols of hexylresorcinol should, not would, prevent cross-infections.

From the practical point of view, support to the laboratory work has been given by Dickson,⁴ who reports reduction of absenteeism and duration of morbidity among a large group of office-workers exposed to continuous-flow aerosols of hexylresorcinol. Further support is furnished by McGrath's experiences in the Dublin Zoo monkey-house.⁵ Moreover, in the plasma-rooms of blood-transfusion centres, the contamination-rate has been considerably reduced since the aerosol system was introduced.

Altogether there is so much evidence in favour of continuous-flow aerosols that we feel there must be some explanation for the reported failure, and Dr. Williams and his team are best placed to suggest reasons. If some peculiar local conditions obtained, then it is important that these be known so that if they occur elsewhere steps might be taken to counteract them.

Avebury Research Laboratories,
Goring-on-Thames.

A. HOWARD BAKER.

HASHIMOTO'S STRUMA LYMPHOMATOSA

SIR.—If sought in the highways and byways, this fascinating condition is not as uncommon as is generally believed. The patient is usually a middle-aged or elderly woman with an abnormally firm, and therefore outlined, thyroid gland, which is often obviously enlarged; and there is evidence, both clinical and laboratory, of subthyroidism.

There is wide agreement about the histological changes in the thyroid—apart perhaps from how much fibrosis to allow before changing the name to Riedel's disease. These changes include diffuse infiltration with lymphocytes and plasma-cells, and the presence of well-formed lymphoid follicles. On the other hand, clinicians are far from unanimous about what they are looking for; Crile⁶ mentions 50 patients (and other evidence suggests that these cases were collected over, at the most, a few years), but he dismisses Riedel's struma as "such a rare disease that for practical purposes it can be disregarded"; Spence⁷ says that Hashimoto's struma is rarer than Riedel's, which itself is rare; and Simpson⁸

1. Mackay, I. *J. Hyg. Camb.*, 1952, 50, 82.
2. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1948, no. 262.
3. Dickson, C. *Irish J. med. Sci.* Sept., 1953, p. 337.
4. McGrath, J. *Ibid.* p. 343.
5. Crile, G. Jun. *Ann. R. Coll. Surg. Engl.* 1954, 14, 3, 158.
6. Spence, A. W. *Clinical Endocrinology*. London, 1953.
7. Simpson, S. L. *Major Endocrine Disorders*. Oxford, 1948.

considers the condition very rare and only to be diagnosed at operation.

In this department, 8 or 10 cases (not all proved by biopsy) have been watched over the past few years, and in those treated steadily with oral thyroid extract the same diminution in size of the gland has been seen as was described by Crile, who now considers this the specific treatment instead of the hitherto widely practised thyroidectomy. It is strange that this simple treatment has apparently received scant attention, although Lerman⁸ knew of it.

We have observed a persistent abnormality in the serum colloidal gold test, of which we have found no mention in case-reports. Curves of the order of 555554 and, in another case after a year on thyroid, 555410 have been obtained. Nothing comparable has been seen in the most florid "typical" myxœdemas. In one case, in which the remote possibility of amyloidosis of the liver and thyroid gland had been considered, the histological picture of a wedge of liver was normal.

This abnormal blood chemistry may assist in diagnosis; and if others have met it we shall be interested to hear their views.

Department of Pathology,
General Hospital,
West Hartlepool.

R. T. COOKE
E. WILDER.

TRICHOBEZOAR

SIR.—The article by Mr. Trafford in your issue of April 10 reminds me of a similar case operated on by Mr. C. Raison at Birmingham Children's Hospital in 1926. The girl, aged about eleven, was admitted with intestinal obstruction and was diagnosed as having a hair-ball on the story of her mother, who said she was always chewing her blankets. The obstruction was at the lower end of the ileum.

V. S. MITCHESON.
Folkestone.

HEPARIN AND HYALURONIDASE

SIR.—I was interested to read Dr. Riley's paper (April 24) on the mast cells. A study of the literature on the relation between heparin, hyaluronidase, and collagen led to the following hypothesis which was put forward about a year ago.⁹

Heparin is known to be a powerful natural inhibitor of the enzyme hyaluronidase,¹⁰ and serum contains a non-specific inhibitor of hyaluronidase.¹¹ The only tissue from which this inhibitor can be extracted is stated to be one rich in mast cells.¹² The level of this inhibitor in the serum has been found to be raised in "stress" states, in acute lupus erythematosus and rheumatic fever, after corticotrophin (A.C.T.H.) injection¹³ and after operations in animals.¹⁴ It is interesting to note that in many of these conditions the activity of heparin in preventing coagulation of the blood is diminished. This is so after operation and the administration of corticotrophin,¹⁵ in rheumatic fever,¹⁶ and in acute lupus erythematosus.¹⁷

It seems that these observations may be explained by assuming that the substance produced by the mast cells can act either: (a) as heparin, when combined with its co-factor; or (b) as hyaluronidase inhibitor, when combined with a lipoprotein.¹² This combination of heparin with a lipoprotein, thus diverting it from its anticoagulant activity, may be favoured by the adrenal

8. Lerman, J. *New Engl. J. Med.* 1952, 247, 259.
9. Garrett, J. V. D.M. Thesis, Oxford University, 1953.
10. Swyer, G. I. M. *Biochem. J.* 1948, 42, 32.
11. McClean, D. *J. Path. Bact.* 1942, 54, 284.
12. Glick, D., Sylvén, B. *Science*, 1951, 113, 388.
13. Glick, D. *J. Mt Sinai Hosp.* 1950, 17, 207.
14. Cole, J. W., Shaw, D. T., Fraser, P. *Surg. Gynec. Obstet.* 1950, 90, 280.
15. Garrett, J. V. *J. clin. Path.* 1953, 6, 294.
16. Abrahams, D. G., Glynn, L. E., Loewi, G. *Clin. Sci.* 1951, 10, 1.
17. Borrie, P. *Brit. J. Derm.* 1951, 63, 21.

cortical hormones. In this connection it is interesting to note that heparin,¹⁸ salicylates, and cortisone all have a therapeutic action in rheumatic fever, and that salicylates are stated to have an inhibiting action on hyaluronidase, probably due to their stimulation of pituitary and adrenal activity.¹⁹

If the action of corticotrophin and cortisone in the collagen diseases is related to the inhibition of breakdown of hyaluronic acid and the above hypothesis is correct, one might expect, in some cases, a potentiation of the therapeutic action of the hormones if heparin were given simultaneously, an extra supply of part of the anti-hyaluronidase system thus being made available.

I am well aware that many objections to this hypothesis can be produced, but there is no room to discuss them in a short letter.

St. James's Hospital,
Leeds, 9.

J. V. GARRETT.

Parliament

Science to the Rescue

IN the House of Lords on April 28 Viscount SAMUEL drew attention to the rapid increase in world population and the consequent need to produce more food and raw materials. A hundred years ago the population of the world was 1000 million; today it was 2500 million; next century it would probably be 5000 million. The pessimistic school of neo-Malthusians held that the fertility of the human race was outstripping the fertility of the plant. Lord Samuel believed that this need not be so. He looked to science, which had brought about the danger, to bring about the means of averting it. If there were millions more mouths to feed—100,000 more every day—every mouth brought two hands to work, and if there was a stomach there was also a brain. Opportunities to extend the area of soil under cultivation were enormous, and those to increase its yield were even greater. For instance, by replacing draught animals by machinery immense quantities of food were released from animal consumption for human consumption. But the most important equipment on the farm was human labour, and in the tropics many workers were incapacitated by chronic disease. We could bring them health not only by providing drugs but by educating the women. Their homes were too often squalid and unhealthy, and he believed that the problem of Asia and Africa was largely a problem of the liberation and education of women.

Lord BOYD-ORR agreed that, if the present trend of population continued, we must double food production in the next 25 years, and nearly double it again in the following 25 years. There were two views on its feasibility. Some held that it was impossible and pointed to the food lost through soil erosion. Others held that with modern engineering and agricultural science it was difficult to set limits to the amount of food which could be produced. Even if land resources failed to produce enough the chemist could make food from sawdust. Protein could be produced from yeast and from algae and other plankton. But though it was easy in theory to increase food, it was not so easy in practice. Social, religious, and economic difficulties stood in the way. He thought it might be a good thing if an informal committee of the House were set up to consider what might be done in the interests not only of this country but of the world.

Lord BEVERIDGE pointed out that the growth of population was due to death control. The saving of lives through the development of science had become one of the major factors in the world population problem. Was it not clear that death control automatically required in some form or another birth-control? Lord SIMON OF WYTHENSHAWE agreed that the problem facing the world was to help the people of underdeveloped countries to complete the cycle, as we in this country had, from the state of high births and high deaths to low births and

18. Glazebrook, A. J., Wrigley, F. *Brit. med. J.* 1949, ii, 789.

19. Pelloja, M. *Lancet*. 1952, i, 233.

low deaths. When we had started death control two hundred years ago medical and sanitary science was in its infancy. In Eastern countries the death-rate was falling to Western levels in a few years and the people had no time to adapt themselves.

Lord HADEN-GUEST asked for a detailed survey of world conditions. People did not always act rationally; they did not take food because it had certain proteins and carbohydrates, but for all kinds of reasons. We also needed a more detailed survey of the world population, because some form of birth-control was a necessity, and it would be difficult to persuade primitive peoples to accept it.

Lord STAMP suggested that preventive inoculation, and other public-health measures, could be a mixed blessing to over-populated areas, if the end-result was to increase malnutrition and deaths from starvation. But the problem of feeding the world could be tackled from many angles and, as a medical microbiologist, he was particularly interested in the so-called unconventional methods of food production. Among some of these forward-looking developments he mentioned the suggestion that yeasts might be grown on industrial wastes such as molasses or on the hydrolysed products of wood pulp or of seaweed and used as accessory human food. This had already been done on a small scale in the West Indies. Another group of organisms which might serve as food for animal livestock were the algae. These unicellular plants produced high yields of fats and protein of nutritive value when grown under controlled conditions on simple inorganic nutrients under the photosynthetic influence of sunlight or artificial light. Considerable progress had already been made in developing this idea on a pilot-plant scale both in this country and, even more so, in the United States. It was also possible that, as the result of genetic studies, the yield of substances of nutritive value might be increased by the selection of variant strains of yeast and chlorella. Another possibility was to use the photosynthetic action of sunlight to extract proteins from leaves of plants at present largely wasted, such as potato and beet tops. This process might be especially suitable in tropical countries where the photosynthetic action of sunlight was intense and vegetation was lush. Again, in Denmark progress had been made in harvesting plankton from the sea by an ingenious process of electrolysis, which attracted them to the surface of large metal plates. The Danes had also treated fish and other offal with cultures of bacteria, thus rendering it palatable to animals. The mass production of micro-organisms and chemical analysis of their products was likely to have wide applications. Some of these processes were already being used on a large scale for the production of antibiotics, such as penicillin, and also vitamins, such as vitamin B₁₂, which could not be synthesised commercially. By lowering costs of production they might substantially reduce the cost of the health service.

Earl DE LA WARR, postmaster-general, replying to the debate, said that the real problem was for agriculture to keep pace with medicine. But it could do so only by a great effort. Birth-control was primarily a matter for the countries concerned and then for the individuals concerned. He could not see India thanking us, or the United Nations, for teaching their people methods of birth-control. Turning to help that we could properly offer, he said that just under £1 million of F.A.O.'s £4 million income came from Great Britain and the Commonwealth. We were also sharing in the Colombo plan. In our own Colonial territories in 1953 the grants and loans for projects to increase production amounted to about £123 million, besides what the local governments in those territories were doing.

He would like to end on a hopeful, but not complacent, note. In 1950 it was estimated that world food production was falling behind the increase in the population, but two years later it had outstripped that increase. The increase in food production was not large, but it did show that the problem was soluble if it was faced. Her Majesty's Government were determined to make their maximum contribution internationally, but above all in this country and in the Colonies for which they were primarily responsible.

Committee on Homosexuality

On the motion for the adjournment in the House of Commons on April 28, Mr. DESMOND DONNELLY asked for the appointment of an royal commission on homosexuality. Sir ROBERT BOOTHBY thought that homosexuality in this country was more prevalent than was admitted and that it was tending to increase. All the laws relating to it were enacted before the discoveries of modern psychology. They were outmoded and they failed either to limit the incidence of homosexuality or to mitigate its evil effects. Youth must be protected, but there, in his opinion, the law should stop, and he believed that if it did so there would be at once a vast improvement in the existing situation. To send confirmed adult homosexuals to overcrowded prisons for long sentences was not only dangerous but mad.

Sir HUGH LUCAS-TOOTH, under-secretary of State for the Home Department, said there were no reliable means of assessing the prevalence of homosexual practices. The number of cases which came to the notice of the police and the number of convictions had increased. There would be general agreement that the criminal law ought to provide effectively for the protection of the young and for the preservation of public order and decency. The question was whether the law should confine itself to securing those two objects or whether it should be amended so as to permit unnatural relations between consenting adults in private. Such activities were no crime in many countries of the world today. The Home Secretary had received from the Cambridge Department of Criminal Science a report on a survey of all sexual offences reported to the police in 1947 in 14 police areas. It showed that 986 persons were convicted of homosexual and unnatural offences. Of these 257 were indictable offences involving 402 male victims or accomplices, as the case might be. Most of these victims or accomplices were under the age of 16. Only 11% of the whole were over 21, and there was only 1 conviction involving the case of an adult with an adult in private. These figures showed that the result of the law, whatever its intention might be, was not so very different from what Sir Robert Boothby had pleaded for.

Turning to medical treatment, Sir Hugh said that visiting psychotherapists had been appointed at certain prisons. Prison medical officers elsewhere submitted the names of any prisoners serving substantial sentences, whom they thought likely to benefit by treatment, for transfer to a prison where treatment was available. Prisoners serving shorter terms could be seen by visiting psychiatrists from regional hospital boards, and treatment was often started with a view to continuation after release from prison. The Prison Commissioners proposed to build a special establishment for mentally abnormal prisoners; sexual and homosexual cases would certainly be included.

Sir Hugh ended by announcing the decision of the Home Secretary and the Secretary of State for Scotland to appoint a committee to examine homosexual offences and the parallel problem of the law relating to prostitution and solicitation generally. The Home Secretary felt that a committee would be more appropriate than a royal commission, but he was anxious to secure the services of able and experienced men and women to serve on it. It might be some time before the membership and terms of reference could be announced.

Pay of Mental Nurses

In an adjournment debate on May 3 Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, announced the improvements in the remuneration of nurses and assistant nurses in the mental health service, recommended in the arbitration award, which are being submitted to the Whitley Council. The basic rates, she explained, are to remain unchanged, but the student mental nurse would receive an increase of £40 in total in the proficiency allowances payable on passing her preliminary and final examinations. By the time the mental student nurse reaches the end of her training she would thus have received £175 more in pay and allow-

ances than the general student nurse, or nearly £60 a year. There would also be increases in dependants' allowances, and in allowances to married men. The new rates would increase the "mental lead" from £20 to £45, so that a qualified mental nurse would receive £45 more than her counterpart in the general hospital. The revised salaries would be £405 rising to £505 for women, and £415 rising to £515 for men. There were other and comparable increases for ward sisters and the like. The nursing assistant would start at £280 instead of £250, and after two years' satisfactory service she would advance to £335 and thereafter to the existing maximum of £425. Miss Hornsby-Smith added that the Whitley Council had still to announce their decision on the award.

QUESTION TIME

World Health Organisation Funds

Sir RICHARD ACLAND asked the Minister of Health whether he would instruct the representative of H.M. Government on the relevant committee of the World Health Organisation, at the next appropriate meeting of the committee, to press for a substantial increase in the regular budget of the organisation and to pledge this country to pay its fair share in the increase.—Miss PATRICIA HORNSBY-SMITH replied: The proposed regular budget of the organisation for 1955 shows a substantial increase over that approved for 1954, but the Minister is not satisfied that this increase is justified. The matter will be further considered at the next World Health Assembly. The United Kingdom contributes to the budget on a scale approved by the assembly. Our representative will not press for an increase in the total budget unless we are satisfied that it is justified.

Private Beds

Mr. ARTHUR MOYLE asked the Minister what steps were taken to ensure that private beds were not reserved for the use of fee-paying patients when there were urgent or chronic cases on the general waiting-list.—Miss HORNSBY-SMITH replied: The National Health Service Act, 1946, specifically provides for patients in urgent medical need of treatment to be admitted to a pay bed without charge if no alternative accommodation is available. The Minister has brought this to the notice of hospital authorities, and has also asked them to ensure that pay beds not in full use for private patients are used for other patients whether urgent cases or not.

Mr. MOYLE: Will the Parliamentary Secretary say what view the Minister takes of the heavy fees that are paid by private patients for minor operations like the removal of tonsils, for which they are able to get immediate attention within a week of the arrangement being made with the specialist or consultant, whereas children who, in the opinion of their parents are suffering from defective tonsils, have to wait as long as six months before they can get the operation done? Miss HORNSBY-SMITH: I hope the hon. Member will not exaggerate these claims, because in the case of hospitals in which he himself is interested the Minister has assured him that whereas 25 tonsillectomies were done a week under the National Health Service there were only 4 a year done on private fee-paying patients. I do not think it is fair to suggest that there is this widespread abuse when the case which was investigated for the hon. Member was not justified.

Labelling of Poisons

Lieut.-Colonel WENTWORTH SCHOFIELD asked the Home Secretary if, where the law provided that any poisonous fluid or substance must be marked or labelled Poison, he would make it compulsory that the antidote to the poison should also be clearly stated.—Sir DAVID MAXWELL FYFE replied: The Poisons Board has advised against the introduction of such legislation. Undue emphasis on antidotes might result in the loss of valuable time in obtaining medical help. Barbiturate poisoning, for example, which has been the commonest form in recent years, requires immediate hospital treatment, and any delay may be fatal. I hope no-one will rely on antidotes to the exclusion of getting immediate medical advice.

Recruitment of Sanitary Inspectors

Sir HAROLD SUTCLIFFE asked the Minister what action he proposed to take on the report of the Working Party on the recruitment, training, and qualification of sanitary inspectors.—Mr. IAIN MACLEOD replied: I and my colleagues who are

concerned in the work of sanitary inspectors have now considered the report and I propose to discuss it with the interested bodies with a view to implementing the Working Party's proposals. It should not be inferred that I necessarily accept all the detailed recommendations of the Working Party.

Obituary

LUDWIK HIRSZFELD

M.D. Berlin, Prague, and Zürich

Professor Hirsfeld, who died at Wrocław on March 7, was known far outside his own country and his own discipline, for his discoveries on blood-groups had offered to the growing sciences of anthropology and genetics the support of medicine.

He was born in Warsaw in 1884, and he studied medicine in Würzburg, qualifying in Berlin in 1907. His first interest was in cancer research and he worked in Heidelberg with Emil von Dungern and later in Zürich, where he became Privat-Dozent in 1914. But he was already interested in blood-groups, and he and von Dungern in 1910 published their important paper establishing that blood-groups are inherited according to mendelian laws.

On the outbreak of the first world war he volunteered to work with the Serbs in the Central Bacteriological Laboratory, first at Belgrade and later at Nish, where he vigorously supported Dr. William Hunter's crusade against typhus exanthematicus. His classical description of *Bact. paratyphosum* C, "Hirsfeld's bacillus," appeared in our columns in 1919. But his interest in blood-groups had not slackened. At first sight, conditions in war-time Macedonia might seem unfavourable for research; but with his wife, Dr. Hanka Hirsfeld, he took advantage of the heterogeneous character of the armies and their prisoners to investigate the racial distribution of blood-groups. They were able to show that on the whole the factor producing group A is prevalent among European peoples and the factor producing group B among those from Asia and Africa (*Lancet*, 1919, ii, 675).

On his return to Poland in 1920 he was appointed director of the Serum Institute in Warsaw and later of the Institute of Hygiene. In 1931 he became a professor in the medical and pharmacological faculty of the University of Warsaw, but after the German invasion in 1939 he was interned in the ghetto. There he organised a bacteriological laboratory, lectured in the secret school of medicine, and again had to fight typhus. He escaped in 1942 and hid under a foreign name. In 1944 he helped to organise the University of Lublin where he accepted the chair of microbiology. The following year he moved to Wrocław where he was appointed dean of the faculty of medicine and, later, president of the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences, which since his death has been renamed in his honour.

Throughout this not uneventful life Hirsfeld steadily pursued his scientific work. He foresaw the possibility of incompatibility between the maternal and foetal blood-groups long before this hypothesis was confirmed by the discovery of the Rh group, and in his latest studies he was investigating the mechanism of habitual abortion which he believed was often due to this cause. On the hypothesis of an allergic basis for abortion he gave anti-histamine drugs in this condition with apparent success.

The universities of Prague and Zürich had conferred on him the honorary degree of M.D., and he was a foreign member of the French Society of Allergy and of the Academy of Sciences, New York.



[Merckx]

STUART SPENCE MEIGHAN
B.Sc., M.B. Glasg., F.R.F.P.S.

Dr. Spence Meighan died on April 20, at the age of 65 years, a short time after his retirement from his appointments as surgeon to Glasgow Eye Infirmary and ophthalmic surgeon to Stobhill Hospital.

His father, Dr. T. Spence Meighan, had preceded him as surgeon to the Glasgow Eye Infirmary, and he was educated at Glasgow High School and Glasgow University. The award of the Weir scholarship to him in his third year proved a reliable prognostic sign, for he graduated B.Sc. in pure science in 1909 and M.B. with honours in 1912, and still found time to play rugger for the university xv. He was also a powerful swimmer and captained a Glasgow water-polo team.

As a houseman at the Western Infirmary he had the exhilarating experience of serving under Sir William MacEwen and Ralph Stockman. After holding other junior posts, including a clinical assistantship at the Glasgow Eye Infirmary, he was commissioned in 1915 in the R.A.M.C. (T.F.). He served in France with a field ambulance in the 51st Highland Division, and he was twice mentioned in despatches before he was taken prisoner-of-war.

On demobilisation in 1919 he returned to the Glasgow Eye Infirmary as assistant surgeon. Later he became visiting surgeon to the Eye Infirmary and ophthalmic surgeon to Stobhill Hospital. In 1926 he was appointed professor of ophthalmology at the Anderson College of Medicine in the extramural school. In 1920 he was elected a fellow of the Royal Faculty of Physicians and Surgeons and he was an examiner in ophthalmology for the faculty. He also held office as president of the Scottish Ophthalmic Club and vice-president of the Ophthalmological Society of the United Kingdom. He was a member of the board of management for the Glasgow Northern Hospitals.

S. A. writes: "Spence Meighan became a legend in his own life-time. He was a comfortable soul—generously proportioned, ruddy complexioned, and by disposition genial and friendly. His outlook and temperament seemed essentially bucolic, but at heart he had an almost Johnsonian love of towns and cities. For a few years before he died he lived in the beautiful Blane valley, on the road to Killearn; but he could always find a good reason for driving into Glasgow, and Sauchiehall Street was his spiritual home. Nevertheless he could enjoy the open air and it was his delight to have sailing holidays on the Clyde with his neurosurgical colleague. Not the least engaging of his qualities was his loyalty to his friends and to the hospitals which he served—a loyalty so unwavering that it became a source of inspiration to all who worked with him."

Dr. Spence Meighan leaves a widow and two sons, one of whom is a senior registrar in medicine.

JOHN EDMUND BOWEN

M.A., M.B. N.U.I., D.P.H., D.M.R.E.

Dr. J. E. Bowen, who died in Dublin on April 19, at the age of 69, was a native of Galway City. He was educated there at St. Ignatius College and at Queen's (now University) College. After he had taken an M.A. degree in 1910, he was appointed assistant lecturer in physics and, although of retiring nature, he quickly won a well-deserved popularity for patient and lucid exposition of his subject. About 1919 he was appointed lecturer in physics at King's College, London. During his last few years in Galway he studied medicine and he completed his course in London at Middlesex Hospital and St. Bartholomew's Hospital. He graduated M.B. N.U.I. in 1921, and he took the D.P.H. in 1922 and the D.M.R.E. in 1923. Almost the whole of his medical career was spent in Shanghai, where he was superintendent and radiologist to the Country Hospital and chief radiologist to the Shanghai municipal council. During the war he was interned in Japan. He passed the last years of his life in Dublin.

J. C. writes: "John E., as he was affectionately called, left Galway in dark and troubled times and he was destined to travel 'far off ways,' but his heart, perhaps, remained in the City of the Tribes and it is there that he was buried."

He is survived by his wife, Miss Nettie Grealish, of Galway, whom he married in 1916.

Diary of the Week

MAY 9 TO MAY 15

Monday, 10th

WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8.30 P.M. (1, Wimpole Street, W.1.) Sir William MacArthur : Pepys and the Plague. (Cavendish lecture.)
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Mr. Geoffrey Keynes : Second (and Third) Thoughts on Surgery of the Thymus Gland. (Annual oration.)

Tuesday, 11th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. J. Forest Smith : Nutrition and Child Health. (Second of two Croonian lectures.)
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. L. M. Franks : Latent Carcinoma. (Imperial Cancer Research Fund lecture.)
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. Section of Experimental Medicine. Dr. F. V. Flynn, Dr. J. Hardwicke, Prof. A. C. Frazer, Prof. N. H. Martin : The Serum Proteins.
8 P.M. Section of Psychiatry. Dr. L. Stein, Mrs. Mary Williams, Miss Theodora Alcock : Stammering.
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Prof. P. B. Medawar, F.R.S. : Wound Healing with Special Reference to the Skin.
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. J. O. Oliver : Antibiotics.

CIBA FOUNDATION

5 P.M. (26, Portland Place, W.1.) Sir Macfarlane Burnet, F.R.S. (Melbourne) : Problem of Virulence in Virus Disease.

UNIVERSITY OF EDINBURGH

5 P.M. (University New Buildings, Teviot Row.) Prof. Evarts A. Graham : Cancer of Lung. (Sir John Fraser lecture.)

Wednesday, 12th

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. J. A. Dudgeon : Virus Diseases.

MANCHESTER MEDICAL SOCIETY

4.30 P.M. (Medical School, University of Manchester.) Section of Pathology. Prof. R. A. Willis : Use and Abuse of Eponyms.

UNIVERSITY OF DUBLIN

4.30 P.M. (School of Physic, Trinity College.) Prof. E. B. Verney, F.R.S. : Water Diuresis. (John Mallet Purser lecture.)

Thursday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Prof. M. L. Rosenheim : Treatment of Nephritis.

ROYAL SOCIETY OF MEDICINE

5 P.M. Section of Ophthalmology. Mr. H. E. Hobbs, Mr. W. E. S. Bain : Hormone Treatment in Macular Disease. Dr. C. H. Greer : Pre-cancerous Melanosis.

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. Dudgeon : Virus Diseases.

ALFRED ADLER MEDICAL SOCIETY

8 P.M. (11, Chandos Street, W.1.) Dr. Franklin Bicknell : Diet and Behaviour.

UNIVERSITY OF ST. ANDREWS

5 P.M. (Medical School, Small's Wynd, Dundee.) Dr. R. W. G. Wyckoff : Use of Electron Microscope in Biology and Medicine.

SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION

5.30 P.M. (Roffey Park Rehabilitation Centre, Horsham, Sussex.) Dr. V. W. Wilson : Occupational Problems of the Neurotic. Dr. L. S. Davies : Value of Funkenstein Test. Dr. T. M. Ling : Psychological Problems Involved in Population Shift.

Friday, 14th

POSTGRADUATE MEDICAL SCHOOL OF LONDON

2 P.M. Mr. E. P. Brookman : Disabilities of the Foot.
4 P.M. Prof. R. B. Hunter : Control of Anticoagulant Therapy in Myocardial Infarction.

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. P. F. Borrie : Vascular Anomalies.

VARRIER-JONES LECTURE

5 P.M. (26, Portland Place, W.1.) Dr. H. G. Trimble (California) : Current Therapy in Pulmonary Tuberculosis.

UNIVERSITY OF CAMBRIDGE

5 P.M. (Department of Pathology, Medical School.) Sir Macfarlane Burnet : Influenza Virus Genetics.

UNIVERSITY OF LEEDS

3.30 P.M. (University Union.) Dr. Alfred Blalock (Baltimore) : Expanding Scope of Cardiovascular Surgery. (Moynihan lecture.)

Saturday, 15th

BIOCHEMICAL SOCIETY

11 A.M. (Department of Physiology, University, Bristol, S.) Scientific papers.

Births, Marriages, and Deaths

BIRTHS

MICHELL.—On April 12, at the Middlesex Hospital, W.1, to Annie, wife of Dr. Guy Michell—a daughter.

DEATHS

BRODIE.—On April 21, in Malaya, Dr. Mabel Garland Brodie, wife of Dr. W. H. Brodie.

Notes and News

WORLD HEALTH ORGANISATION

THE Seventh World Health Assembly, governing body of W.H.O., opened in Geneva on May 4 and will remain in session until May 22. More than 60 of its 84 member and associate member States have sent delegations.

Outstanding questions on the agenda will be the proposal for an increase in W.H.O.'s regular budget from \$8,500,000 in 1954 to \$10,300,000 for 1955, put forward by the director-general, Dr. M. G. Candau; a proposal from several member States that the members of the executive board should be increased from 18 to 24 to give a wider geographical distribution of seats; and a request for admission of the Federation of Rhodesia (comprising Northern and Southern Rhodesia and Nyasaland) as an associate member.

Prof. Jacques Parisot of France is to be awarded the Léon Bernard Foundation prize in social medicine, and Dr. G. Robert Coatney (U.S.A.) and Prof. George MacDonald (U.K.) will receive awards from the Darling Foundation for their work on malaria.

Technical discussion will again be held during the assembly session, starting on May 8. This year's theme is Public Health Problems in Rural Areas.

THE BURDEN OF PENSIONS

"THE Growth of Pension Rights and their Impact on the National Economy" is discussed by a research group set up jointly by the Institute of Actuaries and the Faculty of Actuaries in Scotland.¹

The proportion of our population who are over sixty-five years old is likely to rise (the report says) from 1 in 9 at present to 1 in 6 in twenty-five years' time. About 5,000,000 men and 1,300,000 women are covered by existing pension schemes, including the various schemes for public servants and the mineworkers' scheme, and the annual contributions paid under these schemes amount to £240 million of which £90 million is paid by the members themselves and the rest by their employers. There are now 600,000 pensioners with pensions amounting to £105 million. In addition there are National Insurance pensions and certain other State pensions, which bring the annual total of pensions paid up to £600 million—about 4% of the national income. In thirty years' time, it is estimated the total annual expenditure on pensions of all kinds in respect of pension rights already contracted for (including National Insurance) will have grown to £1200 million, on the basis of the present levels of wages and salaries.

It is not possible to estimate to what extent pension schemes will spread; but an upper limit to the potential growth may be obtained by assuming that in thirty years' time employed persons will receive by and large a retirement pension (including National Insurance) of two-thirds of their average earnings throughout their working life and that widows will receive a pension equal to half of their husband's pension. On these assumptions pension payments will grow to £2100 million—equal to 14% of the present national income; but about half of this amount would in any event be required to maintain the increased number of old people on a minimum subsistence level, which will have to be provided whether or not they are entitled to pensions. The growth in pension rights will necessitate a reduction in the standard of living of the rest of the population over the next thirty years, unless it proves possible to make a drastic reduction in the present cost of defence expenditure or unless the national income increases substantially. Before the war productivity per head was increasing by about 1½% per annum, while in several post-war years the rate has been as high as 3%. Even the lower rate, if continued for thirty years, would increase the national income by over 50%, which should permit of a substantial increase in the standard of living, in spite of the growth in the numbers and claims of the old people. One of the most important factors in increasing productivity per head is an increase in the amount of capital equipment per worker, and the growth of pension funds provides an important contribution to the volume of savings available to finance new capital investment.

In the long run, the report says, the money burden of pensions is not substantially altered by general late retirement, as in the State scheme, since individual pensions are frequently augmented when retirement is postponed. Some increase in

1. A limited number of copies are available from the Institute of Actuaries, Staple-Inn Buildings, Holborn, London, W.C.1.

the national product will be contributed by those who retire late, and retirement should therefore be postponed as long as possible without harmful effects on health or efficiency; but, as the number of elderly workers who could be added to the labour force is probably not more than 300,000, only a limited benefit can yet be expected from this source. Incentives to encourage deferment of retirement appear to be preferable to compulsory deferment of minimum pension ages.

In most private pension schemes contributions are accumulated in a fund, out of which the pensions are subsequently paid. The primary object in building up a fund is to safeguard the benefits by making sure that the money to provide them has been saved in advance; and the report considers the question whether the same principle should be applied to National Insurance pensions. The National Insurance scheme differs from private schemes in that the Government have power to raise money by taxation or borrowing to pay the benefits, and the deciding factor in determining the level of benefits is therefore likely to be the prevailing trend of opinion about the proper provision that should be made for old people. From the standpoint of the national economy, the funding of pension schemes is of value only if it helps to increase the future level of national production, since in real terms the consumption of pensioners during any period must be met out of the current production of that period. Hence the funding of the National Insurance scheme would not help to alleviate the ultimate burden of pensions unless it provided a genuine addition to the volume of savings—not a mere substitution for savings which would otherwise have been made in some other form—and results in a real increase in capital investment. If the National Insurance retirement pensions were to be funded, the initial annual cost would be between £550–700 million, which would presumably have to be found mainly from taxation. These figures suggest that any attempt at a full funding of the National Insurance retirement pensions would be largely at the expense of other forms of saving.

SMOKING AND LUNG CANCER

THE April issue of *Medical World*¹ is devoted to a single topic—smoking and lung cancer. Dr. Richard Doll writes on incidence and aetiology, Dr. C. H. C. Toussaint on problems of early diagnosis, and Dr. W. P. Cleland on treatment and prognosis. The second half of the journal contains a symposium of the opinions of 7 family doctors, 7 consultants, and 7 medical officers of health and administrators.

WELFARE FOODS AFTER RATIONING ENDS

REVISED arrangements for the welfare milk scheme will be introduced on Oct. 31. Between Sept. 20 and that date, beneficiaries will receive a book of welfare milk tokens in exchange for their ration-books. These tokens can be used with any milk retailer anywhere; each token will enable the housewife to get 7 pints of milk at the welfare price (now 1½d. a pint) or 1 tin of national dried milk (equivalent to 7 pints of liquid milk) at the welfare price (now 10½d.). Books of tokens will be issued by the local offices of the Ministry of Pensions and National Insurance, and of the Ministry of Labour and National Service. Expectant mothers will receive books of up to 26 tokens, and children, books of 52 tokens. Application forms will be posted to everyone entitled to liquid milk under the scheme. Forms for those beneficiaries taking dried milk will be available at welfare foods distribution centres. The name and address and national insurance number of the expectant mother or of the parent or guardian of a child will be required on these forms.

Rationing ends on July 3, but those entitled to welfare milk must keep their books; for they will need them whenever they wish to change their retailer—e.g., when going on holiday—and will also have to produce them if they wish to get national dried milk.

The issue of other welfare foods (orange juice, cod-liver oil, and vitamins A and D tablets) will also continue after rationing ends. There will be no change in the present entitlements. Beneficiaries have already been notified that new books of coupons for orange juice and cod-liver oil are now obtainable from local food offices for use after May 15, when the coupons in the child's current green ration-book (B.B.2) will have been used up.

Local authorities in England and Wales have agreed to take over the distribution of welfare foods (other than liquid milk) when the local food offices close, and they have been

1. Published at 55, Russell Square, London, W.C.1. 4s.

asked to arrange to take over all local distribution from June 28. Similar arrangements are being made with local authorities in Scotland.

University of Glasgow

On Saturday, May 1, the degree of M.D. was conferred on the following:

* Donald Maclae (high commendation); James Walker (honours); H. G. Easton, J. T. Hutchinson.
In absentia.

Royal College of Physicians of London

At a cornitia held on April 29, with Sir Russell Brain, the president, in the chair, the following were elected to the fellowship:

M. K. GRAY, Christchurch; I. G. DAVIES, Leeds; E. T. D. FLETCHER, London; O. R. J. MURPHY, Brisbane; C. L. STOTE, Shrewsbury; L. G. BELL, Winnipeg; H. M. RENNIE, Sydney; RALPH WHISHAW, Hobart; A. C. E. COLE, Dar-es-Salaam; E. C. ALLIBONE, Leeds; H. B. MAY, London; E. M. DARMADY, Havant; H. A. DEWAR, Newcastle upon Tyne; J. M. HOLFORD, surgeon commander R.N.; A. P. DICK, Cambridge; D. H. G. MACQUAIDE, Northampton; JAMES CARSON, Sheffield; RAYMOND GREENE, London; R. J. G. MORRISON, lieut.-colonel R.A.M.C.; GEORGINA M. BONSER, Leeds; C. E. DENT, London; J. M. NAISH, Bristol; T. N. MORGAN, Aberdeen; K. S. MACLEAN, London; JOHN LOWE, London; A. P. NORMAN, London; J. HAMILTON PATERSON, London; G. MACG. BULL, Belfast; L. G. BLAIR, London; ROBERT KIRK, Khartoum; D. V. HUBBLE, Derby.

The following were elected to the fellowship under by-law 39b, which provides for the election of non-members "who have distinguished themselves in any branch of the service or practice of medicine":

A. P. MURPHY, F.R.A.C.P. Brisbane; Sir ERIC PRIDIE, London; H. E. SIGERIST, Zürich and Yale University.

The following, having satisfied the censors' board, were elected to the membership:

K. D. Bagshawe, M.B. Lond., Katharine M. Baker, M.B. Lond., F. H. Burns, M.B. Sydney, S. I. Cohen, M.D. Lond., John Colvin, M.B. Glasg., P. B. Cook, M.B. Lond., J. J. Daly, M.B. Camb., Hout. R.A.M.C., J. R. Edsall, M.B. Camb., I. E. Evans, M.B. Lond., Yvette A. P. Franklin, M.B. Lond., R. G. Gibbs, M.B. Camb., A. J. Glebe, M.D. Melbourne, J. D. S. Hammond, M.B. Sheff., P. J. D. Heaf, M.D. Lond., Cherry D. Heath, M.D. Lond., J. B. Hickie, M.B. Sydney, Alison Hunter, M.B. N.Z., J. D. Hunter, M.B. N.Z., John Knox, M.B. Glasg., P. J. Lawther, M.B. Lond., D. G. Le Roux, M.B. Cape Town, D. Y. Mackenzie, M.D. Lond., J. McE. Neilson, M.B. Glasg., Patience Proby, B.M. Oxf., A. J. Proust, M.B. Sydney, P. M. Roze, L.R.C.P. J. F. Soothill, M.B. Camb., M. D. Turner, M.B. Brist., H. E. Webb, B.M. Oxf., Eric Wilkes, M.B. Camb., M. M. Zion, M.B. Witwatersrand.

Licences to practise were conferred upon the following 129 candidates who have passed the final examination of the conjoint board:

S. L. Adesuyi, L. N. Allen, T. D. Annear, Diana Austin, Jacqueline E. Banbury, Laurence Barsey, D. G. Bennett, Abraham Berry, H. R. Bissoon Dath, A. S. Blake, Gwyneth J. D. Botherway, Angela I. Brooks, Jean Brown, D. C. L'E. Burges, Patricia Burne, P. M. C. Camm, Jean Carberry, June M. Cheetham, Brenda A. P. Clark, R. M. Clark, David Constad, I. J. Cope, I. C. Cree, M. R. Crompton, R. N. Davis, Brian Dawson, Jean E. Drake, Peter Dromgoole, D. P. Dunfield, Lise L. Elnor, R. A. Ellis, P. A. S. Evans, C. D. Farrier, A. S. E. Fowle, J. K. Frost, Peter Garmon-Jones, Grace M. Gee, Mary H. Godwin, Peter Gortval, R. A. Grande, Brenda Grant, W. B. Hanley, Leonard Harbin, L. M. Hart, David Hide, G. M. R. Holliday, P. E. Hoogewerf, A. B. Hugo, L. H. Hurrell, W. M. Huie, Isidoro Ingleby, Barbara M. Isles, D. C. Jackson, P. D. C. Jarman, Peter Jenkins, A. R. Jones, Erice J. Jones, F. W. Jones, H. D. Jones, J. A. Kay, Peter Kellett, C. E. Langham, Diana E. Lethbury, N. A. G. Leadbeater, J. E. Leaneay, J. J. Lewis, D. C. Linahan, Patricia J. Lindop, B. A. Lowe, Colin Lowson, J. A. McMillan, W. M. Mee, Margaret S. Meyer, H. N. Middleton, K. F. Mole, A. A. D. Moore, Janet E. Morgan, Oswald Morton, Patricia E. Moul, Sheila M. Mullally, D. D. Munro, T. W. Nicholson, Wendy E. Noble, Patricia Painter, M. S. K. Palmer, Arnold Pearce, K. I. Pearce, Valerie J. Perkins, J. M. Phillips, C. W. Pook, Denys Pownall, J. A. Purcell, J. R. Rawstron, Dorothy S. Read, Kathleen M. Reid, J. E. S. Relton, Corinne J. Richardson, D. F. Rideout, G. D. Ripley, Derrick Roberts, Margaret Russell, J. G. Sanderson, A. C. Skarbek, J. C. Smith, R. W. Smith, D. L. Smithson, B. K. Sood, G. P. St. C. Starck, Leo Stimmer, Jane Sweetman, Eileen N. Thompson, T. M. Tibbets, W. R. Tidy, E. E. D. Tomlin, Annie M. N. Tustin, Heather F. A. Vickery, Dragomir Vuckovic, J. G. Wall, D. R. Whitehouse, D. H. Williams, H. R. Willings, J. H. P. Willis, A. J. Winterton, Joan M. Woodley, Celia B. M. Wooley, Enid M. Wozencroft, R. T. Yip-Choy, A. Youatt, C. F. A. Younger.

The following diplomas and those mentioned in our issue of April 17 (p. 840) were conferred jointly with the Royal College of Surgeons:

D.A.—A. J. Sims.

D.C.H.—Susanne M. Salvisberg.

D.T.M. & H.—Rahim Muhsin Ajina, Evelyn C. Cummings, J. S. Dodge, Nandkumar Damodar Gosavi, A. E. Gunders, Vishwanath Ganesh Nivsarkar, Hla Kyaw Pe, C. E. P. Samarasinghe, Suranjan Sen Gupta, T. K. Sweeney, Syed Abu Talib.

Hunterian Society of Great Britain

Dr. W. S. C. Copeman has been elected president of this society in succession to Sir Heneage Ogilvie.

Royal Medical Benevolent Fund

The annual general meeting of the Fund is to be held on Friday, June 4, at 5 p.m., at 11, Chandos Street, London, W.1, when Lord Webb-Johnson, the president, will take the chair.

Institute of Social Psychiatry

Dr. J. L. Moreno of New York will deliver a lecture to the institute at 1, Wimpole Street, London, W.1, on Monday, May 17, at 8 p.m., on Recent Advances in Sociometry.

State Medicine in the Nineteenth Century

Prof. W. M. Frazer will give three Newsholme lectures on this subject at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1, on May 24, 25, and 26, at 5.15 p.m.

Ministry of Health

The Minister of Health, Mr. Iain Macleod, has appointed Mr. R. B. Mayoh to be his assistant private secretary. The Parliamentary Secretary to the Ministry, Miss Hornsby-Smith, has appointed Miss P. M. Ibbotson to be her private secretary.

Association of Optical Practitioners

Mr. Stanley Wells, F.S.M.C., is delivering the Ettles lecture to this association on Wednesday, May 19, at 8 p.m. at the London School of Economics and Political Science, Houghton Street, London, W.C.2. He is to speak on Visual Problems of Older Workers in Industry.

The Concept of Race

On Saturday, May 15, at 2.30 p.m., at 45, Russell Square, London, W.C.1, the Medical Association for the Prevention of War is holding a conference on this subject. The speakers include Prof. Lionel Penrose, F.R.S., Dr. N. A. Barnicot, Mr. S. Sachs, and Dr. Duncan Ley.

Royal Society

The four new foreign members elected to this society include Prof. Karl von Frisch (Munich) and Prof. Otto Loewi (New York). Professor von Frisch is honoured for his work on the physiology of the chemical and visual sense organs of animals, especially insects and fish, and Professor Loewi for being the first to demonstrate the transmission of the effects of nerve-impulses by the release of chemical transmitters.

The Metropolitan Ear, Nose and Throat Hospital (outpatient department) has been transferred to St. Mary Abbots Hospital, Marloes Road, Kensington, W.8.

Appointments

JONES, LILIAN F., M.B. Birm., M.R.C.P.: house-physician, The Hospital for Sick Children, Great Ormond Street, London.

LAIDLAW, C. D'ARCY, F.R.C.S.: surgical registrar, Southmead Hospital, Bristol.

LAURENCE, ROSEMARY W., M.B. Edin.: house-surgeon to orthopaedic and plastic departments, The Hospital for Sick Children, Great Ormond Street, London.

MAY, C. R., L.M.S.S.A.: surgeon lieutenant R.N.: asst. m.o., British Transport Commission (London Midland Region).

TRUSCOTT, D. E., M.B. Lond., D.M.R.D.: consultant radiologist, West Cornwall clinical area.

WHINCUP, H. H., M.B. Lpool.: asst. m.o., British Transport Commission (London Midland Region).

Appointed Factory Doctors:

MYERS, CARL, M.B. Sheff.: Preston, Lancs.

REA, A. H., M.B. Camb.: Halstead, Essex.

TAYLOR, WILLIAM, M.B.: Castletown, Caithness.

WILSON, C. L. L., L.R.C.P.I.: Newington, Kent.

Colonial Medical Service:

CAMERON, J. G., M.B. Witwatersrand, M.R.C.O.G.: specialist (obstetrician and gynaecologist), Medico Department, Gold Coast.

FUNG-A-FAT, A. G. E., M.B.: m.o., British Guiana.

GREENAWAY, D. G. G., M.R.C.S.: m.o., Falkland Islands.

MCMAHON, F. S., M.B. N.U.I.: house-physician, Colonial Hospital, Windward Islands.

RUGGLI, P. A., M.D.: m.o., Gold Coast.

TAYLOR, JAMES, M.B. Glasg., D.P.H., D.T.M.&H.: D.D.M.S., Sarawak.

VARDY, E. C., M.D. Durh.: D.D.M.S., Sarawak (Brunei).

North East Metropolitan Regional Hospital Board:

ATHERSTONE, R. N. G., M.A., M.B. Camb., F.R.A.R.C.S., D.A.: part-time consultant anaesthetist, King George and Ilford Isolation hospitals.

BALME, H. W., M.B. Camb., M.R.C.P.: full or maximum part-time consultant physician, Whipp's Cross Hospital.

ENTICKNAP, J. B., M.D. Lond., D.C.P.: full-time consultant pathologist, East Ham Memorial Hospital.

RUSSELL, ALEXANDER, O.B.E., M.D. Durh., M.R.C.P., D.O.H.: part-time consultant paediatrician, Harold Wood and Ilford Maternity hospitals, and Ilford Public-health Offices Clinic.

THICK, G. C., M.B. Lond., F.R.A.R.C.S., D.A.: part-time consultant anaesthetist, Hertford group of hospitals.

THE THRESHOLD OF AGE

JAMES M. MACKINTOSH

M.A., M.D., LL.D. Glasg., F.R.C.P., F.R.C.P.E.

PROFESSOR OF PUBLIC HEALTH IN THE UNIVERSITY OF LONDON
AT THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

SOCRATES : "To tell you the truth, Cephalus, I am very fond of conversation with elderly folk. They have gone before us on the road over which perhaps we also shall have to travel and I think we ought to try to learn from them what the road is like—whether rough and difficult or smooth and easy. And now that you have arrived at that period of life which poets call 'the threshold of age,' there is no-one whose opinion I would more gladly ask."

PLATO : *The Republic*. Book I.

In the field of health and welfare one of the most striking changes in the short span of two generations in the United Kingdom is the increased number of the elderly members of the community. This simple table gives quite a vivid picture of the situation ; it shows three age-groups and the percentage changes that have taken place between 1891 and 1951 :

Age	1891	1951
0-14	35 %	21 %
15-64	60 %	68 %
65	5 %	11 %
Total	100	100

In the same period the total population has gone up from thirty-three million to fifty, and by 1980, it is estimated, a fifth of us will be of pensionable age. Hence it is not surprising that we have become conscious of the social and economic embarrassments of old age. We can no longer afford to ignore the personal needs of the elderly, partly because there are so many of them and partly because we ourselves are vulnerable.

In recent years a large number of studies have been made of the problems affecting the aged—statistical, social, economic, and clinical.

In 1940 the National Council of Social Service called together a group of voluntary societies engaged in helping the aged and formed a special "National Old Peoples' Welfare Committee" under the chairmanship of Eleanor Rathbone. Voluntary bodies are always in the van of social effort.

It soon became evident that the most pressing need was for investigation. Accordingly in 1944 the Nuffield Foundation appointed a survey committee to study the social and medical aspects of the ageing process, and the work already undertaken by public authorities and voluntary bodies. This committee reported in 1946.¹ An early result of this movement was the establishment, by the Foundation, of the National Corporation for the Care of Old People.

In the medical sphere one of the most striking surveys was that of Dr. J. H. Sheldon, of Wolverhampton.² Especially valuable also was the pioneer work by the late Noah Morris in Glasgow, the clinical observations by Dr. Marjory Warren, and the statistical studies of McKeown and Lowe in Birmingham.

These investigations aroused for the first time a sense of urgency, and a feeling of social and medical responsibility ; a national health service cannot ignore the welfare, housing, and other needs of five million people. At the same time it became clear to scientific investigators that social and economic planning for the aged was not enough ; we needed more knowledge of the biology of ageing so that we could take effective delaying action. Research had to be directed towards the maintenance of health and productivity beyond the normal threshold of age.

These efforts began gradually to resolve themselves into a public-health project in four essential phases :

- (1) To learn more about the normal health needs of ageing people—e.g., in terms of diet, rest, recreation, and the physical effects of mental and manual work.
- (2) To study the question of how best to prepare for the period of age—to enable people to make adjustments early and so proceed by easy gradations to the years of retirement.
- (3) To develop means of preventing, or at least stabilising, the chronic diseases and disabilities which tend to speed up the ageing process.
- (4) To develop methods of rehabilitation after illness among the elderly so as to bring them back as quickly as possible into "normal circulation."

On the psychological and educational side much work has still to be done on the maintenance of morale—e.g., as regards clean habits, proper methods of preparing and eating food, pride in clothes, and so on—and also to break down public prejudices about the elderly so as to induce more favourable attitudes among employers, the community, and the elderly themselves.

Some encouraging clinical facts have been brought to light by Sheldon, Morris, Marjory Warren, and others. In the Wolverhampton survey,² for example, in which old people in their own homes were the primary subjects of study, it was shown that only 3% were undernourished, and only 25% of 450 persons of over sixty-five were bedridden : at sixty only 28% were receiving medical care ; and though at eighty-five years and upwards the percentage rose to 43, at the age of seventy about 30% neither sought nor required medical attention. No very elaborate tests of mental capacity were carried out by Sheldon, and indeed the whole subject of mental testing needs further thought and study ; but he found that more than 75% needed no supervision from the mental point of view. A few were eccentric but harboured only gentle bats in the belfry—little furry things that hang upside down.

There was another side to the picture, partly coloured by physical disability. 40% had difficulty with stairs and general trouble in movement ; 40% had foot trouble of some severity, two women to every man. (This tells a tale ; is it Mistress Fashion or overmuch standing—or both ? In this respect a woman is probably at a disadvantage compared with a man because she may have to stand all day at a bench and then does not get an opportunity of putting her feet up on the mantelpiece when she returns home.) Rheumatism affected more than 55%, mainly in painful and creaking joints. 80% needed dentures and 60% wore them. 40% were worried with respiratory conditions, mainly bronchitis. At that time, before the National Health Service Act had swung into full operation, over 30% of elderly people were wearing bad or useless glasses and no less than 17.5% of their glasses had been obtained "by gift or inheritance."

The Threshold

Much of the research into the problems of old age has been obscured by a lack of division into categories. We should not think of lumping together in a single syllabus of education the infant, the school child, and the adolescent ; in old age a similar grouping holds good in reverse. So many of our guides have drawn no distinction between a person who reaches the fixed point of sixty-five while still in the full tide of his activity, the senior who is becoming garrulous and repetitive, and the doddering ancient.

We are faced with the process of decline and most of its incidents. Of course one finds precocious senescence : "there be some have an over-early ripeness in their years, which fadeth betimes" ; and on the other hand the

1. Old People : Report of a Survey Committee on the Problems of Ageing and the Care of Old People, under the chairmanship of B. Seehoem Rowntree, LL.D. London, 1946.

2. The Social Medicine of Old Age : Report of an inquiry in Wolverhampton. London, 1948.

decline may be long delayed. A few may burn brightlier toward their setting day.

For these reasons among others I have confined my subject to the threshold of age. At this critical time we may discern some special requirements: firstly, the wish to retain independence as long as possible; secondly, the need to feel of use as long as possible; thirdly, the need to be ready for retirement and adjusted to it long before the actual event. The portrait of a man or woman at the retiring age varies greatly; in its more vivid colours it presents those who are still in the active habit of life and look forward with zest to a new world of interest. An excellent example of this was Sir Harold Stiles, who gained distinction in geology after having made the splendid contributions of a lifetime to the art of surgery. At the other end we have the drab picture of a man who has made no preparation, has no inward interests: his retirement leads to a desert of loneliness; he shrinks mentally and even physically when the blow falls.

The study of the threshold of age is of immediate practical value; in the clinical field, at any rate, excellent progress has been made by showing that many crippled and even bedridden folk can be put on their feet again and helped to live useful lives. Nevertheless rehabilitation, valuable as it is, must be regarded as a form of therapy. When we come to examine the retiring age, our minds should be directed towards the prevention of disability, or at least postponement of the wearing-out process. In our present economic stresses we cannot afford to waste the talents and working capacities of any type of worker; we have to face the practical issue of how to maintain productivity without interfering with either the economic structure of our working society or the reasonable prospects of younger people.

During the past year or two there have been several important publications concerned with the elderly worker, notably *The Employment of Elderly Workers*, based on the practice and experience of 400 member firms of the Industrial Welfare Society, and *Older People and their Employment*, by G. Thomas and B. Osborne, published by the Social Survey. These reports should be consulted by those who wish to study the figures and the details of the investigation. I can deal only with the outstanding features of the landscape.

The Fixed Retiring Age

The first point to note is the remarkable decline in the employment of men over sixty between the years 1945 and 1951. Whereas for women there was practically no change, the proportion of men between sixty and seventy-five who were still at work fell from 44% to 30%.

Compared with the general population, fewer men over retiring age were manipulative workers and operatives, and more were on managerial staffs or came into the category of unskilled workers. The Social Survey made a distinction between those working in the larger firms (with more than 9 employees) and those working for smaller firms or self-employed. In the larger firms superannuation schemes are becoming increasingly common, and many of them provide for senior executive staff as well as for workers. Such a scheme enables employers to feel that they have made provision for all employees at the retiring age, and at the same time it gives a greater control over the elderly worker. But the insurance company becomes the arbiter of the worker's destiny, and a new pattern of employment is emerging. The existence of a superannuation scheme tends to hold younger workers at their job, so that they may retain benefits of insurance, but it tends to operate against workers over forty-five who wish to enter a particular employment for the first time.

The fixed retiring age has now extended widely beyond the full-time professional group and is an accepted policy in many industrial firms. It is also spreading into smaller

firms. In the Social Survey it was shown that some 37% of the larger firms had established a definite retiring age and 33% had superannuation schemes. In smaller firms the figure had reached about 14%. The result of this is an increasing pressure to retire at a fixed age and greater economic security in retirement. Of those working in firms that had established a retiring age it was found that about half the workers would have preferred to stay on beyond that period:

With a superannuation scheme	42%
Without a superannuation scheme	52%

It is clear that economic factors played a part in the wishes thus expressed. About half the men and women in full and part-time work said that they worked because they must; 40% of men and 30% of women said that they were obliged to work but at the same time preferred it to idleness. The remainder simply said that they preferred work. Nearly two-thirds of the men in full or part-time employment said that they intended to go on working for as long as they could; ill health seemed to be the most likely bar to continuing employment.

Waste of Potential Workers

In the Industrial Welfare Society pamphlet it was shown that the proportion of male elderly workers (compared with all workers) employed was

1945	4.3%
1950	2.7%

This indicates that the potential sources of labour are not being used today so effectively as in 1945. The factors which act against working beyond pensionable age are stated to be: (1) that the higher National Insurance pension at seventy for those who continue working is hardly worth the effort; (2) the growing feeling of being unable to compete with younger men; (3) the alleged resentment of younger men to the older people who block promotion; and (4) the whole sense of diminished physical capacity, the fear of having to learn a new job, and the desire for leisure. On the other hand many workers want to go on working because they dread the loneliness of retirement or because they desire to remain useful members of society. Employers as well as workers had some doubts about the economic value of postponed retirement. There was the fear of increasing accident-rates and of diminishing attendance at work; embarrassment about the trade-union attitude; and considerable doubt as to what work was appropriate for the ageing worker. Unless the employer had very strong feelings about his duty towards older people he was disinclined to face these problems.

The survey dealt with 400 member firms, employing 260,000 men and 87,000 women. In the total sample of workers elderly men counted for 2.7% and women for 2%; a distinction made between small, medium, and large firms showed a higher proportion of elderly workers in the small firms. This is to be expected partly because of the higher proportion of pension schemes in the larger industries and partly because of the more intimate relations between the workers and the management in the smaller groups. The general findings about superannuation policy agreed on the whole with those of the Social Survey that schemes were more common in the larger firms, thus leading to a bias in favour of compulsory retirement. They also eased some of the economic difficulties which lead men to continue work.

There is some disquieting evidence that the spread of pension schemes has a tendency to encourage premature retirement. The existence of a scheme lends force to the feeling of both management and workers that the elderly man will step down at about sixty-five years of age. The firm has little incentive to look further into the matter and try to create jobs for older men or to adjust existing processes to suit the slower pace of the elderly worker.

It is difficult to assess the feeling of the elderly worker himself towards retirement. What I tell you at the age of sixty-three about my future may be entirely different from my opinion a few months before actual retirement at sixty-five. I am ready to urge an early retiring age so long as I feel that the elders stand in the way of my promotion; my view will be sharply modified when I myself become the obstruction. Again, I may have felt that I needed a rest and so looked forward to retirement, but when the time comes and a few weeks or months have gone by, I may well take the view of Elia:

"I am no longer . . . clerk to the Firm of, &c. I am Retired Leisure. I am to be met with in trim gardens. I am already come to be known by my vacant face and careless gesture, perambulating at no fixed pace nor with any settled purpose. I walk about; not to and from. They tell me, a certain *cum dignitate* air, that has been buried so long with my other parts, has begun to shoot forth in my person. I grow into gentility perceptibly. When I take up a newspaper, it is to read the state of the opera. *Opus operatum est.* I have done all that I came into this world to do. I have worked task-work, and have the rest of the day to myself."

CHARLES LAMB, *Last Essays of Elia.*

Alternatives to Enforced Leisure

We must now turn to another aspect of the retiring age and try to discover if there are any appropriate alternatives to enforced leisure.

Let us assume that we are dealing with a manual worker who when he reached the age of retirement had been employed on work at which with his increasing skill he has become dexterous. If the firm, as is often the case, has a rigid rule about the age of retirement, it is unlikely that the workman will be able to secure alternative employment that complies with the simple, desirable conditions of continued satisfaction. The essentials of a good retirement job can be set down as follows:

- (1) The job should be paid.
- (2) The job should be on a part-time basis (becoming, if possible, gradually less onerous with increasing years) or should be lighter in the sense of relieving physical strain or, what is more important, slowing the pace.³
- (3) The job should be on a mental level not substantially less than his previous work. We do not wish to draft thousands of intelligent workmen to inferior duties which give them no real satisfaction. A job should be such as to offer interest and stimulation and avoid monotony.
- (4) The worker should be prepared to coöperate in simple and effective tests of his mental and physical capacity and, if necessary, undergo a course of training for new employment.

The selection of an elderly man for his new job should be based on his positive capacities and not on a list of disabilities.

If the question of retirement were merely a matter of years there would be little room for argument; but, just as the child has special characteristics and aptitudes, so too have the aged their special features. We should look at these positively, as we do with a disabled person, and our interest must be directed towards discerning what the man or woman of pensionable age can still do well, perhaps better than his juniors. Rough tests have been devised from time to time to determine the capacity of the ageing as the years go by, but so far there has been little attempt at accurate ascertainment, as in childhood and adolescence. What a glorious field for the psychologist! I am not for a moment suggesting that these tests of capacity would be easy to devise or to put into

3. "Within the limits of our sample, however, it was clear that older people tended to be found doing work where there was an absence of time-stress—in other words, work which could be done at their own pace, unhurried by pressure for speed, and where there was opportunity for accuracy to be displayed to advantage." From *Skill and Age: an Experimental Approach* by A. T. Welford and colleagues at the Nuffield Research Unit into Problems of Ageing. London, 1950; p. 144.

use; many of them perhaps will have to be applied not to the worker in relation to a job but rather to the circumstances of his everyday life. Amongst professional people the trouble often is that the adult is so much more sophisticated than the child and at a personal interview he knows so many of the answers, at least verbally. We may be driven to the kind of tests put forward by Bacon:

"Men of age object too much, consult too long, adventure too little, repent too soon, and seldom drive business home to the full period, but content themselves with a mediocrity of success."

Another useful kind of test is to compare present accomplishments with the work of the past. Sometimes the thought and speech of the ageing betray them. I always listen carefully to the man who says: "I am as good a man as ever I was," for that is one of the first symptoms of declining mental powers. The dear man has begun to whistle in the growing intellectual dusk. I suspect that Dr. Johnson was one of my examples. He had been to dinner with Allan Ramsay, who was about sixty-five years of age at that time—and then Boswell takes up the story:

"Next day, Thursday, April 30, I found him at home by himself. JOHNSON: 'Well, Sir, Ramsay gave us a splendid dinner. I love Ramsay. You will not find a man in whose conversation there is more instruction, more information, and more elegance, than in Ramsay's.' BOSWELL: 'What I admire in Ramsay, is his continuing to be so young.' JOHNSON: 'Why, yes, Sir, it is to be admired. I value myself upon this, that there is nothing of the old man in my conversation. I am now sixty-eight, and I have no more of it than at twenty-eight.' BOSWELL: 'But, Sir, would you not wish to know old age? He who is never an old man, does not know the whole of human life; for old age is one of the divisions of it.' JOHNSON: 'Nay, Sir, what talk is this?' BOSWELL: 'I mean, Sir, the Sphinx's description of it; morning, noon, and night. I would know night, as well as morning and noon.' JOHNSON: 'What Sir, would you know what it is to feel the evils of old age? Would you have the gout? Would you have decrepitude?'—Seeing him heated, I would not argue any farther; but I was confident that I was in the right."

Compulsory Retirement

We must now consider the desirability of a compulsory retiring age; and here some distinction must be made between those employed mainly in physical labour and those engaged in professional work making heavy demands on the mind.

For the manual worker a retiring age is desirable if only as a fixed period for the consideration of physical and mental capacity. Obviously there is nothing physiologically significant about the sixty-fifth birthday; it is just a matter of convenience. A good pension scheme ought to permit of considerable latitude about the age of retirement, say between sixty and seventy. This would encourage the stronger man to continue work without at the same time forcing the weaker to engage in competition beyond his physical powers. It is easy to convince oneself that the brain matures with age but even the most gullible will not deny that the suitcase becomes heavier. The man himself benefits by continuing his work beyond the retiring age partly from financial gain and partly because he is presumably doing something that gives him satisfaction. The community benefits because, to some extent, it gathers the fruits of his labour.

The important thing to remember is that the man himself must not be the arbiter; unless we accept, and he accepts, a dispassionate, independent assessment of his capacities, physical and mental, we shall go not one inch further towards a reasonable plan for retirement.

In the case of the professional worker who is mainly dependent on his mental powers the picture is different. The older man may find that his output is increasing with age and it is natural that he should mistake this for wisdom, since the tongue is perhaps the only organ of the

body that is not slowed down by advancing years. Physical suffering is endured; mental infirmity is enjoyed.

Indeed perhaps the greatest difference between the manual and the mental worker is the capacity for the latter to do harm. It is a sobering thought that the product of manual labour is mostly good, whereas the results of mental exertion may be disastrous. By the time the mental worker reaches retiring age he is often in a position of authority where his opportunities for doing ill are extensive; as a rule there is no-one in a position to tell him to go home. One might suggest therefore that a retiring age for professional people should be compulsory; the difficulty to be solved by mental health experts is what age should be chosen.

At any rate, as Dr. Johnson said:

"There is no state more contrary to the dignity of wisdom than perpetual and unlimited dependence, in which understanding lies useless, and every motion is received from external impulse."

RESISTANCE OF THE BREAST-FED INFANT TO GASTRO-ENTERITIS

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It is generally recognised that breast-fed babies are relatively resistant to gastro-enteritis (Levi 1941, Alexander 1948). The predominance of *Lactobacillus bifidus* in the stools of the suckling might suggest that the intestinal environment of the breast-fed infant is unfavourable to the establishment of *Escherichia coli*, particularly the types associated with infantile gastro-enteritis. The experiments described here were an attempt to study some of the features of the intestinal environment of the infant in relation to the growth of *Esch. coli*.

The Experiments

GENERAL PLAN

Metabolic Products in the Intestinal Tract

Previous study had shown that there is a qualitative difference in the faecal excretion of amino-acids by the breast-fed infant and by the artificially fed baby (Ross 1951). This suggested that certain amino-acids might either stimulate or inhibit the growth of these types of *Esch. coli*. An investigation of the growth of a laboratory strain of *Esch. coli* NCTC5928 on single amino-acids as the sole source of nitrogen in a glucose-salt medium (Dawes 1952) was now extended to certain types of *Esch. coli* associated with infantile gastro-enteritis.

Several investigators have found that a single amino-acid added to a medium otherwise capable of supporting growth may inhibit growth, but that this effect can be presented by the simultaneous presence of certain other amino-acids (Gladstone 1939, Porter and Meyers 1945, Davis and Maas 1949). A study of the growth of different types of *Esch. coli* on single amino-acids would therefore be of limited value in assessing their ability to grow in the complex mixture of amino-acids present in the intestines of infants. To overcome this difficulty the growth of these organisms was studied in sterile faecal extracts from artificially fed babies, breast-fed babies, and babies with gastro-enteritis associated with a specific type of *Esch. coli*. This experiment enabled the growth-promoting effect not only of the amino-acids but also of all the metabolic products in the faeces to be assessed.

Influence of pH

The striking difference between the pH of the faeces of breast-fed infants and of infants fed on preparations of cow's milk is well known (Tisdall and Brown 1924, Ross 1951). It therefore seemed relevant to study the pH of the stools in infantile gastro-enteritis and the influence of pH on the growth of these types of *Esch. coli* in vitro.

Dagley et al. (1953) found that, with *Esch. coli* in glucose-ammonium sulphate medium, low pH values alone could not account for the cessation of growth, and thought that certain products of metabolism might exert a toxic effect. In particular they showed that formic acid, which is produced during the growth of *Esch. coli*, increased rapidly in toxicity as the pH value decreased.

MATERIALS AND METHODS

The organisms used in the investigations were three type strains of *Esch. coli* (0-111, 0-55, and 0-26) obtained from the State Serum Institute, Copenhagen, and an untypable strain of *Esch. coli* from a healthy artificially fed infant.

Growth with Single Amino-acids as Sole Source of Nitrogen

The growth medium contained potassium dihydrogen phosphate 5·4 g., glucose 12 g., magnesium sulphate ($MgSO_4 \cdot 7H_2O$) 0·4 g., and either ammonium sulphate 1·2 g. or the required amino-acid 0·6 g., and made up to 1 litre with glass-distilled water and adjusted to pH 7·1. The medium was distributed in 25-ml. amounts in 'Pyrex' boiling tubes (6 x 1 in.) previously cleaned by boiling with nitric acid and washing with glass-distilled water.

The growth of *Esch. coli* was studied by the method described by Dagley et al. (1950). Bacteria for inoculation were prepared by three serial subcultures in glucose-ammonium-sulphate media; 0·1 ml. of the third culture, taken at the onset of the stationary phase, was used as inoculum. The tubes were incubated at 37°C without aeration because this would approximate more nearly to the conditions obtaining in the intestines. Samples of about 2 ml. of the growing culture were withdrawn with a Pasteur pipette and killed by the addition of 2 drops of formalin. Bacterial growth during culture was estimated turbidimetrically with a Spekker photo-electric absorptiometer (filters H508 and OB2) calibrated to convert turbidity readings into bacterial counts obtained with a haemocytometer.

Growth in Sterile Faecal Extracts

As our first purpose was to assess the effect produced on growth by the faecal extracts, independently of their natural pH, phosphate buffer containing potassium dihydrogen phosphate 9 g. and 5N sodium hydroxide 10·4 ml. per litre at a pH of 7·1 was used as the extracting fluid. In preliminary experiments the ratio of fresh faeces to extracting fluid was adjusted to the dry weight of the faeces; but it was found that the stools of the suckling were always more fluid than those of the artificially fed infant, and that the equalisation of specimens as regards dry weight often necessitated considerable dilution of the faeces of the artificially fed. Further, the test organism might not grow in this diluted extract, whereas there was good growth in an extract from the same specimen diluted on the basis of its fresh weight. We therefore decided to use equivalent weights of wet faeces from all three groups of babies in the proportion of 1 g. of faeces to 5 ml. of phosphate buffer. As sterilisation by Seitz filtration might remove not only bacteria but also some growth substances, portions of each extract were sterilised in three different ways: by Seitz filtration, by tyndallisation at a temperature of 100°C for 20 minutes on three consecutive days, and by Seitz filtration followed by tyndallisation.

To 12 g. of a well-mixed specimen of faeces was added 60 ml. of phosphate buffer. This was shaken for 3 minutes and centrifuged; thereafter the supernatant fluid was divided into three aliquots for sterilisation as described above. The sterilised extracts were then dispensed in 5-ml. portions in bijou bottles under aseptic conditions.

In this set of experiments the organism used was the stock strain of *Esch. coli* type 0-111, which was the type strain most often associated with our severe cases of gastro-enteritis. A subculture of the organism was made in 10 ml. of nutrient broth and incubated for 18-24 hours at 37°C. The bacteria

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TABLE I—GROWTH OF VARIOUS *Esch. coli* STRAINS ON AMINO-ACIDS AS THE SOLE SOURCE OF NITROGEN IN GLUCOSE-PHOSPHATE MEDIA UNDER UNAERATED CONDITIONS AT 37°C

Amino-acid	Stationary population (millions per ml.)				
	Strains of <i>Esch. coli</i>				
	NCTC 5928	Untypable <i>Esch. coli</i>	0-111	0-55	0-26
Ammonium sulphate	720	610	645	630	672
Aspartic acid	600	545	660	585	610
Serine	440	360	324	285	250
Glycine	373	225	290	250	348
Glutamic acid	310	280	170	230	165
Alanine	450	145	130	125	168
Threonine	78	45	200	145	165
Valine	34	65	145	102	117
Lysine	80	55	130	80	148

Little or no growth was obtained with any of the organisms on tryptophane, methionine, tyrosine, or isoleucine.

were harvested by centrifugation and washed three times in saline solution. The final washed-cell suspension in 10 ml. of saline solution was diluted 10¹, 10², and 10³, and 0.02 ml. of each dilution was inoculated into the bottles of faecal extracts, which were then incubated at 37°C. Growth curves were obtained by a modification of the method of Miles et al. (1938). At periodic intervals a sample of each extract was withdrawn with a sterile Pasteur pipette, and one drop was placed on similar numbered sections of each of three plates of dried nutrient agar. After absorption of the drops the plates were incubated at 37°C for 18–24 hours. Colony counts were made in drop areas showing no signs of confluence of colonies, and the mean colony count for the three was determined.

pH of Stools in Infantile Gastro-enteritis

This was estimated with B.D.H. indicator papers in faecal specimens from which *Esch. coli* 0-111, 0-55, or 0-26 had been isolated. The specimens were obtained from 80 infants either shortly after their admission to the gastro-enteritis ward at Knightswood Hospital or after cross-infection with these organisms in the ward.

Influence of pH on Growth in Vitro

The supply of nutrients in the intestines of the infant varies considerably. As the type of medium might influence the pH growth-range, media representative of three differing nutritional conditions were used :

(1) A simple synthetic medium was made as described above with ammonium sulphate as the sole source of nitrogen.

(2) Nutrient broth contained peptone 2%, 'Lab. Lemco' 1%, and sodium chloride 0.5%. To each boiling-tube were added 15 ml. of sterile nutrient broth and 10 ml. of water, and the tubes were then sterilised.

(3) Nutrient glucose broth.—To each tube containing 15 ml. of sterile nutrient broth was added 10 ml. sterile glucose solution 3% (w/v).

A Marconi pH meter was used for the pH estimations, which were adjusted by the addition of 5N sodium hydroxide or 5N hydrochloric acid, so that, for each medium, tubes covering a pH of 3–10 were obtained. Bacteria were pre-

TABLE II—GROWTH OF *Esch. coli* TYPE 0-111 IN FAECAL EXTRACTS

Time after inoculation (hr.)	Mean colony count in faecal extract								
	From baby on National Dried Milk			From breast-fed baby			From baby with gastro-enteritis		
	s	t	s and t	s	t	s and t	s	t	s and t
1	9	5	7	7	8	3	8	7	6
2	O-	O-	C-	C-	C-	C-	C	C	C
5	O	C	C	C	C	C	C	C	C
7	C+	C+	C+	C+	C+	C+	C+	C+	C+
9	O+	C+	C+	C+	C+	O+	C+	C+	C+
11	O+	O+	C+	O+	O+	C+	C+	C+	C+

C, confluent.

C-, partially confluent.

C+, densely confluent.

s, Seitz-filtered.

t, tyndallised.

s and t, Seitz-filtered and tyndallised.

pared for the experiment by three serial subcultures, in the medium to be employed for studying growth, at pH 7. Each tube was inoculated with 0.1 ml. of the third culture and incubated for 18–24 hours. The growth in each tube was determined turbidimetrically.

Formic-acid Content of Faeces

Seitz-filtered faecal extracts from 3 breast-fed babies and 3 infants receiving National dried milk formulae were used for this estimation. The formic acid in each specimen was determined by the method advocated by the Association of Official Agricultural Chemists (1945).

Influence of Oral Lactose on Faecal pH

This was studied in 18 healthy artificially fed infants under 4 months of age by the addition of lactose to a basic National dried milk formula with a protein content (about 1.5 g. per 100 ml.) approximating to that of human milk. A preliminary investigation showed that, if we gave 3% lactose straight away, diarrhoea and vomiting often ensued. Accordingly it became our established routine to start with a small supplement and to increase it every third or fourth day until the infant was receiving 3% supplementary lactose. This dosage was maintained for seven days and then gradually increased to 5%. The pH of the stools from these infants was determined daily with B.D.H. indicator papers, and the proportion of lactobacilli in each specimen was assessed by microscopy of a film of faeces stained by Gram's method.

RESULTS

Growth with Single Amino-acids as Sole Source of Nitrogen

The total growth of *Esch. coli* in media containing single amino-acids is given in table I. For all these

TABLE III—pH OF FAECES OF INFANTS WITH GASTRO-ENTERITIS IN RELATION TO PRESENCE OF SPECIFIC *Esch. coli* TYPES

<i>Esch. coli</i> type	No. of babies with faeces of pH						Total
	4.0–4.9	5.0–5.9	6.0–6.9	7.0–7.9	8.0–8.9	9.0–10	
0-111	0	1	8	29	10	0	48
0-55	0	0	12	14	4	0	30
0-26	1	0	0	1	0	0	2
Total	1	1	20	44	14	0	80

organisms the amino-acids studied could be divided into two well-defined groups :

(1) Those supporting good growth when providing the sole source of nitrogen in the medium (aspartic acid, serine, and glycine), or fairly good growth (glutamic acid and alanine).

(2) Those supporting poor or no growth (threonine, valine, lysine, tryptophane, phenylalanine, tyrosine, methionine, and isoleucine).

The behaviour of the type strains to single amino-acids displayed no significant difference from two "non-pathogenic" strains. With glutamic acid, however, *Esch. coli* 0-111 and 0-26 grew less well than the other three organisms.

Growth in Sterile Faecal Extracts

Table II shows the growth of *Esch. coli* 0-111 at intervals after inoculation of the faecal extracts (at pH 7.1) from a baby receiving National dried milk, a breast-fed baby, and an infant with infantile gastro-enteritis associated with *Esch. coli* 0-111. It will be seen that this organism could grow equally well in all three extracts. There was thus no evidence that its failure to grow in the intestines of the breast-fed baby was due to any lack of suitable nutrients.

pH of Stools in Infantile Gastro-enteritis

The pH range of 78 of the 80 specimens of faeces containing a specific type of *Esch. coli* was 6–9 (table III). As the majority of the babies in this group had diarrhoea

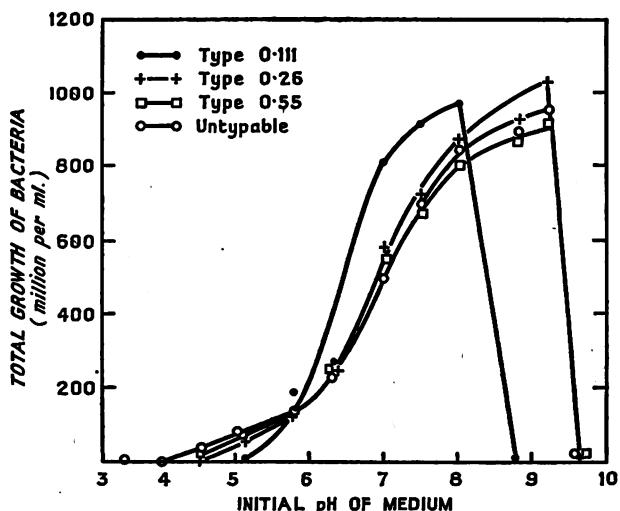


Fig. 1.—Total growth of different types of *Esch. coli* in glucose-ammonium-salt medium as a function of the initial pH of the medium.

of varying degrees of severity, it seems that, in gastro-enteritis associated with these organisms, the stools are generally alkaline and approximate to the pH found in healthy artificially fed infants.

Influence of pH on Growth in Vitro

The total growth of each of the four strains in simple synthetic medium, nutrient broth, and nutrient glucose, at various pH values, is shown in figs. 1, 2, and 3 respectively.

In simple synthetic medium (fig. 1) growth of *Esch. coli* 0-111 was not detected in the tubes of media below pH 5; from this pH there was a gradual increase in growth reaching a maximum at pH 8, with an abrupt decrease thereafter. With the other three strains growth began at pH 4-5 and reached a maximum at pH 9-2, with an abrupt decrease to no growth at pH 9-6. It thus seems that, in the simple synthetic medium, *Esch. coli* 0-111 has a more restricted pH growth-range than the other strains.

In nutrient broth (fig. 2) the pH growth-range for all four organisms was similar, and growth was maximal at pH 7-8. The stationary population attained by *Esch. coli* 0-111 and 0-55 was considerably greater than that reached by *Esch. coli* 0-26 and the untypable organism. The total stationary population for each of the four strains was less than that

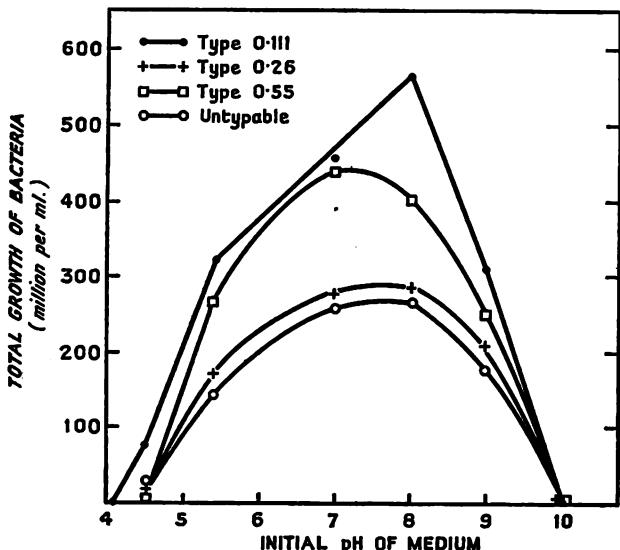


Fig. 2.—Total growth of different types of *Esch. coli* in nutrient broth as a function of the initial pH of the medium.

obtaining in simple synthetic medium, which has a much greater buffering capacity.

In nutrient glucose broth (fig. 3) growth for all four strains began at pH 4-4. For *Esch. coli* 0-111 and 0-55 maximal growth was reached at pH 10, with a rapid decrease thereafter. For *Esch. coli* 0-26 and the untypable organism growth was maximal at pH 10-6 (the highest pH reading). In this medium there was a wide difference between the high stationary populations attained by *Esch. coli* 0-111 and 0-55 compared with those attained by *Esch. coli* 0-26 and the untypable strain. If these curves are compared with those obtained in nutrient broth alone, it is obvious that the addition of glucose had a considerable effect in stimulating growth, and that this effect was greatest with *Esch. coli* 0-111 and 0-55. The addition of glucose to nutrient broth undoubtedly led to the formation of acid by the organisms, which tended to lower the pH of the medium and so to increase the pH growth-range. Unfortunately the pH of the tubes of media after growth had ceased was not recorded.

It thus seemed that, in each of the three media, all the strains grew with difficulty at a pH lower than 5.

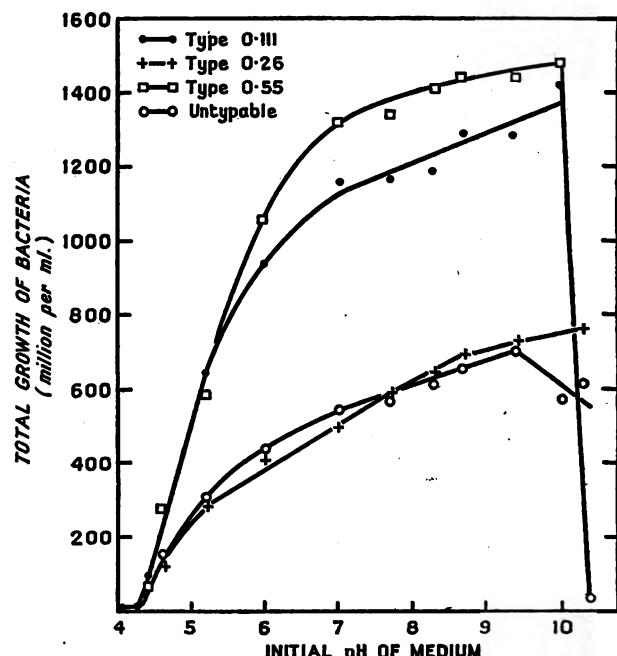


Fig. 3.—Total growth of different types of *Esch. coli* in nutrient glucose broth as a function of the initial pH of the medium.

and that growth was optimal at a pH higher than 7. The low pH of the faeces of the breast-fed infant would therefore be unfavourable to the growth of these organisms.

Formic-acid Content of Faeces

Table IV shows that the formic-acid content of the faecal extracts from 3 breast-fed babies was considerably higher than that of the extracts from 3 infants receiving National dried milk formulae. The concentration of formic acid found in the faeces of these breast-fed infants, in conjunction with the lower pH, would exert a powerful inhibitory effect on the growth of *Esch. coli* (Dagley et al. 1953).

Influence of Oral Lactose on Faecal pH

In view of the importance of a pH lower than 5 in preventing the growth of *Esch. coli*, the factors in breast-milk responsible for the maintenance of a low pH in the intestines were considered. Escherich in 1886 suggested that the high lactose content of human milk was an important factor, and Kendall (1911) emphasised the importance of the relationship of lactose to protein. This relationship was again emphasised by Gerstley et al. (1932), who claimed that the addition of 12%

TABLE IV—FORMIC-ACID CONTENT OF FÆCES OF 3 BREAST-FED BABIES AND 3 BABIES ON NATIONAL DRIED MILK

Formic-acid concentration (mg. per g. of faeces)	
Breast-fed	N.D.M.-fed
0.49	0.19
1.28	0.28
2.31	0.15

lactose to whole cow's milk produced the same quantitative ratio between lactose and protein as in human milk, and gave a stool with a similar aciduric flora to that of the breast-fed infant. These workers, however, did not give precise details of the pH changes accomplished by lactose or of its duration of effectiveness. As these details seemed of considerable relevance to the problem of maintaining a pH lower than 5 in the faeces of the artificially fed infant, we decided to reinvestigate the effect of feeding supplementary lactose.

From table V it will be seen that, before we gave supplementary lactose, the faecal pH was 5.5-9.6, with a mean of 7.7. The lowest pH attained after the addition of supplementary lactose was 4.3-6.7, with a mean of 5.7. The minimal time required to attain the lowest pH was from 5 to 30 days (mean 15.4 days). Moreover the lowest pH values were maintained for only two or three days and rose even while the infant was being given the same dose of lactose. Coincident with the fall in pH the proportion of faecal lactobacilli generally increased; but it was never so great as in the faeces of the breast-fed. Thus the administration of supplements of lactose to artificially fed infants has only a partial and temporary effect in reducing the pH of the faeces.

Discussion

Our investigations show that specific types of *Esch. coli* do not multiply at the pH of the breast-fed infant's stools. The "intestinal medium" of the breast-fed infant is not itself unfavourable to the growth of these organisms at pH 7.1; but formic acid, which is present in much higher concentration in the faeces of the breast-fed than in the artificially fed, may be of considerable importance in limiting growth at low pH values. That other intestinal fatty acids have a similar action on *Esch. coli* at low pH values has been shown by Bergeim (1940), who examined the effects of butyric and acetic acids in concentrations similar to those found in adult faecal extracts, on the growth of *Esch. coli*, and found that an increasing inhibitory effect was obtained with decreasing pH values.

TABLE V—EFFECT OF LACTOSE ON pH OF FÆCES

Patient	Age (weeks)	pH of faeces		
		Before lactose	Lowest after lactose	No. of days on lactose to attain lowest pH
A	8	5.8	5.4	20
B	2	7.9	6.4	12
C	9	7.6	6.7	20
D	10	7.9	6.1	7
E	2	8.2	5.8	8
F	8	7.9	6.7	22
G	2	7.9	4.3	27
H	10	7.6	4.9	7
I	2	5.5	5.2	8
J	11	7.6	5.5	5
K	9	9.6	4.6	10
L	13	8.2	6.7	30
M	5	7.9	4.9	30
N	8	8.5	6.1	15
O	11	7.6	6.4	18
P	2	8.2	4.9	9
Q	9	7.9	5.4	15
R	2	7.9	6.1	14
Mean	..	7.7	5.7	15.4

The difference between the total bacterial populations attained in nutrient broth and in nutrient glucose broth is of considerable interest. The stimulating effect of glucose on the growth of these organisms is important when it is remembered that oral feeds of glucose and saline solution are commonly used in the treatment of infantile gastro-enteritis. In healthy infants glucose would be rapidly absorbed from the upper intestinal tract, which is normally free from coliform organisms. In infantile gastro-enteritis, however, not only may there be invasion of the upper intestinal tract by coliforms (Blacklock et al. 1937) but also intestinal hurry may carry a considerable quantity of glucose further down the intestines. The combination of these factors might well stimulate the growth of a specific *Esch. coli*.

It is not sufficiently well appreciated that even the administration of a single supplementary feed of a preparation of cow's milk caused an immediate rise in the pH of the faeces (Ross 1951). Any resistance to types of *Esch. coli* based on a low intestinal pH would thus last only during the period of complete breast-feeding. Evidence for the transient nature of this resistance was found in the fact that in infants with gastro-enteritis no correlation could be found between the duration of previous breast-feeding and the severity of the illness. This is in keeping with the report by Stewart and Westropp (1953) that gastro-enteritis was rare in infants receiving nothing but breast-milk, but that, when they were removed from the breast, there was no difference in sickness experience between those weaned early and those weaned late.

The prevalence of cross-infection with specific types of *Esch. coli* among artificially fed babies in paediatric units has been shown by Rogers (1951) and Anderson et al. (1954). The ideal solution to this problem is to feed these babies with human milk. Where this is impossible, an attempt to attain an acid pH in the intestines assumes considerable importance. We have shown that it requires from about one to four weeks to reduce the pH of the faeces by adding lactose to National dried milk formulae, and that this reduction is only partial and temporary. Nevertheless, in view of the relationship of pH to growth of these types of *Esch. coli*, any effect produced by lactose in lowering the intestinal pH might in certain circumstances be advantageous.

It seems that in human milk there is another factor besides lactose which is necessary for the maintenance of an acid pH and a lactobacillary flora. György (1953) has reported the presence in human milk of a specific "growth factor" for a strain of *Lactobacillus bifidus*. This factor contains glucosamine, fucose, and galactose. Possibly this factor may also be necessary for the maintenance of a lactobacillary flora, and the production of such a flora would lead to an acid intestinal pH.

Summary

The predominance of *Lactobacillus bifidus* in the faeces of the breast-fed infant suggested a possible relationship between resistance to infection with specific types of *Esch. coli* and certain environmental conditions in the intestines.

With single amino-acids as the sole source of nitrogen in a glucose-saline medium there was no significant difference in total growth between the specific types of *Esch. coli* and the untypable *Esch. coli*.

Esch. coli O-111 grew equally well at a pH of 7.1 in the sterile faecal extracts from all three types of infant. It therefore seemed that there was no lack of suitable nutrients for this organism in the faeces of the breast-fed infant.

The pH of stools from infants with gastro-enteritis from whom these organisms were isolated was 6-9, a range similar to that found in healthy artificially fed infants.

The influence of pH on the growth of these organisms in vitro was investigated in a simple synthetic medium, nutrient broth, and nutrient glucose broth. In all three media the growth of each of the four strains was negligible when the initial pH of the medium was below 5, and optimal when the pH was above 7. It was therefore evident that the low pH of the breast-fed infant's stool would inhibit the growth of these organisms. Moreover it was found that formic acid, which is toxic to *Esch. coli* at a low pH, was present in much higher concentration in the faeces of the breast-fed than of artificially fed infants.

Oral feeds of lactose had only a partial and temporary effect in reducing the pH of the faeces of artificially fed babies. Human milk seems to contain another factor necessary for the maintenance of an acid pH and a lactobacillary flora.

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Secondly, different factors either enhance the severity of poliomyelitis and similar diseases, or shorten the incubation period, or promote the localisation of disease to a particular region of the nervous system. Among the first of these to be recognised was vaccination (Hochhaus 1909). Since then many others have been discovered, including tonsillectomy (Francis et al. 1942, Southcott 1952, and others), trauma (German and Trask 1938, Le Févre de Arric and Millet 1929), diphtheria prophylaxis (McCloskey 1950, and others), pertussis inoculation (Dean et al. 1951), and injections of cortisone (Schwartzman 1950), guanine, bismuth, and arsphenamine (Horstmann 1952, Findlay 1952), and penicillin (Banks 1954, Trueta 1954). It is also known that muscular activity during the preparalytic stage enhances the severity of poliomyelitis, and that paralysis affects particularly those limbs exercised most actively (Wickham 1913, Levinson et al. 1945, Russell 1947). In addition pregnancy has been implicated as a predisposing factor in poliomyelitis by Aycock (1941), and several other workers.

Experiments

We began our experiments on the assumption that the various influences mentioned above might conceivably work by a common mechanism. We thought that these different provocative procedures might all alter the vascular pattern within the nervous system and increase the permeability of the blood-brain barrier. We reasoned further that, if the virus gained access to the blood-stream while the vessels of the central nervous system were unusually permeable or even perhaps disrupted, pathological agents would then be afforded easy access to the vital neural elements beyond the isolating barrier.

As Trueta (unpublished) had observed the occurrence of poliomyelitis in a patient operated on for osteomyelitis and later placed in a plaster cast, one of the first experiments undertaken was the application of plaster casts to the hind limbs of rabbits. The rabbit whose spinal cord is shown in fig. 1 was killed, after immobilisation of the right leg for a fortnight, by an injection into the thoracic aorta of a mixture of Berlin-blue and barium. The representative samples in fig. 1 illustrate the increased vascularity of the right half of the cord which was consistently found in the lumbosacral enlargement.

Because of the importance of exercise as an enhancing influence in poliomyelitis, experiments were undertaken to determine its effect on the vascular state of the cord. Fig. 2 shows that exercise in the intact mouse is accompanied by a vast increase in the number of patent blood-vessels in the spinal cord. The lumbar enlargement of the spinal cord of the control mouse and that of the exercised mouse, injected with Berlin-blue in the left heart two hours after swimming for forty-five minutes in tepid water, show the striking contrast between the blood-vessels of the spinal cord at rest and after work.*

Our other experiments were concerned with the effect produced on the blood-vessels of the spinal cord by the injection of various irritants into the extremities (Speransky 1934). Only two of the most striking experiments will be mentioned here.

(1) The intramuscular injection of 10% formol-saline 0.05 ml. into the right hind limb of an adult white mouse was followed by paresis of the injected limb within an hour.

* These results throw light on certain unpublished incidental findings of Hodes and Shearer, the significance of which for the current problem was not appreciated at the time. These investigators, working in America on the preferential destruction of large motor neurones in poliomyelitis (Hodes 1949, Hodes et al. 1949, Sharrard 1953), observed last year that prolonged electrical stimulation of the motor cortex or individual dorsal roots of anaesthetised cats often produced macroscopically visible hyperæmia and extravasation of blood subdurally and within the medullary substance of the activated spinal segments.

and by death in four days. Gross inspection of the cord showed tremendous vascular engorgement limited exclusively to the vessels of the right lumbosacral region. Extravasation of blood from the dural vessels of this side was clearly visible on low-power magnification.

(2) The injection of 1% formol-saline 0.05 ml. into the thigh of another mouse was followed by paralysis, with death in seven days.

The reason for the death of these mice as well as of those that died after injections of other irritant substances into the periphery is now being investigated.

The second example of the effect of peripheral injections on the vascular tree of the spinal cord was provided by our experiments with croton oil, a powerful irritant. An injection of 1 in 50 croton oil 0.5 ml. into the muscles of the upper left thigh of a rabbit was followed four days

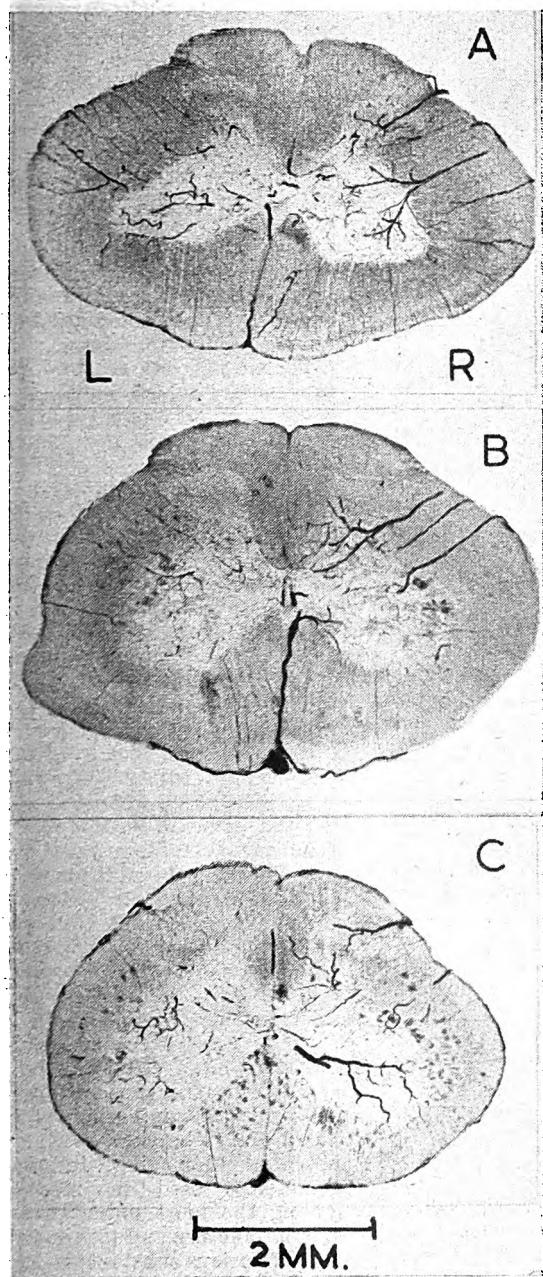


Fig. 1.—Representative unstained 300 μ sections through upper (A), middle (B), and lower (C) lumbar regions of spinal cord of a rabbit, showing greater vascularity on right side. A plaster cast had been applied to the animal's right leg for a fortnight before it was killed. L, left; R, right.

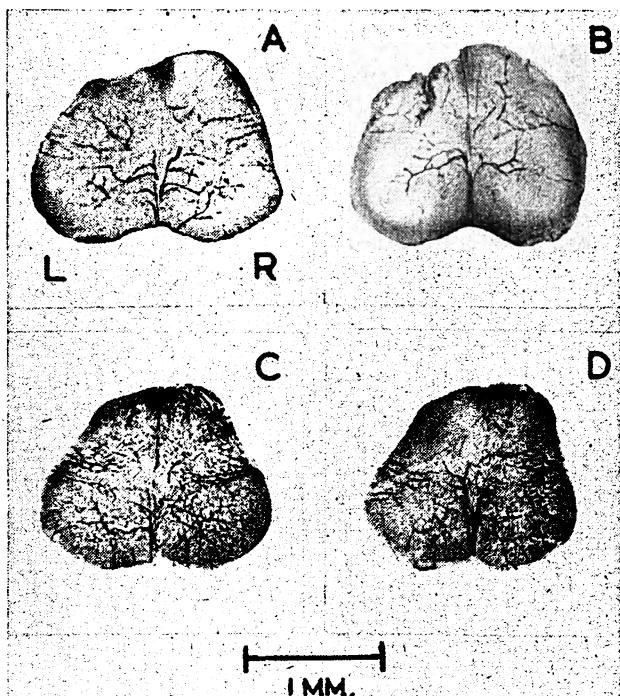


Fig. 2.—Injected vessels of 200 μ sections of lumbosacral cord of two mice : A and B, unexercised control ; C and D, after exercise. In C the entire section is filled with vessels ; in D the hyperæmia is most prominent in the ventral half of the cord. L, left ; R, right.

later by an injection of 1 in 10 croton oil 0.5 ml. into the same region. Weakness of the injected extremity persisted throughout the experiment, which ended twenty-four hours after the second injection. The thoracic aorta was then perfused with a mixture of Berlin-blue and barium, the spinal cord was fixed in formol-saline, and later thick frozen sections were prepared (fig. 3). The sections show red streaks of blood, marked engorgement and rupture of the vessels, blood in the central canal, and bright-red deposits of haemoglobin, sometimes spotty, sometimes massive, confined largely to the grey matter of segments L1-3.

Although the histological examination is not yet complete and therefore details are still lacking, it seems clear that the areas of the spinal cord that are most affected are those supplying the nerves to the injected portion of the limb. Their condition strikingly resembles the description of early lesions in fatal human poliomyelitis given by Wickman (1913).

"The changes in the spinal cord are usually obvious to the unaided eye. If they are at all marked, the cut surface protrudes, the grey substance is hyperæmic, either as a whole when it appears as a red H, or only in circumscribed areas, especially in the anterior horns. Besides this diffuse colouring, generally tiny blood streaks and specks also are perceptible ; they resemble capillary haemorrhages and have been so reported. But in most of the cases they are only vessels distended with blood. As mentioned already these macroscopical changes are most marked in the anterior horn, especially in the protuberances ; but they occur also in the posterior horns and occasionally in the posterior horns alone."

Discussion

The fact that widely different types of stimuli—plaster casts, exercise, and peripherally injected irritants—produce macroscopic changes in the circulatory patterns of the spinal cord suggests that many of the factors which enhance the severity of poliomyelitis, or localise the paralysis, may operate through local vascular changes in the brain and spinal cord. The extent of alteration of the blood-vessels of the spinal cord may vary, as in the

experiments described here, and may perhaps explain the greater provocative or localising action of some agents than of others.

It has long been recognised by several workers that many influences can reduce the normal impermeability of the blood-brain barrier, and that such influences tend to increase the severity of disease caused by a variety of pathogens. Thus, Flexner and Amoss (1917), Le Fèvre de Arric and Millet (1929), and Speransky (1934) showed that spinal puncture, intraspinal injections (including physiological saline solution), trauma, and the injection of various substances (particularly irritating agents given either subcutaneously or intramuscularly) increase the

permeability of the blood-brain barrier. When these diverse influences were combined with injection of the causal agents of poliomyelitis, herpes, rabies, and tetanus, death or serious disease resulted, whereas control animals, not so treated, either presented significantly reduced symptoms or were entirely free from the clinical disease.

In the light of our present work the words of Flexner and Amoss (1917) seem to us remarkable :

"The meningeal mechanism, which includes the choroid plexus, has indeed proved to be not only determinative in respect to the effect of an inoculation of the virus, but also of remarkable delicacy of adjustment. Pathological changes of almost incredibly slight character may set aside its protective function."

Implications

The results of our experiments encourage us to publish them without waiting for a detailed analysis of the data that we are gathering about the most effective ways of altering the permeability of the blood-brain barrier, either by increasing it—a factor which may help to prevent infection of the central nervous system in the prodromic phases of poliomyelitis—or by lowering it, a change which may facilitate the arrival of injected antibodies at the vulnerable cells. The evidence suggests that many of the factors which enhance the severity of poliomyelitis or localise the paralysis may operate through vascular changes in the spinal cord and brain, and that these alterations may be much more localised than one would have expected. Thus, in our opinion, exercise, pregnancy, minor or major peripheral or central trauma, injections, and many of the miscellaneous insults of daily life may well produce their deleterious effects in poliomyelitis by "slight changes" of the nature envisaged by Flexner and Amoss (1917).

If the concept advanced above is valid in broad outline, certain practical considerations arise immediately. In addition to the precautions necessary to reduce the chance of infection with poliomyelitis virus (Agerholm 1953) it would appear of prime importance that the physician should avoid inflicting on the patient any procedure which might seriously affect the blood-supply of the nervous system and endanger the integrity of the blood-brain barrier. Of the potential damaging influences commonly used in medicine, among the most potent are (1) spinal puncture and (2) the injection of various substances. Pending the results of further investigation of the effects of these procedures in human neurotropic disease, medicaments should whenever possible be given other-

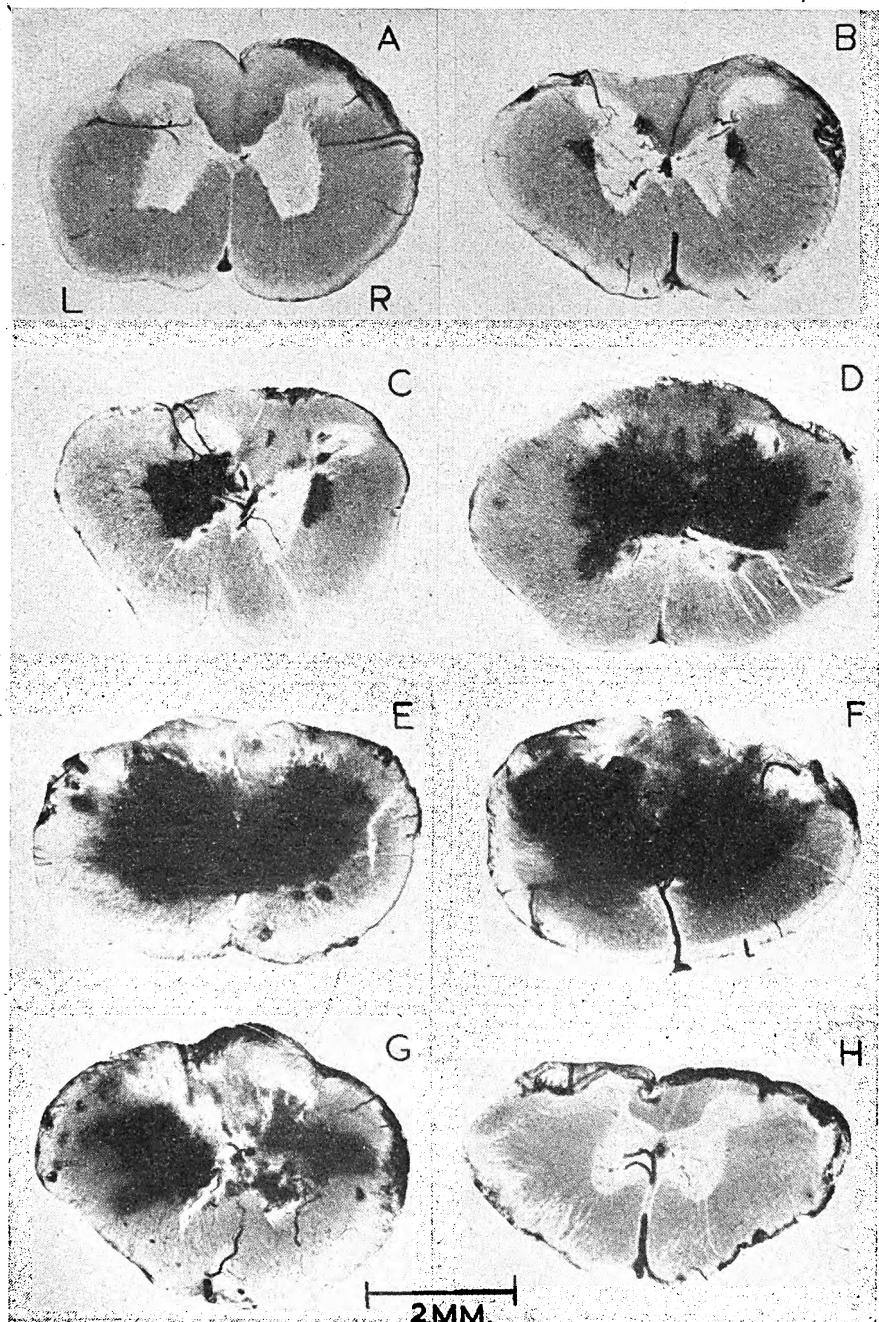


Fig. 3.—Spinal cord of rabbit after injection of croton oil into muscles of left upper thigh. Unstained 300 μ sections through cephalic portion of L4 (A); caudal (B and C) and cephalic (D and E) portions of L3; cephalic portion of L2 (F); middle of L1 (G); and caudal edge of T12 (H). L, left; R, right. Black borders on surface are Indian ink painted on right side; black areas within cord are deposits of haemoglobin. Note greater prominence of lesions on left side, its preponderant localisation in the grey matter, and blood in central canal in B and H.

wise than by injection. Where injection is unavoidable, it would be well to consider the advisability of finding less dangerous sites or less irritant substances to inject than those customarily used.

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POTENTIALLY DANGEROUS GROUP-O BLOOD

A SCREENING TEST

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ALTHOUGH, ideally, group-O blood should be transfused only to group-O recipients, in practice the emergency transfusion of blood of this group to patients who may be group A, B, or AB remains a necessity. Whenever such a transfusion is given, the potential danger exists that the transfused anti-A or anti-B antibodies from the group-O plasma may react with the recipient's A or B red-cell antigens, causing a haemolytic transfusion reaction. Reactions of this type have been reported by Ervin and Young (1950), Dausset and Vidal (1951), Mollison (1951), and Grove-Rasmussen et al. (1953), and in all these cases the transfused group-O blood contained anti-A antibodies exhibiting immune characteristics. Increasing attention has therefore been paid to the feasibility of providing a routine laboratory test for detecting a dangerous concentration of such antibodies in group-O donors. Alternatively purified A and B group-specific substances can be added to a bottle of group-O blood for emergency transfusion. Ervin and Young (1950) have shown, however, that even then a dangerous titre of immune antibody may still remain.

Grove-Rasmussen et al. (1953) claim that a concentration of immune anti-A or anti-B agglutinins greater than 1 : 16 in a group-O donor's serum must be regarded as significant, since this titre is the highest that can be expected to be rendered innocuous by dilution in the recipient's blood-stream. They recommend the use of a routine screening test based on partial absorption with group-specific substances followed by an indirect anti-globulin (Coombs) test. This is an elaborate procedure for a busy laboratory to apply to all bottles of group-O blood. In our experience serious reactions following the transfusion of group-O blood are not sufficiently common to justify the increased labour and materials involved in adopting this test, especially when economy has to be considered.

Crawford et al. (1952) suggest that among the various "immune" characteristics of anti-sera their ability to

lyse A or B cells in vitro gives a good indication of their potential lytic power in vivo. They therefore conclude that a routine haemolysin test would be valuable as a screening procedure for the selection of group-O blood, but that this would be a troublesome laboratory procedure. As an alternative, and because of the high incidence of immune anti-A antibodies in persons recently inoculated, they recommend that it would be a wise precaution to refuse as donors all people who have received an injection of any vaccine or animal serum during the previous three months.

When investigating samples of serum from expectant mothers for anti-A and anti-B haemolysins we observed that sera containing the strongest haemolysins would haemolyse group-A₁ or group-B cells during the course of the routine check for anti-A and anti-B agglutinins and without the addition of complement. Crawford et al. (1952) have shown that most group-O sera containing anti-A haemolysins contain also immune anti-A agglutinins.

An investigation was therefore undertaken to determine whether, if the routine test for anti-A and anti-B saline agglutinins used by all major blood-banks were extended to include a check for haemolytic activity, most of the bloods containing a significant concentration of immune anti-A or anti-B antibodies, agglutinins as well as haemolysins, could be detected. We describe here the results of this investigation, which shows that a simple screening test for anti-A and anti-B haemolysins, involving a blood-bank laboratory in little additional labour and no additional materials, will detect most group-O bloods containing a significant concentration of immune anti-A or anti-B antibodies.

Methods

DETECTION OF HAEMOLYSINS

Within twenty-four hours of collecting the blood, one volume of the serum under investigation was placed into each of three tubes measuring $3 \times \frac{1}{8}$ in. and standing in three rows in a metal rack. To each tube was added one volume of a 5% suspension in saline solution of red cells of groups A₁, B, and O respectively. The O cells were included as a control. The tubes were left to stand for an hour at room-temperature (18°C) and, after naked-eye examination of the sera for anti-A and anti-B agglutinins, were placed (in their racks) in an incubator at 37°C for a further hour. Each rack was next held before a source of light and, with the minimum of disturbance, the supernatant fluid in each tube was scrutinised for haemolysis. The results were recorded as follows :

Complete haemolysis,	+++
75% haemolysis,	++
50% haemolysis,	++
25% haemolysis,	+
Trace of haemolysis, tr.	
No trace of haemolysis, 0.	

It was found subsequently that the haemolysins detected could be divided into two groups : "strong," embracing ++++, ++, and +++; and "weak," embracing + and tr., and this grouping has been adopted in classifying the results.

In tests involving the addition of fresh serum to provide complement a single group-O donor was used whose serum contained weak anti-A and anti-B agglutinins and no haemolysins. Equal volumes of test serum, cell suspension, and fresh serum were used in the test. Contrary to the recommendation of Crawford et al. (1952), suspending the A₁ cells in fresh A serum was found to be unsatisfactory.

INDIRECT ANTI-GLOBULIN TESTS USING
"PARTIALLY NEUTRALISED" SERUM

The technique was essentially similar to that of Crawford et al. (1952), except that only one volume of A or B saliva was added to the serum under test, and group-O cells were included in the examination of each serum as a negative control. In reading the results

each test was examined for agglutination at intervals of two minutes, five minutes, and ten minutes after mixing the washed cells with an anti-globulin reagent on an opal tile, and the results were recorded as follows:

Cells agglutinated in uniform clumps, no free cells,	3
Cells agglutinated in small clumps, some free cells,	2
Weak agglutination, many free cells,	1
No agglutination, 0.	

By this method the strongest anti-globulin result could "score" 9 points ($3+3+3$) and the weakest 1 point ($0+0+1$), when readings were recorded at intervals of two, five, and ten minutes. To all sera giving negative results ($0+0+0$) was added one volume of red cells sensitised with Rh antibody. Unless the sensitised cells showed strong agglutination within two minutes of mixing, the indirect anti-globulin procedure was repeated on the group-O serum under examination to exclude a false negative reaction.

TITRATION OF SALINE AGGLUTININS

A direct dilution of the serum of 1/200 was made with physiological saline solution. One volume of this dilution was mixed with an equal volume of a 5% suspension of cells, and the mixtures were examined microscopically for agglutination after two hours at room-temperature. The reciprocal of the highest dilution which produced clumps of 8-12 cells was recorded as the titre of the serum.

Results

DETECTION OF HÆMOLYSINS

The sera from 1960 group-O blood-donors selected at random were examined by the methods described above for anti-A and anti-B hæmolsins. The results of these examinations are given in table I: 27 of the 29 sera containing anti-B hæmolsins also contained anti-A hæmolsins.

The technique used was selected so that, if it proved reliable, its adoption as a "screening test" would give a blood-bank the minimum of additional labour. The close correlation between the proportion of sera containing anti-A hæmolsins detected by this simple procedure (20·2%) and that detected by the more elaborate method used by Crawford et al. (1952) (18%) provides clear evidence that this technique is satisfactory in the detection of lytic sera.

Crawford et al. (1952) suggest that an anti-A serum which, diluted 1 in 4 in fresh serum, will not lyse group-A₁ cells after two hours' incubation at 37°C will not cause appreciable destruction of red cells when transfused to a group-A recipient. In the present investigation 70 of the sera found to contain anti-A hæmolsins were therefore examined by the technique proposed by Crawford et al. After two hours' incubation at 37°C 3 of the sera (4·3%), diluted 1 in 4 in fresh serum, had hæmolysed group-A₁ red cells, and 15 of the diluted sera (21·4%) showed a weak or partial hæmolysis of group-A₁ cells. Tested undiluted, and without the addition of fresh serum, by the procedure outlined above, these 18 sera all hæmolysed group-A₁ cells "strongly" at 37°C and at room-temperature. It may therefore be concluded

TABLE I—INCIDENCE OF ANTI-A AND ANTI-B HÆMOLYSINS IN RANDOM SAMPLE OF GROUP-O DONORS

Donors	No. of sera examined	No. of sera showing hæmolsins			
		Anti-A		Anti-B	
		Weak	Strong	Weak	Strong
H.M. Forces	819	93 (11·4%)	89 (10·8%)	7 (0·85%)	11 (1·3%)
Civilians ..	1141	133 (11·7%)	81 (7·1%)	7 (0·61%)	4 (0·35%)
Total ..	1960	226 (11·3%)	170 (8·7%)	14 (0·71%)	15 (0·76%)

that the type of anti-A₁ hæmolsin considered to be "significant" by Crawford et al. is readily detected by this simpler method.

The following further check was included, however, to confirm that it is not necessary to add fresh serum to detect significant hæmolsins: 153 sera, selected because most of the donors had recently received inoculations of T.A.B. vaccine, were examined for anti-A and anti-B hæmolsins within twenty-four hours of collection with and without the addition of fresh serum; 27 of the sera hæmolysed group-A cells strongly, and 48 weakly, without additional fresh serum; whereas after the addition of fresh compatible serum no further strong hæmolsins were detected, and an additional 12 sera showed only very weak hæmolytic activity.

Since it might not always prove practicable for a blood-bank to do the screening test for hæmolsins on the day following the collection of the blood, 60 sera found to contain strong anti-A hæmolsins were stored for three days at 4°C and then retested by the screening method against group-A₁ cells from the same donor. 12 of the sera were found now to possess only weak hæmolytic activity, and 1 serum which when fresh had shown 50% hæmolysis of group-A₁ cells did not now hæmolysed these cells. The addition of fresh serum from a group-O donor fully restored the hæmolytic power of all 13 sera. It is therefore evident that, when the screening test for hæmolsins cannot be completed within twenty-four hours of collecting the blood, fresh group-O serum containing weak agglutinins but not hæmolsins should be added to each test serum to provide complement.

TABLE II—INCIDENCE AND AVIDITY OF IMMUNE ANTI-A AGGLUTININS IN HÆMOLYSING AND NON-HÆMOLYSING GROUP-O DONOR BLOODS

Sera	No. tested	Total immune anti-A agglutinins	"Score" of anti-globulin reaction							
			0	1	2	3	4	5	6	7
<i>Hæmolysing :</i>										
Strong ..	196	144 (74%)	52	54	25	20	14	11	8	6
Weak ..	82	31 (38%)	51	17	10	3	1	0	0	0
Non-hæmolysing ..	690	55 (8%)	635	36	7	9	2	1	0	0

Finally, to determine whether group-A cells vary in their reactivity to anti-A hæmolsins, cell suspensions made from 23 bloods of group A₁ and 8 of group A₂ were tested against an anti-A serum containing a "strong" hæmolsin. The 23 group-A₁ cell suspensions were all hæmolysed strongly to about the same degree, but the 8 from A₂ cells showed a considerably weaker hæmolysis. Provided, therefore, that it is confirmed to be group-A₁, a cell suspension from any donor of this group may be used as test cells for the hæmolsin-screening test.

DETECTION OF IMMUNE AGGLUTININS

The above-mentioned results having shown that the routine test for anti-A and anti-B saline agglutinins could satisfactorily be extended as a test for the detection of significant hæmolsins in group-O donors, the following further investigations were undertaken to determine to what extent a hæmolsin test would also detect group-O bloods containing immune anti-A and anti-B agglutinins.

214 group-O sera containing "strong" hæmolsins (including many of those detected in the above series), 89 sera containing "weak" hæmolsins, and 1088 non-hæmolysing group-O sera were examined for immune anti-A and anti-B agglutinins by an indirect anti-globulin technique after "partial absorption." The results are recorded in tables II and III. The method of "scoring" the anti-globulin reactions was adopted as the most convenient way of indicating the strength of the reaction when many positive tests were being recorded.

TABLE III—INCIDENCE AND AVIDITY OF IMMUNE ANTI-B AGGLUTININS IN HEMOLYSING AND NON-HEMOLYSING GROUP-O DONOR BLOODS

Sera	No. tested	Total immune anti-B agglutinins	"Score" of anti-globulin reaction								
			0	1	2	3	4	5	6	7	8
Hemolyzing:											
Strong ..	18	11 (61%)	7	8	1	2	0	0	0	0	0
Weak ..	7	2 (29%)	5	1	1	0	0	0	0	0	0
Non-hemolyzing ..	398	16 (4%)	382	15	1	0	0	0	0	0	0

To enable a comparison to be made with the "screening test" of Grove-Rasmussen et al. (1953), 15 of the partially neutralised sera containing immune anti-A agglutinins were also examined at a final saline dilution of 1 in 16. These results are to be found in table IV and indicate that a serum giving a "score" of 4 or 5 by our method would have a concentration of immune agglutinins equivalent to 1 in 16 by the dilution method of Grove-Rasmussen et al.

It will be seen from table III that, in 423 sera examined, no immune anti-B agglutinins with a titre of 1 : 16 were detected. It may therefore be concluded that immune anti-B agglutinins are negligible as regards dangerous group-O blood. Consequently, a comparison has been made in table V of the incidence and strength of the immune anti-A agglutinins found in 196 group-O donor bloods containing "strong" haemolysins and 772 bloods lacking strong haemolysins. The results have been expressed in each case as a percentage incidence to enable a direct comparison to be made. Not only do they confirm the findings of Crawford et al. (1952) that immune anti-A agglutinins are most often found in association with anti-A haemolysins, but also they establish that the strongest immune agglutinins (concentration greater than 1 in 16) are confined to sera containing strong anti-A haemolysins. 10% of the 196 strongly lytic sera were found to contain immune anti-A agglutinins giving a score of 6 or more—i.e., a titre greater than 1 in 16.

Discussion

Since all the evidence published during the past five years supports the contention that the immune characteristics of a serum indicate its ability to destroy A or B cells in vivo after transfusion, it appears to be a wise precaution for all blood-banks to adopt a method for safeguarding the recipient from the possible harmful effects of a transfusion of group-O blood containing a significant concentration of immune anti-A and anti-B antibodies. The procedure we propose is that described above.

After the routine examination for saline anti-A and anti-B agglutinins the tubes containing the cell-serum mixture should be incubated for a further hour at 37°C, and the supernatant fluid should be examined for visible haemolysis. The bottle corresponding to any tube showing strong haemolysis should then be labelled to indicate that it should be transfused to only a group-O recipient. The tests for haemolysins should preferably be completed by

TABLE IV—CORRELATION BETWEEN "SCORE" OF INDIRECT ANTI-GLOBULIN REACTION AND TITRE OF IMMUNE ANTI-A AGGLUTININS (15 SERA)

No. of sera examined	Indirect anti-globulin "score"	Titre of immune anti-A agglutinins
2	3	< 16
1	4	< 16
2	4	16
2	5	16
4	6	> 16
3	8	> 16
1	9	> 16

the day following the collection of blood, the serum samples having been stored at 4°–6°C until the time of testing. If necessary the testing may be deferred up to seventy-two hours after the collection of blood, but in this event an equal volume of fresh compatible serum should be added to each test serum to provide complement. In the present investigation the strongest haemolysins showed complete haemolysis of group-A₁ cells at room-temperature, and it may therefore be concluded that a wide margin of safety is provided in the detection of haemolysins when the tests are made at 37°C.

Clinical and experimental investigations have not yet established whether the dangerous component of group-O blood is the haemolysin or the immune agglutinin. Whereas Crawford et al. (1952) suggest that an anti-A serum which, diluted 1 in 4 in fresh serum, does not lyse group-A₁ cells after two hours' incubation at 37°C will not cause a haemolytic reaction when transfused to a group-A recipient, Grove-Rasmussen et al. (1953) place reliance on the elimination of group-O bloods containing

TABLE V—INCIDENCE AND AVIDITY OF IMMUNE ANTI-A AGGLUTININS IN GROUP-O BLOODS SHOWING "STRONG" HEMOLYSINS AND "WEAK" HEMOLYSINS, EXPRESSED AS APPROXIMATE PERCENTAGE

Sera	No. tested	Percentage containing immune anti-A	"Score" of anti-globulin reaction								
			0	1	2	3	4	5	6	7	8
"Strong" hemolyzing	196	73.5	26.5	27.5	12.7	10.2	7.2	5.6	4.1	3.1	2.6
"Weak" or non-hemolyzing	772	11	89.0	6.8	2.2	1.5	0.37	0.13	0	0	0

immune anti-A agglutinins in a titre greater than 1 in 16. The present investigation has shown that by the adoption of our simple test for haemolysins both types of immune antibody will be detected when they are present in concentrations considered significant by Crawford et al. and Grove-Rasmussen et al. Whereas none of 772 group-O bloods lacking potent haemolysins contained immune anti-A agglutinins in a concentration greater than 1 in 16, 20 of 196 sera which haemolysed group-A₁ cells strongly—i.e., about 10%—showed a titre of immune anti-A agglutinins greater than 1 in 16.

Not only is the proposed test for haemolysins technically simpler than the indirect anti-globulin technique of Grove-Rasmussen et al. but also, if the haemolytic property of a serum in vitro proves to be a sound indicator of its potential lytic power in vivo, nearly 80% of sera containing strong haemolysins do not give a positive indirect anti-globulin test when tested at a dilution of 1 in 16 ("score" of less than 4, table V) and will therefore pass undetected when an anti-globulin test on diluted serum is applied as the screening procedure. Our investigations suggest that 1 in 6 of these sera may contain haemolysins which are still active when diluted 1 in 4 with fresh serum.

Crawford et al. (1952) suggest that it would be a wise precaution to refuse as donors all persons who had received an injection of a vaccine or animal serum during the previous three months. Because of the regular inoculations given to members of the Armed Services, however, the organisation of visits of blood-collecting units to Service stations would become gravely over-complex and probably very seriously jeopardised if this recommendation were adopted. Moreover of 70 Service donors whose serum contained strong haemolysins when

examined by us 17 (nearly 25%) had received inoculations more than three months before they gave their blood.

Some blood-banks regard a titre of saline anti-A and anti-B agglutinins greater than 1 : 200 as the criterion for dangerous group-O blood, based on published reports of haemolytic reactions following the transfusion of blood containing such agglutinins in high titre. In the present investigation the association between high-titre saline anti-A agglutinins, anti-A haemolysins, and immune anti-A agglutinins was studied. The results, given in table VI, show that saline anti-A agglutinins in a titre

TABLE VI—ASSOCIATION BETWEEN HIGH-TITRE SALINE AGGLUTININS, ANTI-A HEMOLYSINS, AND IMMUNE ANTI-A AGGLUTININS

	Hæmolyzing anti-A sera	Non-hæmolyzing anti-A sera
No. tested	226	861
No. showing high-titre saline anti-A*	21 (9.3%)	38 (4.4%)
Proportion of high-titre saline antibodies containing immune anti-A	18 : 21 (86%)	7 : 38 (18.4%)

* Titre greater than 1 : 200.

greater than 1 : 200 were found twice as often in group-O bloods containing anti-A haemolysins as in non-hæmolyzing bloods. Furthermore, when high-titre saline agglutinins were present, 86% of the hæmolyzing-containing group-O bloods contained immune anti-A agglutinins. Possibly, therefore, if the group-O bloods associated with the haemolytic transfusion reactions and containing high-titre saline agglutinins had been examined for anti-A haemolysins and immune anti-A agglutinins, these would have been found and might have been the true cause of the reactions. Grove-Rasmussen et al. (1953) have given details of a haemolytic reaction in a group-A patient resulting from the transfusion of group-O blood containing strong anti-A haemolysins and immune anti-A agglutinins, but the titre of saline anti-A agglutinins was only 1 : 64. It therefore seems to us that, though there may not yet be sufficient evidence for abandoning a screening test for high-titre saline agglutinins in group-O bloods, the adoption by blood-banks of the simple test here described for the detection of haemolysins may provide for the greater safety of the patient who has to receive an emergency transfusion of group-O blood.

Summary

Samples of serum from 1960 group-O donors taken at random were examined within twenty-four hours of collecting the blood by a simple screening test, and 185 (9.4%) were found to contain strong anti-A or anti-B haemolysins.

Whereas 10% of group-O sera containing strong anti-A haemolysins contained also immune anti-A agglutinins in a titre greater than 1 in 16, no immune agglutinins in this concentration were found in 772 group-O sera lacking strong hæmolyzing.

It is therefore recommended that blood-banks adopt this simple test for haemolysins as a screening procedure for group-O donors, since its routine use could ensure that group-O blood containing haemolysins or immune agglutinins (anti-A or anti-B) in high concentration is transfused only to patients known to belong to group O.

We are very grateful to Dr. W. d'A. Maycock for helpful comments and suggestions; and to Mr. H. N. Thomas, Mr. E. M. Day, and other members of the laboratory staff of the South-Western Regional Transfusion Service for their valuable technical assistance.

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BLOOD-AMMONIA LEVELS IN RELATION TO HEPATIC COMA AND THE ADMINISTRATION OF GLUTAMIC ACID

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In 1927 Burchi noted raised blood-ammonia levels in cirrhosis of the liver. Van Caulaert and Deviller (1932) and Fuld (1933) reported that in some patients with cirrhosis the administration of certain ammonium salts led to drowsiness, convulsions, coma, and delirium, and that these symptoms were associated with high blood-ammonia levels. Experimentally Monguió and Krause (1934) showed much the same in dogs with Eck fistulae, when extremely high blood-ammonia levels were found; and, since the symptoms were similar to those seen in Eck-fistula dogs on a protein-rich diet, they concluded that meat intoxication was an ammonia intoxication.

Kirk (1936), using a somewhat more accurate method of determining ammonia, reported abnormal blood-ammonia levels after the administration of ammonium salts in 23 of 28 patients with hepatic cirrhosis. Delirium and convulsions were never seen, however, even when the levels were high. Only 3 patients became semi-comatose after the administration of ammonium salts, and no symptoms developed in the patients with the highest blood-ammonia. Kirk noted that in acute hepatitis and obstructive jaundice the blood-ammonia was normal. From these observations he concluded

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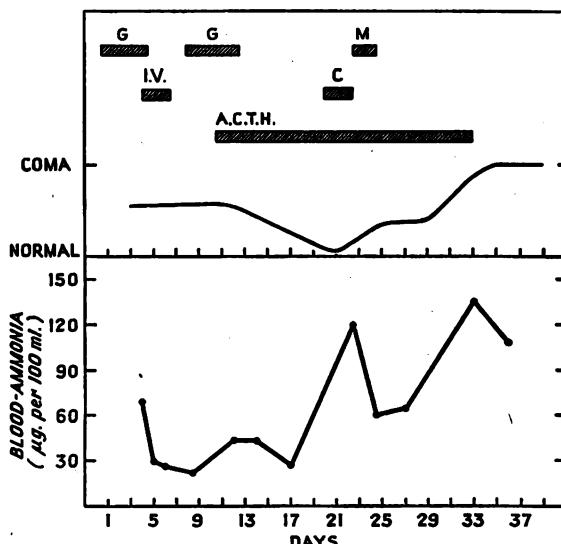


Fig. 1—Blood-ammonia levels, degree of consciousness, and effect of therapy in case I: A.C.T.H., corticotrophin (25 mg. four times daily); C, choline 10 g. by mouth daily; G, glutamic acid 20 g. by mouth daily; I.V., sodium glutamate 23 g. intravenously over four hours daily; M, methionine 10 g. by mouth daily.

TABLE I—BLOOD FINDINGS AND LIVER-FUNCTION TESTS IN TWELVE PATIENTS WITH HEPATIC CIRRHOSIS

Sex	Age (yr.)	Ammonia nitrogen (μg. per 100 ml.)	Glutamine (mg. per 100 ml.)	Albumin (g. per 100 ml.)	Globulin	Free cholesterol (mg. per 100 ml.)	Ester cholesterol (mg. per 100 ml.)	Alkaline phosphatase (Kling-Armstrong units)	Bilirubin (mg. per 100 ml.)	Cephalin cholesterol	Thymol turbidity (units)	Colloidal gold *	Remarks
F	61	69	6.1	3.7	2.3	76	134	7.7	Neg.	+	1.0	2	Necropsy
F	23	111	8.25	3.3	2.8	93	117	11.5	0.5	+++	4.0	3	Biopsy
M	47	60	6.95	2.6	3.6	98	150	8.5	2.2	+++	3.0	3	Biopsy
M	53	68	4.8	3.4	4.6	66	106	10.8	2.3	++	8.0	5	..
M	45	75	7.8	2.9	3.1	108	64	21.5	1.1	++	6.0	5	..
F	69	100	8.0	2.6	2.2	69	70	45.0	3.4	++	5.0	2	..
M	57	58	8.0	2.8	3.4	119	75	14.4	2.6	++	19.0	5	Necropsy
M	47	45	6.2	3.0	1.9	100	132	4.4	3.7	++	3.0	2	..
F	46	112	8.6	3.0	4.2	83	82	17.7	2.3	+	3.0	4	..
M	69	35	4.5	2.3	2.3	76	125	7.8	3.2	+	5.0	3	Biopsy
M	40	30	8.5	4.2	3.8	75	200	61.0	1.1	Neg.	6.0	3	Biopsy
F	51	60	6.24	3.6	3.7	76	44	12.9	1.4	++	6.0	5	Biopsy

* 0 = no flocculation; 5 = complete flocculation.

that raised blood-ammonia levels in hepatic cirrhosis were due not to functional impairment of the liver but to abnormal anastomoses between the portal vein and the inferior vena cava.

Recently, Phillips et al. (1952) again questioned the significance of blood-ammonia and its relation to hepatic coma, since they had observed ill effects after the administration of urea to some of their patients. Walshe (1951) suggested that a high level of intracellular

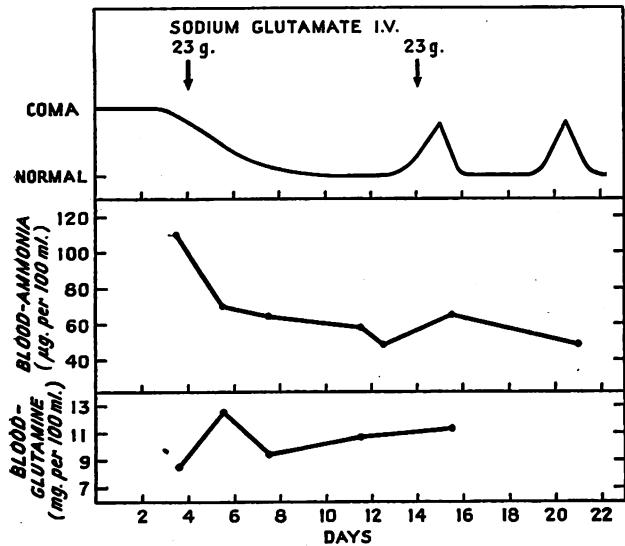


Fig. 2—Blood-ammonia levels, degree of consciousness, and intravenous administration of glutamic acid in case 3.

ammonia was a possible cause of hepatic coma. Subsequently he suggested that the administration of glutamic acid might lead to the formation of glutamine, neutralise the free ammonia, and consequently cure the coma. By this therapy he obtained satisfactory results in 3 patients (Walshe 1953). Woodrow et al. (1953) have also reported favourably on this treatment.

We present here further evidence in support of the views put forward by Kirk (1936) and discuss the effect of the administration of glutamic acid on the blood-ammonia.

Methods

Blood-ammonia levels were determined by the micro-diffusion method described by Conway (1935) and modified by Conway and Cooke (1939), and were expressed as ammonia nitrogen in $\mu\text{g.}$ per 100 ml. Special precautions to ensure that the syringes were used at a low temperature and contained carbon dioxide were important to obtain consistent results. Precautions were also taken to ensure that the laboratory in which the levels were determined was not only free from ammonia vapours but also from volatile acids. The estimations were made within ten minutes of withdrawal of the blood. The error entailed in collecting the specimens

was less than 10%. The error of the method on standard ammonia samples was less than 7% of the mean.

Blood-glutamine levels were determined by the method of Harris (1943). Whole blood was used throughout, but in some patients the glutamine level was determined in both plasma and blood. The plasma-glutamine level was approximately 0.5 mg. per 100 ml. lower than the level in whole blood.

Control blood samples were collected from the antecubital fossae of healthy people; from patients undergoing routine cardiac catheterisation for the assessment of rheumatic and congenital heart-disease; from patients with hepatic cirrhosis (diagnoses based on liver-function tests, biopsy, or subsequent necropsy findings, or strong clinical and radiological evidence); from the caput medusae of 2 patients; and from the hepatic and renal veins by catheterisation in 1 other patient.

Results

Blood-ammonia

The mean level in 34 observations in 23 controls was 10.6 (s.d. 3.15, range 2.0–20.0) $\mu\text{g.}$ of ammonia nitrogen per 100 ml. The levels found in 12 successive patients with cirrhosis of liver, together with the relevant liver-function tests, are given in table I. They range from 30 $\mu\text{g.}$ to 105 $\mu\text{g.}$ per 100 ml.

The highest level was found in a patient who is subjectively well and working and who has previously been reported (Whitfield and Arnott 1951, case 3). Other high levels were found in patients apparently well, and there appeared to be no direct clinical correlation between the blood-ammonia and the clinical state, as has been noted by Schwartz et al. (1953) and Kirk (1936).

A high level of 95 $\mu\text{g.}$ of ammonia nitrogen per 100 ml. was found in a man, aged 56, with hepatic cirrhosis who had undergone portacaval anastomosis for portal hypertension ten months previously. He was well and working. In 1 patient with severe infective hepatitis and grossly abnormal liver-function tests blood-ammonia levels of 8.18 $\mu\text{g.}$ per 100 ml. were found, and in 2 patients with obstructive jaundice levels of 15 $\mu\text{g.}$ and 18 $\mu\text{g.}$ were found.

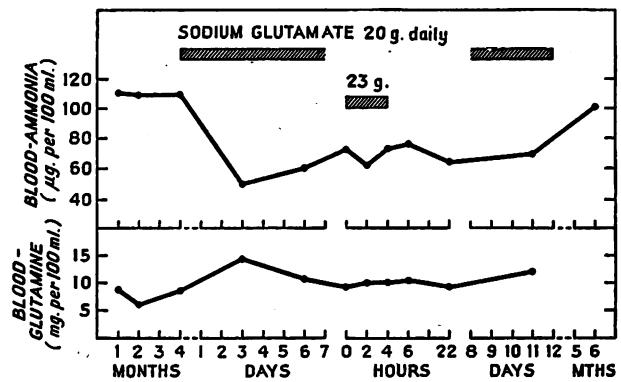


Fig. 3—Effect of admission to hospital and of treatment with oral and intravenous glutamic acid on blood-ammonia levels in case 4.

TABLE II—BLOOD-AMMONIA LEVELS FROM DIFFERENT SITES

Source	Ammonia nitrogen (μg. per 100 ml.)											
	Ante-cubital vein	Right auricle	Pulmonary artery	Hepatic vein	Renal vein	Inferior vena cava below renal vein	Inferior vena cava above renal vein	Superior vena cava	Brachial artery	Caput medusae	Ascitic fluid	
Case 4	95	100	..	71	80	151	107
Case 5	46	68/74	48
Case 6	35	70	..
Cardiac catheterisation :												
1	28	..	26	23	..
2	30	23	..
3	15	80
4	18	23	32	37	32
5	18	16
6	17	18
7	20	..	35	25
8
9
10
11	18/23
									19/22	10	26/28	..
									8/10

Effect of Glutamic Acid on Hepatic Coma and Blood-ammonia

The effects of the administration of sodium glutamate in doses of 23 g. intravenously over four hours, or of 20 g. daily by mouth are shown in figs. 1-3.

Case 1 (fig. 1).—A woman, aged 63, with multilobular hepatic cirrhosis of unknown aetiology showed no real clinical response, though the blood-ammonia levels appeared to fall. Clinical improvement temporarily followed the administration of corticotrophin given partly to counteract the high serum-potassium and low serum-sodium levels. Deterioration set in rapidly, coincidentally with the administration of choline and methionine. The blood-ammonia levels showed the clinical course of this patient.

Case 2.—A brewer and publican, aged 58, with multilobular hepatic cirrhosis came under observation with abdominal pain and vomiting. After the loss of electrolyte fluid had been corrected, he remained semicomatose. His blood-ammonia level was 55-68 μg. per 100 ml. Administration of intravenous glutamic acid had no significant clinical effect, but two days later the blood-ammonia was 45 μg. per 100 ml. The patient went steadily downhill and died.

Case 3.—A woman, aged 46, with progressive jaundice and ascites and known hepatomegaly and splenomegaly of two years' duration, had haematemesis and went into coma. On the fourth day, when she was showing some signs of returning consciousness, the administration of sodium glutamate was followed by a rapid improvement back to normal levels of consciousness. Her clinical course is illustrated in fig. 2. A further episode of increasing coma was rapidly relieved by glutamate without any noteworthy effect on the blood-ammonia levels. A third episode of coma righted itself without administration of glutamic acid.

Case 4.—A woman, aged 25, previously reported by Whitfield and Arnott (1951), entered hospital to determine whether oral or intravenous glutamic acid would make any difference to her clinical status. Since this patient had been in hepatic coma she had maintained satisfactory health and had had no diarrhoea so long as she took capsules of animal protein factor ('A.P.F.' Lederle) or their equivalent, aureomycin 0.25 g., and vitamin B₁₂ 200 μg. by mouth daily. The blood-ammonia levels and the effects of therapy are shown in fig. 3.

Catheterisation Findings

The blood-ammonia levels in blood obtained by catheterisation of the cardiac controls are shown in table II. The levels in blood obtained by catheterisation of renal veins were only slightly higher than those obtained from the liver and from mixed venous blood. The levels found in the patients with cirrhosis showed, however, that the liver was not always an efficient barrier. In case 4 high blood-ammonia levels were found in blood from the hepatic vein (table II). In cases 5 and 6 raised blood-ammonia levels were also found in blood from the caput medusae.

Blood-glutamine

The mean blood-glutamine levels in 19 healthy controls (27 observations) were 6.67 (s.d. 2.5) mg. per 100 ml.

The mean levels in 10 patients with cirrhosis were 7.15 (s.d. 1.2) mg. per 100 ml. There was no significant difference between these two groups. After the administration of intravenous sodium glutamate the blood-glutamine levels showed some increase, but these observations are insufficient to determine whether the increase is significantly outside the experimental error of the method.

Discussion

As a result of these observations it was concluded that glutamic acid may have had some effect on the blood-ammonia levels initially but did not restore them to normal. It was therefore evident that any clinical effect that glutamic acid might have was not due solely to any effect exerted on the blood-ammonia. It might also be concluded that the main source of ammonia is in the intestinal tract, as has been shown by Parnas and Klisiecki (1926). Normally this ammonia is effectively neutralised by the liver-cells. In case 4, possibly as the result of increased portal pressure, much of the blood normally passing up the portal vein is redirected back through the inferior vena cava and hence bypasses the liver-cells. It is, however, evident that blood-ammonia levels in the hepatic vein are excessively high, and that those in the inferior vena cava bear much the same relation to those in the peripheral veins as did those in the blood from the caput medusae in cases 5 and 6. A possible explanation may be in the direct shunting from portal vein to vena cava through the hepatic veins in seriously damaged livers. This is supported by the high levels in the patient with a portacaval anastomosis. Our evidence, such as it is, best fits the hypothesis put forward by Kirk (1936) that the blood-ammonia is more an indicator of the extent of collateral circulation than of cellular dysfunction. For the present we regard the blood-ammonia level in hepatic damage in much the same light as the blood-urea level in chronic renal damage; neither should be regarded as the actual cause of the clinical symptoms, but a raised level of either is evidence of the existence of a grave state of affairs in the respective organ.

Summary

The mean normal blood-ammonia level was found to be 10.16 ± 3.15 μg. of ammonia nitrogen per 100 ml.

Higher levels outside the range of normal were found in patients with cirrhosis of liver but did not necessarily bear any relation to their clinical condition.

The administration of glutamic acid, either intravenously or orally, did not restore the blood-ammonia levels to normal in patients with hepatic cirrhosis.

The blood-ammonia level may indicate the extent of anastomotic circulation between the portal system and the inferior vena cava rather than the amount of damage sustained by the liver-cells.

We are greatly indebted to physicians of the Queen Elizabeth Hospital for facilities to investigate their patients. We wish to thank also Dr. K. W. Donald, Dr. O. L. Wade, and Dr. J. M. Bishop for providing the samples obtained by catheterisation and Mr. Garfield Thomas for the liver-function tests.

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INTRAJEJUNAL DRIP IN GASTRIC SURGERY

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THE sodium, chloride, potassium, and water imbalance following major surgery, especially gastric surgery with its preoperative and postoperative complications due to pyloric stenosis, gastric suction, oedema of stoma, and intravenous infusions, has prompted me to record the advantages of intrajejunal instead of intravenous and rectal feeding.

The disadvantages of intravenous and rectal infusions, in order of importance, are as follows :

(1) In many respects such infusions are difficult to control, especially in a peripheral hospital with shortage of medical and laboratory staff, who are always overworked.

(2) For the same reason potassium therapy is too dangerous.

(3) Both methods are uncomfortable for the patient because they require otherwise unnecessary immobilisation, and the intravenous route is likely to cause painful phlebitis and, occasionally, prolonged discomfort during convalescence. The house-surgeons' and nurses' time is also wastefully used when several such cases are in the wards at the same time.

(4) The use of specially prepared intravenous solutions is expensive.

An intrajejunal drip, given through fine 'Polythene' tubing by the technique described below, circumvents all these disadvantages and has the following advantages :

(1) The tube can be used at any time and disconnected at night or when the patient is up and about.

(2) The patient can be given water, protein, carbohydrate, vitamins, sodium, potassium, and chloride in optimal quantities from the first postoperative day. There is very much less danger of overdosage of sodium, potassium, or chloride. The tube can be used for as long as it is necessary—i.e., until normal oral feeding can be safely resumed—after which it is simply pulled out.

(3) All gastric aspirations with their important electrolytic content, which would otherwise be lost, can be returned to the alimentary tract through the jejunal tube.

I have been most impressed by the comparative comfort and rapid convalescence of the patient and the obvious easing of the staff work during the postoperative phase of seventy-five gastrectomy patients on whom I have used this technique. Its advantages after the Billroth 1 operation are particularly satisfying.

Technique

The insertion of the tube at the completion of the operation adds but ten minutes to the operation time.

A loop of jejunum some 12 inches from the new gastrojejunostomy stoma (or, in the case of a Billroth 1 technique, from the duodenojejunal junction) is picked up, and a point on the antimesenteric border fixed between two pairs of lightly applied tissue forceps. A small hole into the lumen is made between these forceps, and a metal sheath, loaded almost to the tip with gauge-53 polythene tubing 36 inches in length, is pushed distally down the jejunum, the bowel at the same time being "concertina-ed" generously over the sheath. I have been using a Milton's bladder evacuator size 6 (Down Bros.), but doubtless a sheath with a small ball tip could be manufactured for this purpose.

The polythene tube is now pushed so that it projects 1 inch beyond the tip of the sheath, and is grasped firmly through the wall of the bowel while the sheath is withdrawn entirely.

The "concertina-ed" jejunum is next pulled up over the polythene tubing, which is still grasped firmly at its distal end. In this way at least 12 inches of tube is pulled down into the jejunal lumen distal to the aperture by which it enters, and this part of the bowel with its contained tube is returned to the abdominal cavity.

A purse-string suture is used to close the aperture snugly round the polythene tube, and this and some 3 or 4 inches of tube is buried in the wall of the proximal jejunum by the usual Witzel technique with a small curvedatraumatic continuous suture.

After this suture has been tied, the looped and single ends of the knot are left uncut, and the looped end, grasped in a haemostat, is used to support the bowel and stoma while a small trocar and cannula are driven through the abdominal wall into a suitable cup-shaped guard applied to the parietal peritoneum to the left of the abdominal laparotomy wound. The free end of the polythene tube is next threaded through the cannula, which is then withdrawn.

The single end of the uncut atraumatic suture is next used to take alternate bites round the jejunal and parietal peritoneum encircling the emerging polythene tube, and is drawn tight to bring the jejunum up to the abdominal wall and knotted to the loop previously left uncut. This will prevent any risk of the slippery tubing coming out and leaking into the intraperitoneal cavity and is an essential part of the procedure.

The abdomen having been closed, a rolled gauze swab encircling a double strand of nylon is fixed close to the cutaneous stoma by another double nylon stitch, which takes a deep bite of abdominal skin and is tied first round the centre of the roll and then round the polythene tube.

The tube is next made to coil round the gauze roll on alternate sides of the centre anchoring suture some four or five times and then threaded underneath the roll of these coils. The ends of the first double nylon thread are tied together so that the gauze roll loops over the coils in a complete circle and prevents them from slipping off its ends and becoming uncoiled. This method of fixing the tube is secure and has never yet failed.

It is wise to have an intravenous drip during the operation and until the first postoperative morning for anaesthetics and any drugs or blood that may be necessary in this period. From then onwards the jejunal drip alone is used to supply the patient with all necessary fluids, gastric aspirations, vitamins, food (as citrated milk, protein hydrolysates, and glucose), and electrolytes (as sodium, potassium, and chloride) until the fluid-balance chart indicates that oral feeding may be permanently resumed.

This method has been used with success preoperatively in two cases with pyloric stenosis—one with complete duodenal stenosis following repair of a huge perforated ulcer in a contracted duodenum.

URINARY EXCRETION OF ADRENOCORTICAL STEROIDS BY PATIENTS RECEIVING SALICYLATES

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It has been suggested that salicylates act in rheumatic fever by stimulating the adrenal cortex via the anterior lobe of the pituitary to produce adrenocortical steroids, which are considered to be the active agents in the therapy. Many reports have been published comparing the effects of salicylates and of either corticotrophin or cortisone in laboratory animals and in man, and these have been reviewed by Hailman (1952), Smith (1953), and Marson (1953). Although some of the evidence appears to support the hypothesis, certain results are conflicting, and a considerable number of dissimilar effects of the two groups of drugs have been recorded.

Comparison of the effects of salicylates and of either corticotrophin or cortisone in man, particularly in patients with rheumatic disease, provides the most critical data for or against the hypothesis. Van Cauwenberge and Heusghem (1951) claimed that therapy with acetylsalicylic acid caused an increased urinary excretion of reducing steroids, and that this increase corresponded with clinical improvement. However, West (1953) found no increase in the output of 17-ketogenic steroids in adults receiving gr. 80 of salicylate daily, and Bayliss (1953) stated that no change in the level of 17-hydroxycorticosteroids in the plasma was found in people receiving salicylates except in some cases when the dosage reached toxic levels.

We have investigated the urinary excretion of adrenocortical steroids, in patients receiving salicylates, by a paper chromatographic method which enabled separate estimations of Compound E, Compound F, and tetra-

hydrocortisone to be made. A preliminary account of this work was communicated to a meeting of the Society for Endocrinology in December, 1953.

Experimental

Analytical Methods

Urinary adrenocortical steroids were measured in 24-hr. specimens of urine by the method of de Courcy et al. (1953) and plasma-salicylate levels by the method of Smith and Talbot (1950).

Material

Estimations were made on three female patients, aged 18, 22, and 27, with rheumatic fever, and a fourth, aged 56, with rheumatoid arthritis, and on a male, aged 32, with rheumatoid arthritis. In each case the patient was treated with four-hourly doses of sodium salicylate, a total of gr. 150-200 daily being given. In the first three females the urinary adrenocortical steroids were measured on several occasions during and after treatment with salicylate. In the remaining two patients they were serially determined before, during, and after salicylate therapy, and also during the subsequent administration of corticotrophin (40 units of 'Acthar gel,' Armour) on two consecutive days.

Results

The mean urinary excretion of adrenocortical steroids in the three females during and after the administration of salicylates are given in table I.

The results show that, when the salicylates were being given, the urinary excretion of adrenocortical steroids did not exceed the normal range; and, when the salicylates were stopped, there was no decrease in the excretion of the steroids.

Table II shows the results from the male patient with rheumatoid arthritis who was treated with salicylates and later with corticotrophin. The plasma-salicylate levels during salicylate therapy were 30-39 mg. per 100 ml.; plasma-salicylate levels of 30-40 mg. per 100 ml. are usually considered to be adequate for effective treatment (Reid 1948). During treatment the patient showed definite signs of salicylism—i.e., tinnitus, nausea, vomiting, and hyperventilation—and on day 6 his alkali reserve was 38 vols. per 100 ml. The results show that the administration of salicylates caused no increase in the urinary excretion of adrenocortical steroids, but that the subsequent administration of corticotrophin caused a considerable increase. Similar results (table III) were observed with the female patient

TABLE I—URINARY EXCRETION OF ADRENOCORTICAL STEROIDS IN THREE FEMALE RHEUMATIC FEVER PATIENTS DURING AND AFTER TREATMENT WITH SODIUM SALICYLATE (GR. 150-200 DAILY)

(Results are given as means and ranges)

Case no.	—	No. of observations	Adrenocortical steroids (μg. per 24 hr.)					
			Free			Glucuronides		
			Compound E	Compound F	X ₄	X ₄	Tetrahydro E	Unidentified reducing steroids
1	On salicylates	3	80 60-100	50 32-80	80 40-120	580 0-1600	750 640-800	480 400-560
	Off salicylates	5	75 60-100	60 20-80	82 32-120	720 0-1600	1150 240-2000	700 320-1760
2	On salicylates	4	40 20-60	5 0-10	30 20-60	210 40-400	320 200-400	120 40-200
	Off salicylates	2	60 40-80	2.5 0-5	30 30	230 20-240	360 320-400	120 40-200
3	On salicylates	3	95 60-120	60 20-80	70 40-120	810 40-1600	800 200-2000	520 60-1000
	Off salicylates	4	100 60-120	60 40-80	120 100-320	100 40-240	1000 400-2000	400 200-800
Normal range			30-110	10-180	10-320	10-4000	160-4000	0-2200

X₄ and X₄ are unidentified Δ⁴-3-ketosteroids with Rf values of 0.24 and 0.39 in a benzene/50% methanol system (de Courcy et al. 1953).

who, in addition to rheumatoid arthritis, had mild diabetes and a high initial rate of urinary excretion of adrenocortical steroids.

Discussion

The results are in striking contrast to those of Van Cauwenberge and Heusghem (1951), who used the method of Heard et al. (1946) for estimating neutral lipide-soluble reducing steroids in urine. It is possible that salicylates cause an increased urinary excretion of some neutral lipide-soluble reducing steroid which is not estimated in our method. An alternative explanation is that metabolites of salicylate may have been measured. Alpen et al. (1951) have shown that in man 15-40% of ingested salicylate is excreted as conjugated glucuronides. In one type of glucuronide the salicylic acid is linked by its —COOH group to the glucuronic acid, and such a compound may possibly be extracted and cause reduction of the final phosphomolybdate reagent in the method of Heard et al.

The finding that salicylates in full therapeutic dosage did not increase the urinary excretion of adrenocortical steroids such as Compounds E and F and tetrahydrocortisone, whereas in two patients the subsequent administration of corticotrophin caused a large increase, is strongly against the hypothesis that the therapeutic

TABLE II.—URINARY EXCRETION OF ADRENOCORTICAL STEROIDS IN MALE RHEUMATOID ARTHRITIC PATIENT TREATED WITH SODIUM SALICYLATE AND CORTICOTROPHIN

Treatment	Day	Adrenocortical steroids (μg. per 24 hr.)						
		Free			Glucuronides			
		Compound E	Compound F	X ₄	X ₅	Tetrahydro E	Unidentified reducing steroids	Plasma salicylate (mg. per 100 ml.)
None ..	1	100	32	32	0	640	320	—
" ..	2	120	20	20	0	640	240	—
Sodium salicylate gr. 200 per 24 hr. on days 3-8	4	100	20	32	120	800	320	33
	6	32	20	20	160	320	520	39
	7	80	20	60	160	480	560	30
None ..	13	100	10	32	0	400	720	—
" ..	14	80	10	32	0	480	800	—
Corticotrophin 40 units on day 15	16	640	1280	130	0	2560	5760	—
Normal range ..		20-200	10-80	20-120	0-200	240-3000	0-1500	

activity of salicylates is mediated by the anterior lobe of the pituitary and the adrenal cortex.

Other effects of salicylate which are independent of adrenal cortical stimulation via the anterior lobe of the pituitary are the anti-inflammatory action of salicylate observed in the tissues of hypophysectomised animals (Ungar et al. 1952) and the uricosuric effect of salicylates in a patient with severe Simmonds's disease, particularly since this was much greater than that of corticotrophin in the same patient (Marson 1953). Opposite actions of corticotrophin or cortisone and of salicylates on the glycosuria and blood-glucose levels of diabetic animals have been described (Ingle 1950, Smith et al. 1952), and Smith (1952a) has shown that salicylate antagonised the effects of cortisone in depositing liver glycogen in adrenalectomised rats, and in causing glycosuria and hyperglycaemia in normal rats fed on a high-carbohydrate diet.

Conflicting results have been obtained by workers who have studied the effects of salicylate on experimental

TABLE III.—URINARY EXCRETION OF ADRENOCORTICAL STEROIDS IN FEMALE RHEUMATOID ARTHRITIC PATIENT TREATED WITH SODIUM SALICYLATE AND CORTICOTROPHIN

Treatment	Day	Adrenocortical steroids (μg. per 24 hr.)						
		Free			Glucuronides			
		Compound E	Compound F	X ₄	X ₅	Tetrahydro E	Unidentified reducing steroids	Plasma salicylate (mg. per 100 ml.)
None ..	1	80	160	160	1000	640	1000	—
" ..	2	120	240	240	3200	2400	1400	—
Sodium salicylate gr. 150 per 24 hr. on days 3-8	4	80	60	60	160	2000	1200	28
	5	80	40	20	80	2000	1200	38
	8	60	20	20	80	1600	1200	39
None ..	12	100	40	40	80	2000	2000	—
" ..	14	60	40	40	20	1200	1000	—
Corticotrophin 40 units on days 16 and 17	16	160	400	40	1600	3200	6400	—
	17	480	2000	320	1300	16,000	20,000	—
Normal range ..		30-110	10-180	10-320	10-4000	160-4000	0-2200	

systems widely used as indices of adrenocortical function—e.g., eosinophil depression in man (cf. Marson 1953)—and the specificity of salicylate in causing adrenal ascorbic-acid depletion in laboratory animals (cf. Smith 1952b).

We must conclude that, although there are some similarities in the metabolic and clinical effects of salicylates and of corticotrophin and cortisone, the differences are such that the hypothesis that the therapeutic activity of salicylate in rheumatic diseases depends on the intermediary production of corticotrophin is untenable.

Summary

The urinary excretion of adrenocortical steroids has been measured by a specific paper chromatographic method in rheumatic patients receiving salicylate therapy.

Salicylates did not cause an increased excretion of adrenocortical steroids, but a large increase was observed during the subsequent administration of corticotrophin to two of the patients.

The hypothesis that salicylates exert their therapeutic activity in rheumatic diseases by stimulating the anterior lobe of the pituitary and the adrenal cortex is unacceptable.

We wish to thank Dr. R. D. Lawrence for making beds available, and Dr. K. J. Gurling and the nurses of the diabetic wing, King's College Hospital, for their help with the patients.

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SALICYLATES AND THE PLASMA LEVEL OF ADRENAL STEROIDS

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THE arthralgia and pyrexia of acute rheumatic fever are reduced by salicylates and by cortisone. Cochran et al. (1950) report that a patient with rheumatic fever treated with salicylates developed features which they considered similar to those found in Cushing's syndrome. It has therefore been suggested that salicylates act as antirheumatic agents by increasing the secretion of adrenocortical steroids either by stimulating the endogenous production of corticotrophin or by directly

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stimulating the adrenal glands. In either event an increase in the plasma level of circulating adrenocortical steroids would be expected.

The actions of cortisone and corticotrophin have been compared by Hailman (1952) with those of salicylates in a tabulated review of the published reports. Subsequently Van Cauwenbergh and Betz (1952) have confirmed that intraperitoneal injections of salicylates into rats in a dose of 200-300 mg. per kg. of body-weight reduce the ascorbic-acid content of the adrenal glands—an effect indicating increased activity of the pituitary-adrenal system. Increased urinary excretion of reducing steroids has been reported in patients given aspirin (Van Cauwenbergh and Heusghem 1951), and Eades and King (1953) claim to have detected an increase of corticotrophin in the blood of rats given intraperitoneal salicylates.

In contrast to these findings, which suggest that salicylates stimulate the pituitary-adrenal system, no increase has been observed in the urinary excretion of reducing steroids (Böe and Stöa 1953) or of 17-ketogenic steroids (West 1953) after the administration of salicylates. Smith (1952a) has found that the ascorbic-acid content of rats' adrenal glands may be reduced by isomers of salicylic acid having no antirheumatic effect. Salicylates and cortisone have opposing actions on carbohydrate metabolism (Smith 1952b, Smith and Meade 1952), and the ability of salicylates to diminish the glycosuria of diabetic rats is not influenced by either the presence or the removal of the adrenal glands (Ingle et al. 1953).

In the present investigation a more direct approach to the problem of whether or not salicylates stimulate the pituitary-adrenal system was made by measuring the plasma level of circulating adrenocortical steroids before and after salicylate therapy.

Results

Prolonged Treatment with Acetylsalicylic Acid

In 7 patients with either acute rheumatic fever or moderately severe rheumatoid arthritis acetylsalicylic acid was given four-hourly by mouth in the dosages shown in fig. 1. Samples of blood for determining the plasma levels of steroids and salicylic acid were taken before treatment was started and thereafter on the following days four hours after the preceding, and immediately before the next, dose of acetylsalicylic acid. Adrenocortical hormones were measured by the method of Nelson and Samuels (1952), as modified by Bayliss and Steinbeck (1953), which estimates 17-hydroxycorticosteroid compounds, such as cortisone and hydrocortisone, with antirheumatic activity. The plasma level of salicylic acid was measured by the method of Brodie et al. (1944).

During the control period before therapy with acetylsalicylic acid some patients showed considerable day-to-day variation in the plasma-steroid levels. For example, in patients A and F (fig. 1) the steroid level varied from 7 to 14 and from 3 to 14 µg. per 100 ml. respectively. In patients A, E, and G there was no significant increase in the plasma level of 17-hydroxy-

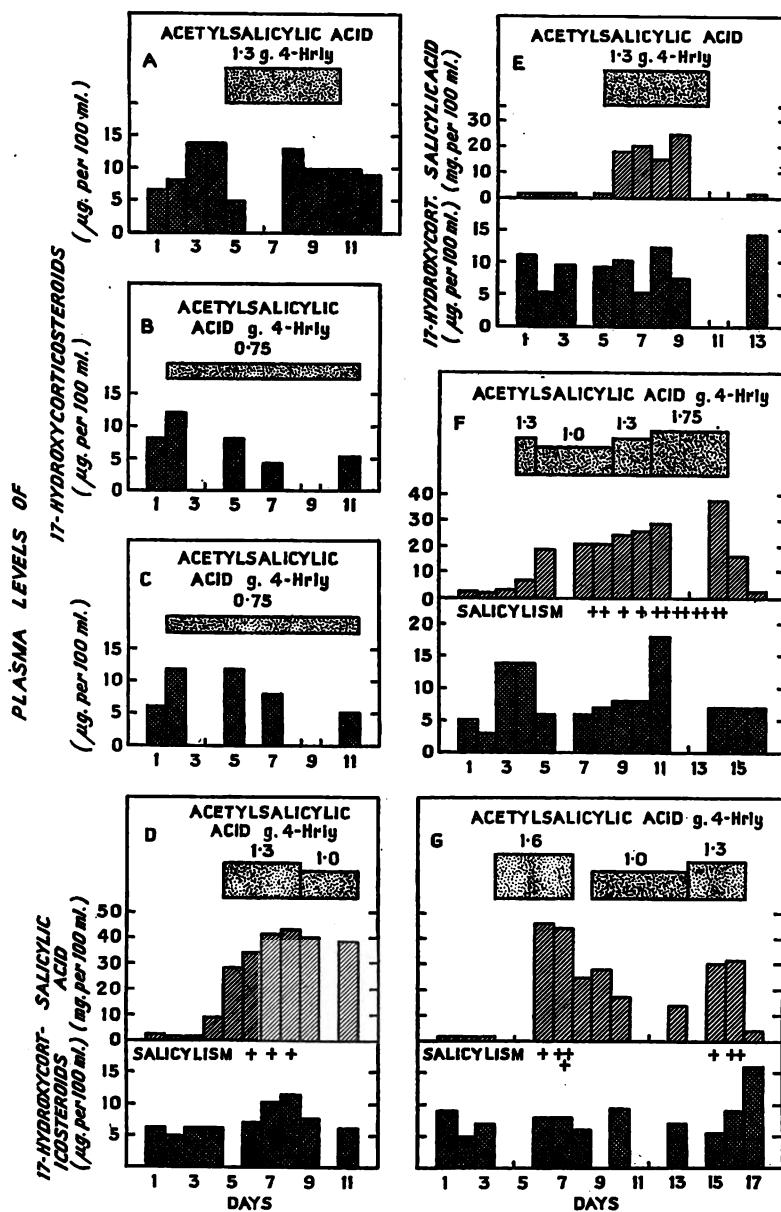


Fig 1.—Plasma levels of 17-hydroxycorticosteroids and salicylic acid before and after treatment with acetylsalicylic acid in 7 patients. Symptoms of salicylism are denoted, according to severity, as +, ++, and +++.

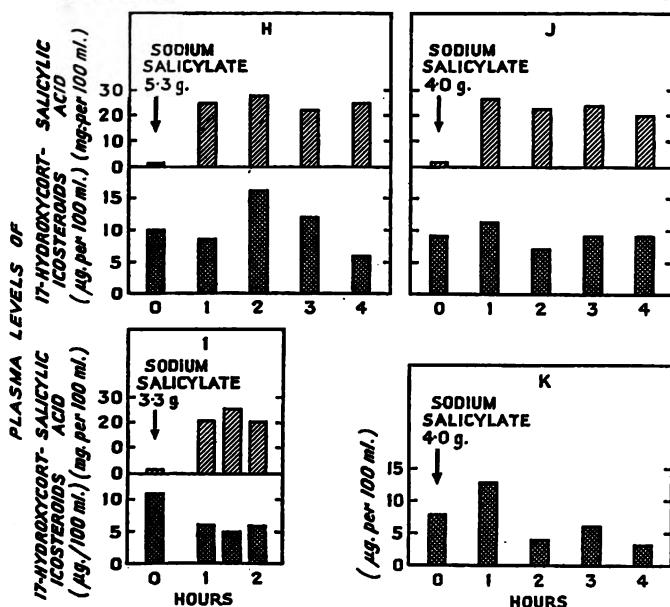


Fig. 2.—Plasma concentrations of 17-hydroxycorticosteroids and salicylic acid immediately before and after a single oral dose of sodium salicylate in 4 patients. The sodium salicylate was given immediately after the blood sample was taken at zero time.

corticosteroids during treatment with acetylsalicylic acid. In patients B, C, D, and F the levels did increase, but the rise was neither consistent nor significant compared with the fluctuations observed during the control period. Statistical analysis showed no significant difference between the mean steroid values during the control and the treatment periods. In patients D, F, and G high plasma levels of salicylic acid were obtained and associated with symptoms of salicylism (deafness, tinnitus, and nausea, but not severe hyperventilation), sufficiently severe in patient G to require reduction of the salicylate dosage.

Single Dose of Salicylate

In the case of 4 other patients a single large dose of sodium salicylate in water was given by mouth, and the plasma levels of steroids and salicylic acid were estimated immediately before and for several hours after the dose. No consistent change in the plasma level of circulating adrenocortical hormones was found after a dose of sodium salicylate sufficient to raise the plasma level of salicylic acid to 20 mg. or more per 100 ml. (fig. 2).

Discussion

These findings indicate that, in adult patients with either rheumatic fever or rheumatoid arthritis, salicylates in either a dosage of 0.75-1.75 g. four-hourly or a single dose of 3.3-5.3 g. did not increase the plasma level of 17-hydroxycorticosteroids. If there was any increase in the secretion of these hormones, the steroids must have been either more rapidly utilised in the tissues or more rapidly excreted from the body, since the level in the plasma remained unchanged.

Although an intraperitoneal injection of salicylate 200 mg. per kg. of body-weight reduces the ascorbic-acid content of the rat's adrenal gland (Hetzel and Hine 1951, Van Cauwenberge and Betz 1952), this amount of salicylate in a man weighing 70 kg. would be equivalent to a single dose of 14 g., which is outside the usual therapeutic range. Hetzel and Hine (1951) noted some ascorbic-acid depletion after smaller doses of salicylate, but Van Cauwenberge and Betz (1952) did not accept the change as significant, and considerable ascorbic-acid depletion may be produced by isomers of salicylic acid which have no antirheumatic effect (Smith 1952a). Although Eades and King (1953) found a significant depletion of adrenal ascorbic acid in rats

given salicylic acid 300 mg. per kg. of body-weight, the depletion in rats injected with the blood from salicylate injected animals is not sufficiently great to provide undoubted evidence of increased amounts of corticotrophin in the donors' blood.

It may well be that doses of salicylate larger than we have given may stimulate the pituitary-adrenal system, and that toxic doses in man will be found to increase the level of circulating adrenocortical hormones. This is the response to any non-specific noxious agent, but from our data there is no evidence that salicylates in sufficient dosage to cause mild or moderately severe salicylism induce a significant degree of pituitary-adrenal stimulation comparable to that found after the administration of corticotrophin (Bayliss and Steinbeck 1954).

Summary

The adrenal response, determined by the plasma level of 17-hydroxycorticosteroids, has been measured in 7 patients given prolonged treatment with acetylsalicylic acid and in 4 patients given a single large dose of sodium salicylate.

No significant increase in the level of circulating adrenocortical hormone was evident.

Salicylates in the clinical dosage of gr. 10-25 four-hourly do not stimulate the pituitary-adrenal system.

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ACUTE BRONCHIOLITIS TREATED WITH DETERGENT AEROSOLS

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BRONCHIOLITIS is responsible for more deaths between the ages of 6 weeks and 2 years than the more widely known and notifiable infectious diseases (Emery 1952). It characteristically attacks the small child and is often overwhelming in the infant.

In two separate epidemics of acute bronchiolitis 68 children, aged from 18 days to 36 months, were admitted to the paediatric wards of three general hospitals in south-east London. The first epidemic, between November, 1952, and February, 1953, involved 41 children, of whom 9 died—a mortality of almost 22%. The second epidemic, between October, 1953, and January, 1954, involved 27 children, none of whom died. The severity of the infection, the age-distribution, and the use of antibiotics and of oxygen were the same in both outbreaks ; but in the second epidemic a detergent aerosol vapour was used in conjunction with the other therapeutic measures. The use of detergent mists may have a very favourable effect on the prognosis of acute bronchiolitis in children.

Pathology

The morbid anatomy of acute bronchiolitis has been described by Newns (1944) and Hubble and Osborn (1941). Macroscopically there is disseminated bronchopneumonia. Histologically the lumen of the finer bronchi

and of the bronchioles is either narrowed or completely obstructed, partly by hyperæmia and infiltration by inflammatory cells of the epithelial lining, and partly by a sticky exudate, which may also fill the alveolar sacs. The alveoli are not usually involved in the inflammation but are either distended by obstructive emphysema or atelectasis.

Aetiology

Though no specific virus has been isolated in bronchiolitis, there is good presumptive evidence that a virus is responsible. Bronchiolitis among children is most common when adults have either influenzal illnesses or "primary atypical pneumonia" (Nelson and Smith 1945), and it is rare in summer. The absence in many cases of a leucocyte response, and the failure of antibiotics to modify the early course, also point to a virus as the cause of bronchiolitis. In the present series no virus studies or cold-hæmagglutination-titre estimations were made.

During the first epidemic a twofold rise in infant mortality took place in London as a result of a severe fog, which lasted from Dec. 5 to Dec. 9, 1952. Though most patients of the first epidemic were admitted some time after the fog, some may well have had a more severe type of illness as a result of their exposure. This seems likely because the mortality from respiratory infections precipitated by the "smog" did not return to normal until January, 1953 (Logan 1953).

Clinical Findings

As would be expected from the morbid anatomy of acute bronchiolitis, the symptoms and signs of progressive bronchial obstruction dominate the clinical picture. At the onset bronchiolitis does not differ from either coryza or mild bronchitis, but soon the child may be desperately ill and gasping for breath. All too often bronchiolitis runs its course within a few hours from the deceptively mild onset to death by suffocation.

Throughout the illness the signs of anoxia are out of all proportion to the other physical findings, which are confined to injection of the upper respiratory tract, and rhonchi and fine crepitations in the chest. Rarely small areas of consolidated or of collapsed lung are detected clinically. Supraclavicular and intercostal recession and cyanosis develop later, often followed by collapse of the patient with an ashy complexion.

The respiratory rate is extremely fast—60–120 a minute. In contrast to the tachypnoea the temperature is often no higher than 101°F, particularly in the very ill child. Similarly, the radiographic findings also fail to reflect the severity of the illness; in this series two-thirds of the films were normal, and the rest showed only minor degrees of consolidation, collapse, or increased bronchial markings.

Treatment

The cause of death in acute bronchiolitis is anoxia due to mechanical obstruction of the bronchioles by inflammatory swelling and sticky exudate. Cold water vapour has been used for some years in an attempt to liquefy the viscid secretions. It was only natural that, after the introduction of synthetic wetting agents, their effect on respiratory diseases should be tried, because these substances could be expected to reduce the surface tension of bronchial secretions, and thereby to facilitate their expulsion by coughing.

Hall (1950) investigated the therapeutic use of detergent mists experimentally, and later (Hall 1952) in bronchiolitis and diphtheria. He felt that these substances were promising and should be given a more extensive trial. He also noted the absence of toxic effects, provided the concentration of the detergent was kept below a certain level.

Towards the end of the first epidemic of bronchiolitis, in February, 1953, several detergents were tried; the

American preparations sodium lauryl sulphate (' Duponol C ') and polyoxyethylene sorbitan mono-oleate (' Tween 80 ') ; and a British detergent consisting of a 0·125% aqueous solution of an oxyethylated tertiary octylphenol-formaldehyde polymer combined with a 2% solution of sodium bicarbonate and a 5% solution of glycerin (' Alevaire '). Duponol C and tween 80 were dissolved or diluted with sterile water to make a 0·1% solution. Alevaire was used undiluted.

In aerosol therapy the mist particles must not be larger than $3\text{ }\mu$ in diameter if they are to reach the finer bronchi and the bronchioles. An 'Oxygenaire' vaporiser was found to deliver a satisfactory vapour. The vaporiser was attached to an oxygen cylinder, and the detergent mist was led to the "sleeve" of the oxygen tent through as short and wide a rubber tube as possible. At first the vapour was blown into the tent for only ten minutes every hour. Later the children were exposed to the vapour continuously until the respiratory rate declined.

Results

In the first epidemic only 6 of 41 children were treated in this way; none died. In the second epidemic 20 of 27 children were so treated. All the children in the second epidemic recovered, whereas there was a high mortality in the first epidemic before the introduction of the detergent mist therapy. In both series various antibiotics (penicillin, streptomycin, chloramphenicol, aureomycin, and oxytetracycline) were used to control secondary bacterial invasion.

No adverse effects were noted. There was no evidence of toxicity, allergy, or depression of bone-marrow. Occasional a child developed redness of the lid margins, presumably due to the fat-solvent action of the detergent, but this disappeared within a few hours of cessation of the treatment.

Summary

Two epidemics of acute bronchiolitis, affecting mainly children aged less than 2 years, occurred in London during the winters of 1952–53 and 1953–54.

In the first epidemic 41 children with bronchiolitis were treated with antibiotics and oxygen. The mortality was 21·9%.

In the second epidemic 27 children were treated in a similar manner, and in addition the 20 most severely ill children were exposed to detergent aerosol vapours. None of the patients in the second epidemic died.

It is suggested that detergent mists should be used in the treatment of acute bronchiolitis.

I am grateful to Dr. George A. Campbell, of Ottawa, for organising the dispatch of detergents; to Messrs. Honeywill & Stein for supplying 'Tween 80,' 'Aerosol OS,' 'Tergitol OS,' and 'Duponol C'; and to Messrs. Bayer Products for supplying 'Alevaire.'

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"... In the United Kingdom we have a moderate experience in methods of health education, but (to tell the truth) I do not think we have a very good publicity sense. We have done much better with intensive campaigns (e.g., for diphtheria immunization) than with general programmes of public education and propaganda. ... I wish we could induce medical faculties in this country to teach medical students about the importance of health education, and how to carry it out in practice. We talk a great deal about the general practitioner as adviser on health, but our schools as a rule make little attempt to teach the student how to exercise this function." —Prof. J. M. MACKINTOSH, Report of European Conference on Health Education of the Public, W.H.O., 1953.

PNEUMOFLATOR ATTACHMENT TO THE BOTH RESPIRATOR

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THE methods of artificial respiration devised at Copenhagen in 1952 (Lassen 1953) used hand power for rhythmic ventilation of the lungs under moderate positive pressure through a tracheotomy tube. Since then several machines have been described which can do this automatically either by utilising an electromagnetic switch to control the flow from a gas cylinder (Bang 1953, Esplen 1952, Macrae et al. 1953, Pask 1953) or by means of a power-operated bag, bellows, or cylinder and piston (Beaver 1953, Russell and Schuster 1953).

Although positive-pressure ventilation may be needed for long periods when given through a tracheotomy tube as the main form of artificial respiration, on many occasions it is desirable for short periods only, notably in a severe case when a cabinet respirator is opened for nursing or physiotherapy. Ventilation can then be given through the mouth and nose with a closely fitting face-mask. Even during these short periods an automatic device is a great advantage not only because it releases a pair of professional hands but also because in these circumstances it seems to be better tolerated by the patient. For example, two cabinet-respirator patients in 1953 (females aged 22 and 20) who had daily intervals of positive-pressure ventilation through a face-mask showed decidedly better tolerance of a power-operated machine than of either of two hand devices, possibly because it is difficult to maintain by hand strict precision of volume and timing. One of these patients could be ventilated by the machine for 20 minutes at a time, and the other for at least an hour.

The present device (figs. 1 and 2) is of the power-operated-bellows variety and is accessory to the modified Both respirator (Smith 1953a); it could, however, also be used for artificial respiration through a tracheotomy tube. Captain G. T. Smith-Clarke, of Coventry, is responsible

for making the apparatus, which consists of the following parts :

(1) A concertina reservoir bellows of about 1200 c.cm. capacity which is fixed by a detachable connection to the horizontal pumping arm of the modified Both respirator (Smith 1953b). By this arrangement, as the Both bellows expand to produce negative pressure inside the cabinet, the downward movement of the pumping arm closes the auxiliary bellows to send a flow of air through its outlet valve and along the corrugated rubber breathing-tube. The bellows are carried on a base which can be swung out of the way when the device is not in use.

(2) A flutter valve specially designed by Captain Smith-Clarke and made of plastic material which fits into the connection of an R.A.F.-type face-mask complete with harness and allows free expiration into the atmosphere.

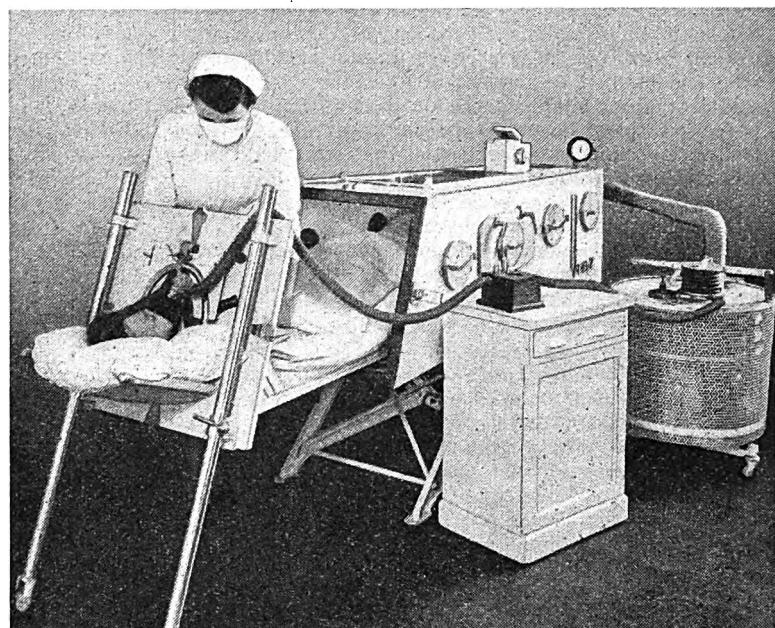


Fig. 2—Pneumoflator in use.

(3) A valve unit comprising (a) a positive gravity-operated safety-valve which prevents pressure from being built up beyond 20 cm. of water, and (b) a second controllable valve which allows the pressure to be set at anything below 20 cm. of water.

(4) A pressure-gauge calibrated in cm. of water.

This pneumoflator appears to have the following advantages :

(1) It is comparatively simple and inexpensive, and could easily be produced on a large scale.

(2) It works off the well-known Both machine as lately modified (Smith 1953b), with which it is precisely in phase whichever of the five available speeds is in use. The pneumoflator can therefore be put into action before the cabinet is opened, and discontinued only after it is shut, thus ensuring a smooth change-over in either direction, which is felt to be a considerable advantage.

(3) It can be used with a split-head respirator.

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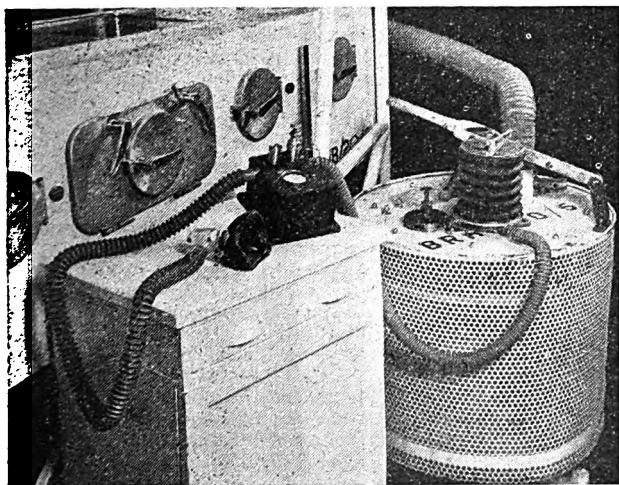


Fig. 1—Pneumoflator assembled for use.

A MACHINE FOR ASSISTED AND POSITIVE-PRESSURE BREATHING

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COUNCIL

EXTENDED experience of the ventilation of patients with respiratory paralysis has emphasised the occasional need of a highly specialised machine, which must be variable in all directions: speed 10-50 r.p.m., volume 200-1200 c.cm. per stroke, phase input, exhaust 1 : 1-1 : 2; and it must be capable of following and assisting the patient's own inspiratory efforts. Mr. H. B. Morton, of the electrocardiography department of National Hospital, Queen Square, suggested that we should make use of electronic control.

Various machines were constructed, and one of us (G. H. B.) considered that thyratron control could best be employed with reversal of a permanent-magnet motor. Two machines were shown at the meeting of the Physiological Society in December, 1953.

The air pump (fig. 1, A) is very simple, and normal bellows deliver about 500 c.cm. per inch movement, 200-1200 c.cm. being available. For maximum efficiency a skew-gear rack-and-pinion gearbox is used, giving a speed ratio of four revolutions of the motor shaft per inch of ram movement. Inertia is thus minimised. The motor has a permanent magnet field and a 450-V armature winding. A Siebe Gorman 'Exnick' valve box is used. Pressure can be adjusted to 10-30 cm. water at any normal speed by varying the stroke volume. In addition there is a spring-loaded blow-off valve. The control box (fig. 1, B) has three dials, and two switches for switching on the set and for selecting automatic (patient) control. The dials control:

- (1) Volume (c.cm.) per stroke. This determines the position at which the ram reverses or stops.

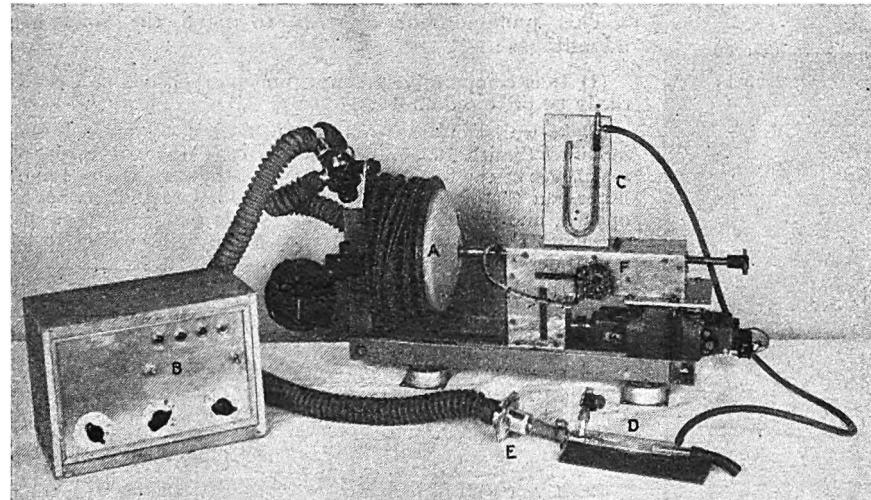


Fig. 1—A, air pump; B, control box; C, mercury U-tube with platinum contact; D, Paul's tubing; E, total expiratory valve; F, rotary wafer switch.

- (2) Pumping-speed (c.cm. per sec.)—i.e., control of motor speed on pumping-stroke—and
- (3) Phase ratio (proportionate speed of motor on return stroke giving ratios 1 : 1 to 1 : 2).

In addition there are four coloured lights indicating the circuits used and assisting hand-timing, or for leads to recording instruments.

A mercury U-tube with platinum contact (fig. 1, C) is used to provide the signal for assisted respiration. To minimise arcing and keep the contact clean, a layer of oil covers the mercury. To provide the necessary negative pressure a length of thin-walled Paul's tubing (D) is introduced adjacent to the mouth-piece or the catheter mount. This remains fully opened during the inspiratory pressure stroke and during expiration. With the inspiration of 5-10 c.cm. the tube collapses and negative pressure is rapidly developed to activate the mercury. This simple device works well, but further developments are proceeding.

A total expiratory valve (E) is included, either of the piston type or the double disc manufactured by the British Oxygen Company. A warm-water humidifier, thermostatically controlled, completes the outfit.

The operation of the mechanism may be explained with the aid of fig. 2.

With assisted breathing the pump remains extended until the patient signal moves the column of mercury

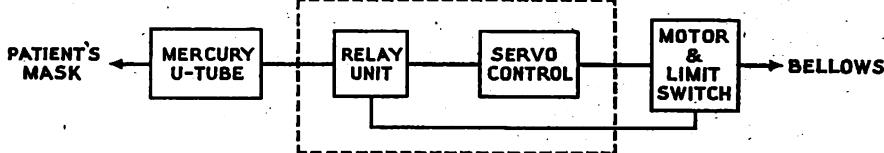


Fig. 2—Schematic diagram of working of machine.

into contact with the adjustable platinum wire. The relay unit passes the appropriate signal to the servo control driving the motor in the desired direction at the appropriate speed. When contact has been made between the mercury and the platinum, the relay system, being self-locking, instantaneously initiates a complete pressure-and-return cycle and switches off the motor ready for the next signal.

The servo is a full-wave thyratron circuit using two thermionic valves causing a rotation of the motor shaft proportional to a small potential applied to the valve grids. In this way a small controlling voltage turns on large current supplies. The interaction between motor armature and valve grids is such that, once the desired controlling voltage has been fixed, a change in motor load causes a change of armature current sufficient to maintain a constant speed. This control unit is one of several which it is hoped to describe shortly elsewhere. The pinion shaft, in the gearbox, carries a radio-type rotary wafer switch (fig. 1, F). This limits the ram travel—i.e., the volume per stroke. It has ten contacts spaced round an arc of some 300°. A central "marrying portion" with a projecting arm in revolving makes connection with the contacts. The left-hand dial switch in the control unit connects any of these contacts to the relay controlling the direction of rotation of the motor. In this way the ram may be reversed between any two positions; but, to reduce the number of variables, the pressure stroke always ends in the same position, volume adjustment being made on the return stroke only. A simplified circuit diagram is shown in fig. 3.

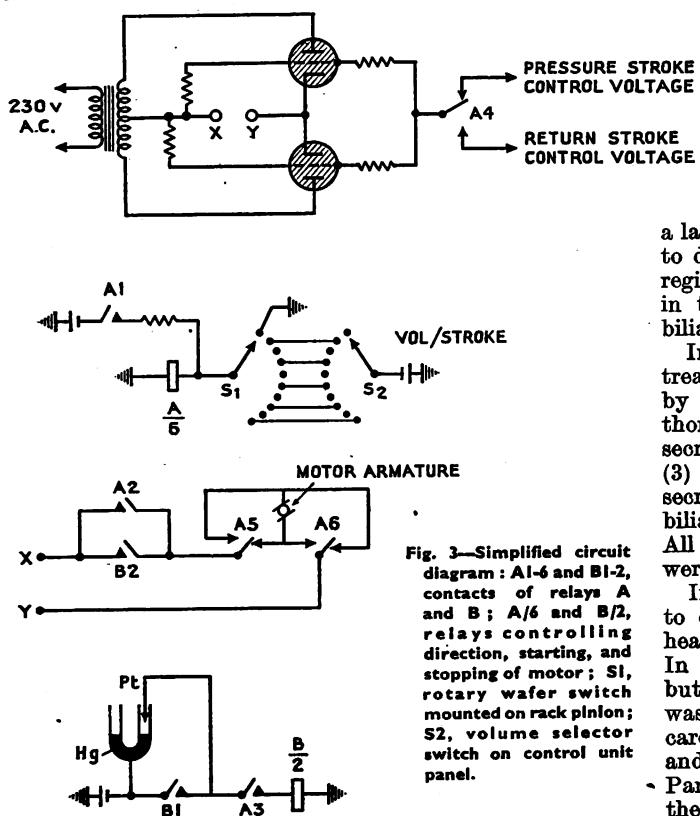


Fig. 3.—Simplified circuit diagram : A1-6 and B1-2, contacts of relays A and B ; A/6 and B/2, relays controlling direction, starting, and stopping of motor ; S1, rotary wafer switch mounted on rack pinion ; S2, volume selector switch on control unit panel.

It is hoped that this machine will help in the problem of the patient whose own ineffectual efforts defeat artificial respiration, and will assist those with marginal ventilation.

We wish to thank Mr. C. S. Hallpike, F.R.C.S., and Dr. W. Cobb, in whose departments much of this work was done; Mr. T. Holmes Sellors, F.R.C.S., and Mr. G. H. Bateman, F.R.C.S., for their patience; and Mr. H. B. Morton and many others for advice and assistance.

Medical Societies

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Diseases of the Pancreas

At a joint meeting on March 4, Dr. H. T. Howat said that the clinical diagnosis of pancreatic disease was at best presumptive and often impossible. In acute pancreatitis a clinical suspicion could be confirmed by the increased amounts of amylase or lipase in serum; but in chronic pancreatitis and in carcinoma of the pancreas these simple tests were less informative. In these cases impaired pancreatic function might be demonstrated by analysis of duodenal contents following stimulation of the pancreas by secretin and pancreozymin; and such stimulation might also raise the level of serum amylase or lipase. These tests were based on sound physiological principles and had proved of value in the diagnosis of chronic pancreatic disease, in conjunction with evidence of impaired glucose tolerance. Tests of this type could be interpreted in terms of morbid anatomy only after closely correlating the findings with the clinical condition of the patient.

Mr. R. L. Holt observed that the surgical treatment of acute pancreatitis was essentially empirical. In the fulminating cases it was doubtful whether any treatment was of any value. In the less severe cases treatment was directed towards : (1) the prevention of oligæmic

shock ; (2) the prevention of paralytic ileus ; (3) the relief of pain by drugs such as hexamethonium or methantheline ; (4) the lessening of pancreatic secretion by atropine ; and (5) the maintenance of electrolyte balance. Constant gastric siphonage was used in the treatment of the paralytic ileus, and it was probably equally important in lessening pancreatic secretion by preventing acid gastric contents entering the duodenum. At a later stage, and then only rarely, it might be necessary to drain abscesses in the lesser sac or subdiaphragmatic region. Nowadays few surgeons believed that laparotomy in the early stages, directed towards drainage of the biliary tract or pancreas, had any beneficial effect.

In chronic pancreatitis the various methods of surgical treatment could be subdivided into : (1) relief of pain by division of the splanchnic nerves or removal of the thoracic sympathetic chain ; (2) reduction of pancreatic secretion by vagotomy combined with gastrojejunostomy ; (3) removal of obstruction to the free flow of pancreatic secretion into the duodenum ; (4) the treatment of biliary sepsis ; and (5) partial or total pancreatectomy. All these methods had their advocates and the results were uncertain.

In malignant disease of the pancreas it was important to differentiate clearly between tumours arising in the head and tumours in the region of the ampulla of Vater. In the former group jaundice was usually a late sign, but in the latter it was reasonably early. The difference was clearly shown in the prognosis. Radical surgery in carcinoma of the head had proved very disappointing, and only very rarely had a five-year cure been obtained. Pancreato-duodenectomy was not worth while when there was evidence of local or metastatic spread. The prognosis was much better in carcinoma of the ampulla, and 40% of cases surviving pancreato-duodenectomy might prove to be cured.

Reviews of Books

Almroth Wright

Provocative Doctor and Thinker. LEONARD COLEBROOK, F.R.S. London : Heinemann Medical Books. 1954. Pp. 286. 21s.

THIS is a first-rate biography—instructive, amusing, exciting, provocative, and readable. It is a study of a remarkable man by one who knew him well and loved him, and had worked in his laboratory for many years. Among much else it describes the origin of antityphoid inoculation, and the fight to get the method accepted ; the not-unjustified distaste of Harley Street for the doctrine that medicine must become applied bacteriology ; the *Doctor's Dilemma* with Wright caricatured as Sir Colenso Ridgeon ; the attacks on women's suffrage ; and the period between the two world wars when his influence on young men diminished while his prestige at St. Mary's Hospital increased.

Wright comes to life again in these pages. Here are some of his remarks : "a man's job in life is to get enough money to get some food and a roof over his head and be able to avoid walking" ; "the best research is done by people who are constitutionally unhappy" ; "if you find yourself when you go to bed, not really tired you should go down on your knees and pray God to forgive you for wasting your day" ; "Shaw has great gifts, but absolutely no desire to get at the Truth—he only wants to do circus tricks" ; "there are no good women—there are only women who have lived under the influence of good men." He still provokes thought—and emotion.

Alethropic Logic

The late Sir ALMROTH WRIGHT, M.D., SC.D., F.R.S. London : Heinemann. 1954. Pp. 346. 25s.

SEARCHING for truth in medicine, Almroth Wright found that he needed the means to recognise it. He also needed the yardsticks with which to measure it

and detect fallacies. Half of this posthumous book is devoted to the definitions and applications of those accurate terms which are the tools of the logician, while the other half contains the "excuses," or practical examples. Assessment of the work is likely to take logicians much time and thought, and the ordinary reader may well be frightened by many strange words for which a glossary of definitions is very necessarily provided. This tells us that the title of the book means "a logic which searches for truth; which concerns itself with truth." The sixteen appendices include forthright views on women, conscientious objectors, the Gospel parables, the secret of inventing, and the need for training in logic.

Chemical Structure of Proteins

A Ciba Foundation Symposium. Editors: G. E. W. WOLSTENHOLME, O.B.E., M.A., M.B.; MARGARET P. CAMERON, M.A., A.B.L.S. London: J. & A. Churchill. 1953. Pp. 222. 25s.

THREE dozen protein chemists met in December, 1952, under the auspices of the Ciba Foundation to discuss the elucidation of the chemical structure of proteins. The well-printed report makes rather heavy reading for anyone not well acquainted with protein chemistry. Although Prof. Cl. Fromageot, the chairman, was somewhat pessimistic about proteins of high molecular weight, the general impression is of rapid progress: it does not seem long since proteins were thought of as messy, gluey things, though, rather surprisingly, some of them could be persuaded to crystallise.

There is much in this book about rigorous standards of purity; about physicochemical methods which can separate peptides and proteins whose molecules differ remarkably little; about various methods, some using chemical reagents and others specific enzymes, to determine the groups at either end of a polypeptide chain; and about chemical and enzymatic tools which can split (and so can detect) particular chemical bonds. R. M. Syngle calls attention to the presence in tissues of peptides as well as of proteins and amino-acids. The presence of these peptides may be more important than their small quantities would suggest, for they may be intermediate stages in the synthesis of proteins, and a "good" intermediate is often present only in small amounts.

Evolution as a Process

JULIAN HUXLEY, F.R.S.; A. C. HARDY, F.R.S.; E. B. FORD, F.R.S. London: Allen & Unwin. 1954. Pp. 368. 25s.

THE whole of organic evolution is shown here, by nineteen scientists studying different branches of natural science, as based on a single mechanism—Darwinian selection acting on the genes. In effect it is a retort to Lysenko and to those nearer home who aver that evolution is not a unitary process.

Professor Huxley starts the book with a comprehensive general survey of evolution. Among the more important of the succeeding articles are Sir Ronald Fisher's review of past criticisms of the theory of natural selection and Prof. J. B. S. Haldane's searchlight beam thrown on to the causes of genetic variation; he plumps for heterosis as the main cause and remarks: "If the views here stated are true, much of the rather speculative human biology which passes under the name of eugenics will turn out to be incorrect." Bernard Rensch, discussing the relation between the evolution of the central nervous functions and body size, claims that smaller animals are more lively and nervous and learn more quickly, whereas larger animals are quieter and more "thoughtful" and can learn more difficult tasks and have a longer memory. P. M. Sheppard attributes nearly all the evolution of bisexual organisms to natural selection as opposed to genetic drift. Prof. J. Z. Young compares the working of the nervous system with the control of communication of information in an engineer's signalling system. He regards environment as the source of information and (like Eugenio Rignano some thirty years ago) calls in memory, both inherited and individual, to direct the reaction to transmitted information. Perhaps he ventures too far when he says: "The mechanisms of natural selection and of the brain may each be said to compute the probability that a given set of circumstances has occurred before." Memory itself he regards as "a persistent

change in the metabolic activity of the nervous system, produced under the influence of the environment." Prof. S. Zuckerman makes a good case for regarding the exciting South African fossil Australopithecine as apes and not man.

Die Variationsmöglichkeiten im Aufbau der Uterusschleimhaut in den einzelnen Phasen des mensuellen Zyklus

Dr. med. HEINZ BEHRENS, M.D. Leipzig: Thieme. 1953. Pp. 88. DM. 9.60.

THIS small book, from the Leipzig University clinic of Prof. Robert Schröder, is an atlas of photomicrographs of endometrium with, where relevant, illustrations of the structure of the corpus luteum on the same day of the cycle. Almost all the material is from operation specimens, not curettings. The first part of the book depicts typical appearances in different stages of the normal menstrual cycle. The second part deals with variations from the usual patterns of both proliferative and secretory phases, which differ from the usual but are not pathologically abnormal, in that they reflect functional disorder—not organic disease.

The paper, printing, and photomicrographs are of high quality, but some of the magnifications might have been increased with advantage.

Spatial Vectorcardiography

GEORGE E. BURCH, M.D., F.A.C.P.; J. A. ABILDSKOV, M.D.; JAMES A. CRONVICH, M.S. London: Henry Kimpton. 1953. Pp. 173. 37s. 6d.

In this excellent summary of the principles of spatial vectorcardiography the technical problems of automatic recording are simply and clearly explained, and the merits of the various methods of presentation of stereovectorcardiograms discussed.

Dr. Burch and his colleagues have devised a special circuit containing unequal resistances capable of recording oblique-plane vectorcardiograms which can be viewed simultaneously on two adjacent cathode-ray oscilloscopes. The advantages and disadvantages of different reference frames are briefly reviewed, and claims are made for the adoption of Wilson's equilateral tetrahedron on the grounds that it is simple and nearly related to the principles of the Einthoven triangle. The studies of the vector loops in normal and the more important pathological conditions are valuable and help to establish adequate criteria for diagnosis. The authors are careful to relate vectorcardiography to electrocardiography and to examine its merits without overlooking its limitations.

The Healing Arts and Their Future (London: Frederick Muller. 1953. Pp. 222. 12s. 6d.).—In this book in The Changing World series Mr. Kenneth Walker has turned his acute but speculative mind to contemporary trends in medicine, surgery, public health, psychomatic and industrial medicine, and psychiatry. He foresees that the problems created by medical skill itself may become more serious with greater power in the hands of the doctors. A longer life-span and lower infant mortality have already aggravated the shortage of world food-supplies. But his fears of an ant-hill World State are mitigated by his profound sense of the power of immaterial and unpredictable elements to mould humanity's destinies.

The World of Learning (London: Europa Publications. 1954. Pp. 1042. 100s.).—It is disappointing to find that this 5th edition does not contain the index of names promised in the foreword of the 4th edition (the lapse is passed over in silence), and that an addition of 78 pages is accompanied by a rise in price of £1 (as happened also with the 4th edition). Nevertheless this is an extremely useful compilation. The different countries have stopped playing general post, but there is one newcomer—Trieste.

Dentists Register (London: Dental Board of the United Kingdom. 1954. Pp. 451. 18s.).—This year the Register contains 15,549 names of dentists (including 216 from the Dominions and Colonies and 258 foreign)—a decrease of 87 in the last year (mostly of dentists qualified in the United Kingdom), but an increase of 222 in the last three years.

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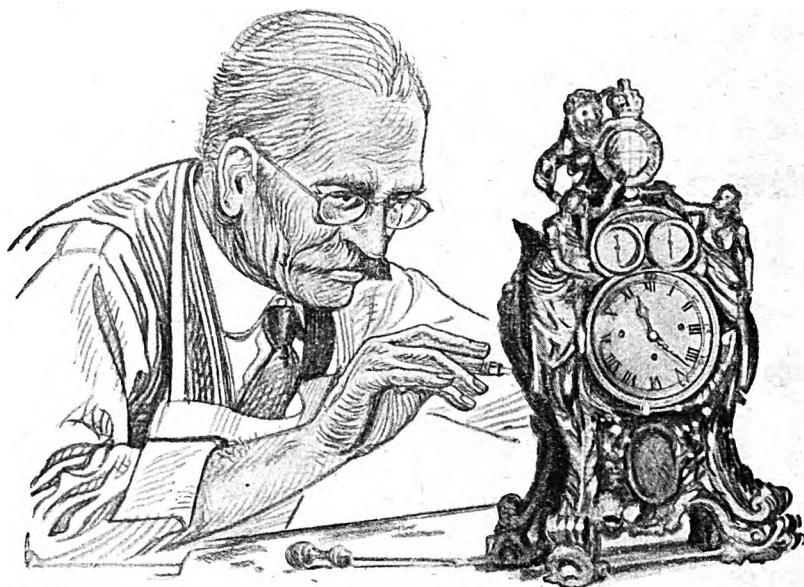
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THE LANCET

LONDON: SATURDAY, MAY 15, 1954

Subacute Bacterial Endocarditis

THE clinical features of bacterial endocarditis are as a rule characteristic, but occasionally the disease may be confused with other disorders—notably in the aged, or when fever or heart murmurs are absent or blood-culture is negative. Embolism of the brain, lungs, abdominal viscera, or a limb may overshadow the endocarditis, and occasionally renal failure or severe anaemia dominates the picture.¹ Early diagnosis often depends on obtaining a positive blood-culture. This, though sometimes difficult, is vitally important since it determines the choice of antibiotic; when no organism is isolated the mortality-rate is higher, since correct diagnosis is delayed and treatment may be postponed or inappropriate.² Sometimes the organism can be isolated only from samples of arterial blood or bone-marrow; and in coarctation of the aorta blood should be collected from the foot rather than the arm.¹ Happily most of the many different organisms that may be found on culture³ respond to penicillin. Of these the commonest is *Streptococcus viridans*.⁴ There is still no conclusive proof that the infecting organism comes from the mouth⁵; but streptococcal bacteraemia is known to follow dental extractions,⁶ which precipitate the disease in at least 10% of cases⁷; and accordingly patients with valvular lesions of the heart who are to undergo dental operations nowadays receive an antibiotic prophylactically. Bacterial endocarditis has also followed quite minor pelvic operations.

In treatment the antibiotic of choice is penicillin. The best results are obtained from intramuscular injection of an aqueous solution of penicillin G in doses of 500,000 units at three-hourly intervals, using the potassium in preference to the sodium salt if congestive failure is present. The resultant high peaks of blood concentration are more effective than the lower yet more sustained levels from equal or smaller total amounts of the repository preparations,

such as procaine penicillin.⁸ When in-vitro tests for sensitivity reveal a more resistant organism—for example, *Strep. faecalis*—the dosage should be increased rapidly to 10 mega-units or more daily, and streptomycin may be added. When very large doses are required their action may be enhanced by inhibiting the rapid renal excretion of penicillin with probenecid ('Benemid') (0.5 g. six-hourly)—a compound similar in action to caronamide but effective in smaller doses and less likely to cause nausea and vomiting.⁹ Salicylates neutralise the action of probenecid and should be withheld during this treatment.² When the organism is particularly sensitive to streptomycin this may safely be given, preferably combined with penicillin, in doses of 1 g. twice daily, reduced after two to three weeks to 1 g. daily; damage to the eighth cranial nerve is unlikely if renal function is unimpaired and if these doses are not exceeded. A two-year follow-up of penicillin-sensitive streptococcal endocarditis treated by a two-week course of penicillin combined with dihydrostreptomycin has shown satisfactory results.¹⁰ Bacitracin is effective only against gram-positive organisms; it may be given in doses of 100,000 units daily with large doses of penicillin, but it is harmful to the kidney and further trials are needed. Aureomycin, oxytetracycline, or chloramphenicol should be used only when the infecting organism is suitably sensitive and perhaps in cases with negative blood-cultures. Chloramphenicol is, however, credited with good results in staphylococcal endocarditis.¹¹ Carbenicillin has so far proved ineffective, but erythromycin, combined with bacitracin or streptomycin,¹² may have a place in the rare infections where the organism is highly sensitive to this antibiotic or where the patient has become sensitised to penicillin; where bacterial endocarditis has been diagnosed clinically but no organism can be cultured from the blood, massive doses of penicillin with streptomycin should not be withheld longer than the forty-eight hours required for intensive clinical and bacteriological study. Cortisone and corticotrophin have been suggested for such cases, but their administration involves a risk of added bacterial infection.

How long should antibiotic treatment be continued? This may be difficult to decide. In Britain the minimum is four to six weeks, with longer courses for second infections or relapses.⁷ The temperature chart is not an entirely reliable guide, for in the later weeks an irregular fever may result from drug sensitivity. Likewise, emboli do not necessarily imply continued bacterial activity, since, even when the infection has been arrested, these may occur at any time in the first three weeks of treatment. Perhaps the only safe criterion of control is a persistently negative blood-culture, judged by the "poor-plate" technique. Relapse is rare more than two months after a course of treatment has been completed. Prolonged rest in bed is important, especially for patients with free aortic incompetence, whose convalescence should be protracted to avert heart-failure.

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5. McEntegart, M. G., Porterfield, J. S. *Lancet*, 1949, ii, 596.

6. Okell, C. C., Elliott, S. D. *Ibid*, 1935, ii, 869. Farmer, E. D. *Proc. R. Soc. Med.* 1953, 46, 201.

7. Cates, J. E., Christie, R. V. *Quart. J. Med.* 1951, 20, 93.

8. Finland, M. *New Engl. J. Med.* 1954, 250, 372.

9. Baker, G. P., Pilkington, J. *Lancet*, 1952, ii, 17.

10. Geraci, J. E., Martin, W. J. *Circulation*, 1953, 8, 494.

11. Miller, G., Hansen, J. E., Pollock, B. E. *Amer. Heart J.* 1954, 47, 453.

12. Geraci, J. E., Martin, W. J. *Proc. Mayo Clin.* 1954, 29, 109.

and embolism. Dental extractions, and surgical treatment of a mycotic aneurysm or of an infected patent ductus arteriosus, should be postponed until the latter weeks of the antibiotic course, and should preferably not be undertaken later under temporary penicillin cover. A blood-transfusion may sometimes render the patient fit for operation or expedite recovery.

The prognosis is rather better in cases of congenital heart-disease, where the myocardium is not irreparably damaged as it may be with rheumatic carditis. Experimental evidence suggests that healing of the lesion is not materially affected by penicillin therapy.¹³ The functional prognosis depends largely on the residual calcification and deformity of the heart-valves—a sequel on which therapy has little influence.

Polyuria

It is the current view that between 150 and 200 litres of water are filtered each day through the glomeruli in the kidneys of a normal adult man. Of this immense volume, all but about 1.5 litres must be reabsorbed by the tubules and returned to the blood, together with most of the solutes present in the original glomerular ultrafiltrate. According to HOMER SMITH,¹⁴ at least two independent processes are concerned with the tubular reabsorption of water. In the proximal tubule about seven-eighths of the filtered water is recovered passively by diffusion, concomitantly with the selective absorption of osmotically active solutes. The remaining water is removed in the distal nephron by an active process that is largely independent of solute absorption. It is the second, distal, component of water reabsorption that can be varied rapidly by the action of the pituitary anti-diuretic hormone (A.D.H.). Change in glomerular filtration-rate is little concerned in the regulation of urine flow in the adult; and developing polyuria results from diminished tubular reabsorption of water. Urine flow may increase by either of two physiologically distinct patterns—"water diuresis" and "osmotic diuresis." Water diuresis, seen characteristically after ingestion of water, results from inhibition of A.D.H. secretion¹⁵ and consequent cessation of active water absorption in the distal nephron: and, since electrolyte absorption in this segment continues normally, the urine excreted is hypotonic and its specific gravity approaches that of pure water. Polyuria in diabetes insipidus is simply water diuresis conditioned by the pathological absence of endogenous A.D.H. secretion, and up to 20 litres of urine may be voided daily. Physiological water diuresis and the polyuria of true diabetes insipidus can be inhibited by the administration of exogenous A.D.H. (vasopressin), and under the influence of this stimulus the kidney excretes urine that is hypertonic to the blood ultrafiltrate—that is, a urine of specific gravity considerably in excess of 1.010. Osmotic diuresis occurs whenever there is need to excrete an excess of osmotically active solute; it accounts for the polyuria of diabetes mellitus and it can be produced experimentally by giving large doses of urea¹⁶ or by the

parenteral administration of many other solutes.¹⁷ As urine flow increases during osmotic diuresis the urine becomes more dilute, but it never becomes hypotonic to the blood ultrafiltrate.¹⁷ Osmotic diuresis cannot be inhibited by administration of vasopressin. The mechanisms responsible for this pattern of diuresis are not certainly known, but HOMER SMITH suggested¹⁴ that an excess of any unabsorbed and osmotically active solute in the urine in the proximal tubule leads to reduction of water and electrolyte absorption in this segment. The resulting increased load of hypotonic or isosmotic urine reaching the distal nephron is not substantially modified in this segment and large volumes of isosmotic urine are excreted. The pattern of water diuresis or of osmotic diuresis can be detected in most instances of polyuria occurring physiologically or arising in patients with intact renal function. It has been suggested¹⁸ that the rhythmic diurnal changes in urine flow represent a third type of natural diuresis; but the evidence seems to indicate that this is a particular example of osmotic diuresis.¹⁹

The simplest form of polyuria in renal disease is that seen during the early phase of recovery from tubular necrosis; for here it has been shown²⁰ that the urine excreted closely resembles glomerular filtrate, and it may be assumed that the regenerating tubular epithelium is incapable of modifying the filtrate. This is the least common form of renal polyuria and all other forms are more difficult to explain. Polyuria, at least as exemplified by the uncomfortable symptom of nocturia, is the most common single symptom of renal failure and it is not surprising that attempts have been made to explain its occurrence in terms of these physiological mechanisms. Foremost among these is PLATT's suggestion²¹ that "isosthenuria" represents a phenomenon of osmotic diuresis. In isosthenuria the urine is isosmotic with plasma ultrafiltrate, its specific gravity is fixed at about 1.010, and the daily volume is 2–3 litres; but the patient is in approximate nitrogen and electrolyte balance so that a normal amount of solute must be excreted daily. PLATT suggests that this normal solute load, passing through a much-reduced number of nephrons, must produce an osmotic diuresis comparable to that induced by RAPOPORT et al.¹⁷ by solute infusions in normal children. This hypothesis is attractive and it may be the correct explanation of isosthenuria resulting purely from loss of nephrons. But most physiologically minded physicians will have seen an occasional patient, usually with "tubular acidosis," in whom the blood-urea level is normal and the filtration-rate very little reduced, but in whom there is isosthenuria. These cases are not readily explained by PLATT's hypothesis, nor is the rare occurrence of isosthenuria in acute nephritis. Certain recent observations suggest that the state of affairs in "renal failure" may be more complicated than is indicated by the osmotic-diuresis hypothesis. ROUSSAK and OLEESKY²² have described two patients in whom renal disease presented with a diabetes-insipidus-like syndrome from failure of the renal conservation of water.

- 17. Rapoport, S., Brodsky, W. A., West, C. D., Mackler, B. *Amer. J. Physiol.* 1949, **156**, 433.
- 18. Borst, J. G. G., de Vries, L. A. *Lancet*, 1950, II, 1.
- 19. Stanbury, S. W., Thomson, A. E. *Clin. Sci.* 1951, **10**, 267.
- 20. Bull, G. M., Joeke, A. M., Lowe, K. G. *Ibid.* 1950, **9**, 379.
- 21. Platt, R. *Brit. med. J.* 1952, I, 1313, 1372.
- 22. Roussak, N. J., Oleesky, S. *Quart. J. Med.* 1954, **23**, 147.

13. McGeown, M. G. *J. Path. Bact.* 1954, **67**, 179.

14. Smith, H. W. *The Kidney*. New York, 1951.

15. Verney, E. B. *Lancet*, 1946, II, 739, 781.

16. McCance, R. A. *J. Physiol.* 1945, **104**, 196.

Each patient excreted up to 5 litres of hypotonic urine daily; and, in each, water deprivation, intravenous hypertonic saline, and vasopressin administration failed to control the diuresis and concentrate the urine. One patient had myelomatosis, and the obligatory hyposthenuria persisted even when the blood-urea level was over 150 mg. per 100 ml.: at necropsy DARMADY was able to demonstrate by microdissection extensive atrophy of the epithelium in distal convoluted and in collecting tubules.²² The second patient had polyuria with hydronephrosis resulting from prostatic enlargement: after relief of the obstruction recovery was complete and the glomerular filtration-rate became normal. ROUSSAK and OLEESKY have called the syndrome "water-losing nephritis," believing that it resulted from failure of the distal component of water reabsorption, and they contrast the condition with isosthenuria in commonplace renal failure. It may be asked why their first patient did not have isosthenuria, since the blood-urea level was high and many nephrons were blocked by casts. The recorded rate of electrolyte excretion was low and the blood-urea level rising, so that the daily solute excretion was probably subnormal. If the rate of solute excretion had been higher, would an osmotic diuresis have masked the "water-losing" lesion of the distal nephron and led to a higher specific gravity of the urine? Experimentally produced osmotic diuresis in patients with untreated diabetes insipidus increases urine osmolarity towards that of the blood.²³ WHITE et al.²⁴ studying water diuresis in chronic nephritis, have found it relatively resistant to the influence of vasopressin. "Water-losing" lesions might then be found more often if more diligently sought. We are accustomed to associate isosthenuria with a urine specific gravity of 1.010; this we measure crudely with a urinometer, paying little heed to the influence of proteinuria. If we were to measure urine osmolarity accurately, it might be found that what is casually called "isosthenuria" was sometimes "obligatory hyposthenuria": careful study might show that a specific gravity fixed at, say, 1.006 indicates a distal "water-losing" lesion. Such observations should help to explain why some patients with renal failure become desiccated without thirst, while others suffer considerably from this symptom.

The concept of glomerular filtration and tubular reabsorption of water is orthodox physiology; another suggestion^{21 22} invokes, in addition, active water secretion into the distal tubule lumen. As a recent review points out,²⁵ most phenomena will accord with either hypothesis, and choice between the alternatives is decided by personal bias rather than facts. DARMADY's finding of distal and collecting-tubule atrophy in a "water-losing" kidney seems likely to reflect a lost function—water reabsorption—rather than a morbidly maintained process of active water secretion. Anatomical examination of other verified instances of "water-losing" kidney and of kidneys from patients with hereditary "vasopressin-resistant" diabetes insipidus is desirable. This may not only illuminate an interesting clinical problem, but also help to answer some of the outstanding questions of renal tubular physiology.

23. Brndasky, W. A., Rapoport, S. *J. clin. Invest.* 1951, 30, 282.
 24. White, A. G., Kurtz, M., Rubin, G. *Amer. J. Med.* 1954, 16, 220.
 25. Berliner, R. W. *Ann. Rev. Physiol.* 1954, 16, 260.

The Concept of Age

MANY approaching the threshold of age wonder what change in their tissues or their reasoning-powers justifies society in classing them one day as workers and the next day as retired. Prof. J. M. MACKINTOSH, on another page, reviews again the puzzling prospects which our greater survival-rate and lower reproduction-rate have opened to us. Already the proportion of those aged 65 and over in the population is more than double what it was in 1891; and by 1980, it is estimated, a fifth of us will have reached or passed retiring age. But perhaps there is some avoidable confusion here: ageing, indeed, is not a factor we can yet control; but at least we have the final say on the length of the retired list. The threshold of age, in fact, is a movable threshold. At present we are hurrying some across it while they still have good work left in them—a policy which in terms alike of humanity, psychology, and economics leaves much to be desired. Nothing compels us to pursue this policy except our own inflexibility. It is reasonable, perhaps, to name some fixed age at which anyone who wants to retire can decently do so; but that is a very different thing from what Professor MACKINTOSH calls "an increasing pressure to retire at a fixed age." Such pressure is already widely exerted, and whereas 44% of men between sixty and seventy-five years of age were employed in 1945, the corresponding proportion in 1951 was only 30%. The fall does not represent the results of free choice, for Social Survey, in their study of firms with a fixed retiring age, found that about half of the workers would rather have gone on working past that age. Nor did the question of a pension make a great difference: in firms without a superannuation scheme the percentage expressing a wish to go on working was 52; in firms with a superannuation scheme it was 42.

For many people the end of the working life means a serious loss of company. Stories are told of retired business men who go on catching the same morning train to town for the sake of meeting their friends. Loneliness, indeed, is one of the commonest hardships of age. The man who retires at sixty-five has an average of twelve and a half years to fill in; a woman who retires at sixty may expect eighteen or more. The 1951 census showed that the number of people living alone has almost doubled since 1931, and more than half a million of them were over forty: no doubt this figure includes a large proportion of people over retiring age. A small survey¹ of eleven Oxfordshire villages, made recently, revealed 135 old people living alone, in a population of only 7500. Old people's clubs, which have multiplied so fast in recent years, are successful largely because they mitigate the loneliness and reduce the fears which, as age advances, distress the old person living alone. Mr. RICHARD COTTAM² quotes the remarks of a man reaching retiring age:

"I am past sixty-five years of age and in a few weeks time must leave my work and live on a pension of 26s. a week. I am partly disabled but could do a light job;

1. *Oxford Times*, March 12, 1954; see *Lancet*, April 3, 1954, p. 718.
 2. Living Longer. A series of lectures organised by the Institute of Public Administration (South-West Regional Group). London: National Council of Social Service. 1954. Pp. 72. 3s. 6d.

it seems a shame I can't go on working ; as it is I have no prospects, no relations to help me and I am all alone. I cannot help wondering what the future has in store for me, especially if my health fails."

This fear of the future is, to COTTAM's mind, one of the greatest causes of unhappiness in age.

"Loneliness, unwantedness, poverty, poor housing, or ill health, are serious enough," he says, "but for every one who suffers from one or more of these there are probably many more whose nightmare is not the hardship itself but the fear of it, a fear accentuated by the feeling that growing infirmity will make it more difficult to face that difficulty when it arises."

Fear and poverty are bad companions. The man who retires at sixty-five still fit to go on working, and lives alone, may—between poor feeding and constant fear—soon become physically and emotionally unfit to work at all. The unhappy ending of stories of this kind can be watched in our chronic wards and mental hospitals.

The converse appears in the good results which come of offering work to the old. Dr. C. O. S. BLYTH BROOKE³ describes a small voluntary scheme in Finsbury, started by the Employment Fellowship with the help of a grant from Finsbury Borough Council. The fellowship rent a house where a group of some 60 elderly people work for two hours daily, either the morning or the afternoon shift.

They do outwork on commission for commercial firms, and also make goods for direct sale to the public. The work has so far included packing corn-pads (50 gross a week), assembling drop-bottles (20 gross a week), making 15,000 thin cardboard wallets weekly, re-indexing the public library, assembling some of the parts of electric irons, and repairing old clothing at the expense of the Old People's Welfare Committee. A fair commercial rate is charged for all work done, and a flat rate of 10s. a week is paid to every worker, irrespective of output.

Altogether there have been 81 workers, of whom 60 (49 women and 11 men) are still attending regularly. The average age of the men is seventy-four, and of the women over seventy. Of the 21 who have left the scheme some have moved from the district, a few fell ill, one left from pique, one died, and some have discovered themselves to be capable of more strenuous work, and have found it elsewhere. The small wage is welcome to the workers, enabling them to buy something besides the bare necessities of life ; but their chief satisfaction is in the renewed experience of fellowship : their work has become what it once was—the centre of their lives—and most of them would like to come for longer hours. But, as this little scheme is not quite self-supporting, it should perhaps be taken as a guide to what is needed rather than a pattern to copy. The economic thing to do, as Professor MACKINTOSH points out, is to let a man go on with his accustomed work—though modified, perhaps, to suit his powers—as long as he is fit to do it. Pension schemes should be flexible enough to allow for variable ages of retirement—say between sixty and seventy: as he says, there is nothing physiologically significant about the sixty-fifth birthday.

But Professor MACKINTOSH's final point also deserves attention. We cannot, he says, be our own assessors of our capacity to go on working past retiring age : that must be decided for us by others. And he issues

a special warning to members of the professional classes and others who work with the mind rather than the hands. They have more power, he thinks, than manual craftsmen to do harm ; and at sixty-five they are often in positions which enable them to do quite a lot of harm. Hence the need for an impartial arbiter. Yet an unfavourable judgment need not throw them out of work : they could accept gracefully both less power and lighter tasks, coupled perhaps with some senior and honourable title. It is inevitable, however, that an adverse judgment should cause some pain, and doubtless it would rouse some elders to heated and open disagreement. Perhaps it would be better to have an understanding that from the age of sixty onwards every senior began to delegate responsibility to others, making his own transition to less responsible work over the course of some five or six years. Those rare ones, who in their seventies are still abler than most, are easy to detect ; and it would be the part of the arbiters to persuade such giants to go on holding the reins.

For the ordinary run of septuagenarians, however, other solutions are possible. ROBERT W. KEEMEIER⁴ describes a community, near Jacksonville, Florida, for retired members of the Loyal Order of Moose and their wives and widows. Bearing the remarkable name of Moosehaven, this community has some 350 residents, drawn from more than thirty different States, and with an average age over seventy-six. More than 200 of them—all who are able, in fact—go on working, and there are more than fifty jobs for them to choose from—kitchen and dining-room work, carpentry, painting, cabinet-making, bartering, clerking, electrical work, wagon-driving, farm and dairy work, and many others. Most of the 200 are happy in their jobs and would not be without them. They receive allowances appropriate to the work they do, but these are not regarded as wages. Many learn new skills and take over jobs they had never learnt before.

The community makes itself completely responsible for their needs, including their medical needs ; and, though the residents have their own homes on the 68-acre estate, there is a "health centre" to which they can be admitted if they fall sick. An optician and a chiropodist visit regularly. A recreation centre provides social diversions—canasta, horseshoe-pitching, barn dances, cinema shows, minstrel shows, and television—and there is a pier for those who enjoy fishing in the river. The residents include about 50 married couples, and 14 of these were married on the premises ; one man who came a bachelor has now been married three times.

But, for all its advantages, Moosehaven is a community for the aged, and death is a frequent visitor : moreover, it is so large that the residents cannot easily step from it into the outside world. For many of them, we suspect, it would really be better to go on living and working in the ordinary community, with the younger generations about them. The constant sight of ageing contemporaries can provoke too much self-concern, too much attention to ailments which might be forgotten in the society of hale young people. Those local authorities who have built bungalows for the old find that they like them to look out on a high road, where the world goes by : they have no taste for a quiet corner.

3. *Ibid.* p. 51.

4. *Amer. J. Sociol.* 1954, 59, 347.

Annotations

NEUROLOGY: A WEAK POSITION

UNLIKE general medicine and the other medical specialties, neurology has not expanded under the National Health Service; and indeed the position is worse now than it was in 1945. The Committee on Neurology of the Royal College of Physicians say in an interim report presented last month that promising graduates now regard the prospects in neurology as "so discouraging that they are becoming increasingly reluctant to enter a branch of medicine in which this country is pre-eminent." The reasons for our failure to expand the neurological services are two. First, of course, the insistent need for economy means that every regional hospital has to meet the demand for more consultant appointments out of a fixed budget. What appointments can be made are apt to be in the specialties which are most in the public eye, and those whose claims are pressed by the most vocal committees. Neurology is often regarded as a luxury which must wait for better times; for the present, the boards seem to feel, the work must be done by general physicians who are interested in neurology, or even by the staffs of the neurosurgical centres which are now springing up. There is a tendency to believe that in the provinces neurology should be undertaken by general physicians; and that both the practice and teaching of general medicine would be impoverished by the appointment of neurologists. But it is in the provinces, in fact, that the shortage of neurologists is most acute: two-thirds of the 50-60 practising neurologists in England and Wales are in the Metropolitan regions, and this leaves only about 20 others, most of them attached to provincial teaching centres. There are, in fact, large well-populated areas where there is no neurologist available within 150 miles. The only three fresh neurological centres set up in the past five years show a steadily lengthening outpatient list, and a rise in the rate of turnover in the restricted number of beds. The committee judge that this strongly confirms the existence of an unfulfilled need for more neurologists in the provinces. Consultant psychiatrists reported almost unanimously to the psychological medicine committee of the college that in the provinces there are not enough neurological consultants to make it possible to train psychiatrists adequately in neurology.

The committee affirm strongly—and we fully agree—that expert neurological opinion should be available for any member of the public who needs it, regardless of his means or his place of residence; and they estimate that not less than 5% of all inpatients in the country are suffering from neurological disorders. By a "neurologist" the committee mean "a trained physician with a higher qualification in medicine who has received the necessary special training and experience and proposes thereafter to devote himself to that specialty." They do not include in this definition general physicians who have gained some experience in neurology in the course of their training in general medicine. To fit himself to be a neurologist, they say, a man should have had the statutory year of resident hospital appointments, a year as a senior house-officer or registrar status in a neurological hospital or the neurological department of a general hospital, and four years as a senior registrar in a neurological hospital or department. He should also have taken a higher qualification, "preferably the M.R.C.P. London." They are opposed to the idea of a diploma in neurology, believing that a man's appointment to a consultant post should depend on his experience of his subject.

The care of inpatients is only a small part of a neurologist's work; most of his time is spent on outpatients and on giving opinions on patients under the care of his

colleagues in other specialties and in general medicine. The committee do not for a moment suggest that such patients should be withdrawn from the care of other physicians and surgeons to be segregated under the care of neurologists: such a policy would have nothing to recommend it. They do, however, think he should be at hand to advise on diagnosis and treatment, and they regard with deep misgiving the growing tendency to set up neurosurgical centres without appointing a neurologist to them. This practice obliges neurosurgeons to take responsibility for medical cases—"a task for which they are suited neither by temperament nor training."

In 1945, the original committee on neurology (made up of many of the same members as this one) thought it certain that under the National Health Service there would be a considerable increase in the numbers of neurologists, and a more even distribution of them throughout the country. In recording their disappointment, they note that after the war many ex-Service graduates trained as neurologists; only 15% of them have been able to find "reasonable employment," and some have emigrated. This is a sad waste of people whom we greatly need at home. The committee confirmed the recommendation of the 1945 committee that active neurological departments should be established in all medical teaching centres, and elsewhere, depending on the needs of the country; and that neurologists attached to teaching centres or neurological departments should be responsible for the care of inpatients and outpatients at their own hospitals and should also be available for consultation at chosen hospitals in the region.

HEPATORENAL SYNDROME

UNEXPECTED deaths after operations on the liver or bile-passages are still fairly common. In some of these cases death apparently results from renal failure, shown by albuminuria, oliguria, or anuria, with raised blood-urea and non-protein nitrogen. The persistence or increase of preoperative jaundice and other evidence of impaired hepatic function justify the term "hepatorenal syndrome" for these cases. Trapnell¹ has described two further examples of this syndrome. He classifies cases in four groups: toxic, infective, postoperative, and dietary. The postoperative group no doubt includes cases from the other groups.

For a toxin to cause this syndrome it must presumably injure both the liver and the kidneys. Substances which can do this include carbon tetrachloride, mersalyl, and sodium chlorate. Similarly some micro-organisms, such as *Leptospira icterohaemorrhagiae* and the yellow-fever virus, have a predilection for these same two organs, and patients infected by them may occasionally show the syndrome. The effect of dietary factors is problematical. In laboratory animals deficiency of choline affects both liver and kidneys, so conceivably diet may be partly responsible for hepatorenal damage in man. The most important of Trapnell's groups is undoubtedly the postoperative; for it is the largest and probably the most easily prevented. The cause of renal damage in these cases is still obscure; but many show rapid and severe destruction of liver cells, so the toxic action of the resulting breakdown products must be considered. An alternative hypothesis attributes the renal damage to failure of the injured liver to carry out its normal detoxicating functions, with consequent accumulation of nephrotoxic substances.

The association of renal dysfunction with hepatic disease raises the question of what these two organs have in common. Both organs consist mainly of specialised closely packed parenchymal cells richly supplied with blood-vessels, with little intervening connective tissue. In both organs the bulk of the blood in the

1. Trapnell, D. H. *Arch. Middx Hosp.* 1954, 4, 58.

capillaries of the parenchyma has already passed through one set of capillaries—in the intestine in the case of the liver, in the glomeruli in the case of the kidney—and it is perhaps hardly surprising that in both organs the cells furthest downstream should be particularly vulnerable to toxæmia, anoxæmia, or deficiency of any essential nutrient. Impairment of the circulation by swelling of parenchymal cells may also be particularly important in these organs with scanty intercellular connective tissue and relatively inelastic fibrous capsule. It is especially interesting that the pathological lesions of the hepatorenal syndrome are almost invariably in the centrilobular zones of the liver and the distal convoluted tubules of the kidney.

In prophylaxis it is essential to avoid any treatment which throws extra stress on the liver. Anoxia must be prevented as far as possible, but it is still more important to withhold drugs that require an intact liver for their metabolism or detoxication. Such drugs include all the barbiturates—not only the derivatives of barbituric acid, but also those of thiobarbituric acid.

EARLIER TISSUE STAGES OF MALARIA PARASITES

FOR many years malarialogists sought the malarial parasite in its development during the ten days between infection and parasitemia. A tissue phase was postulated for some twenty years before Shortt and Garnham demonstrated in 1948¹ the existence of clusters of *Plasmodium cynomolgi* merozoites in liver cells. These forms were soon reported in *P. vivax*,² *P. falciparum*,³ *P. ovale*,⁴ and the simian *P. inui*⁵ (closely analogous to the human infection with *P. malariae*). Malarialogists recognise this phase as confirmed.^{6,7}

With *P. cynomolgi* the minimum period after infection for the blood or liver tissue to become infective on subinoculation is eight days. This was thought to be the time taken by schizonts to develop into adult infective merozoites. To prove this the development of a single generation in the liver had to be demonstrated. Professor Shortt and his colleagues⁸ at the London School of Hygiene and Tropical Medicine now describe in detail this development in the parenchyma cell of the liver from the second to the eighth day.

The glands of mosquitoes (*Anopheles maculipennis*) infected with *P. cynomolgi* were injected intravenously, intraperitoneally, and sometimes directly into the portal vein in monkeys (*Macaca mulatta*). Liver biopsies fixed in 'Carnoy' (with chloroform) and stained with Giemsa-colophonum show clearly on section the sharply defined intracellular two-day form with the nucleus undergoing its first division. At this time the form is only 2.3 μ in diameter, so all sections had to be examined under the oil immersion. The parasites' steady intracellular development is clearly illustrated. A complete lack of hepatic cellular reaction emphasises the adaptation by the parasite during the critical initial ten days when it is establishing itself in a new host. Only with the liberation of merozoites and the start of the erythrocytic cycle do fever and other symptoms begin. Primary schizont forms do not all release their merozoites at the same time: some were found at least fifteen days after infection, when one was estimated to contain 60,000 merozoites. How much longer they can remain will be difficult to prove. Secondary or relapse schizont forms

found in the liver a hundred and five days after infection look very similar to the primary ones.⁹ The eradication of the malaria parasite must depend on the effectiveness of drugs against both these tissue forms and the more easily recognised blood phase.

As a result of this arduous and painstaking work only the first twenty-four hours of the parasite's life in the human body has still to be explained.

MOTIVE AND MOMENTUM

THE first register of qualified practitioners published in this country, in 1859, included the name of a medical woman—Dr. Elizabeth Blackwell. In her presidential address to the Medical Women's Federation, on May 6, Dr. Annis Gillie drew attention to this significant fact. It was significant, however, in the sense that a straw is significant in the wind rather than as evidence of an accomplished revolution or accepted trend. The pioneers—notably Elizabeth Garrett and Sophia Jex-Blake—who opened the doors of British medical schools to women were still to come. Dr. Gillie set their achievement against the social scene of mid-Victorian England, when industrial success for the few had created appalling hardship for the many, and the public conscience was just beginning to rebel against the discrepancy.

In the strong and numerous middle class, prosperity had meant a distressing loss of occupation for women. At the beginning of the century the well-to-do housewife had been personally responsible for feeding and clothing her family and dependants, and for treating their ailments: she took so active a part in household management that she was glad to delegate work to her daughters and daughters-in-law, and to pass on to them her skills and experience. By the middle of the century, however, the aims had changed. The formidable mamma, supported by plenty of servants, was now bent on making her daughter elegant, refined, and idle—accomplished in minor drawing-room arts rather than apt in household management, delicate rather than sturdy. "Many," Dr. Gillie said, "were bored, some were concerned, and a few were disturbed at the state of society as a whole."

Meanwhile a development of a different kind was going on in another section of the community. Ever since the dissolution of the monasteries the wives and daughters of squires and parsons had undertaken the charitable work of relieving the poor and visiting them in their homes—not only to read the scriptures but to give material help and practical advice. This was beginning to grow into a serious form of social work: "by 1820 the young lady in the country was expected to do her district visiting with a register and account book." Octavia Hill, in the 1860s, launched her trained rent-collectors and founded her system of estate management. Trained district visitors were also sent out from the mission dispensaries; and in fact it was becoming clear that women social workers were widely needed. Indeed, it is surprising, Dr. Gillie said, to note "how narrow was the chasm (albeit very deep) which separated the well-developed charitable district experiments from general practice of the same period." It was even becoming clear to some reformers that there was a place for women in medicine.

Like Nonconformists and Roman Catholics at the beginning of the century, women had no vote, and no access to universities; and the schools which catered for their education offered a meagre curriculum. While well-to-do women of limited education were brought up to believe that idleness was a sign of gentility, working-class girls were beginning to enter occupations other than domestic service. "The middle-class daughter had gained a beautiful cage, with little scope inside it and total insecurity without." Dr. Gillie recalled some notable women whose cages could not hold them—Florence

1. Shortt, H. E., Garnham, P. C. C. *Nature, Lond.* 1948, 161, 126.
2. Shortt, H. E., Garnham, P. C. C., Covell, G., Shute, P. G. *Brit. med. J.* 1948, i, 517.
3. Shortt, H. E., Fairley, N. H., Covell, G., Garnham, P. C. C. *Ibid.* 1949, ii, 1006.
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Nightingale, Josephine Butler, Harriet Martineau, Mrs. Gaskell, Barbara Leigh Smith, and Bessie Rayner Parkes. In their various ways, all these did something towards bringing the untrained gentlewoman into the field of social work, and helped to make the concept of the woman doctor less alarming to the public mind. The impetus which carried Elizabeth Garrett and Sophia Jex-Blake through so many unwillingly opened doors was transmitted undiminished to the next generation—to such women as Jane Walker, Louisa Aldrich Blake, and Mona Chalmers-Watson. For these early women doctors and their immediate successors the social conditions of their time were, Dr. Gillie believes, a great stimulus. So, too, were the upsurging of the disfranchised sections of the community, and the movement for women's rights and opportunities. Opposition was a challenge to them, to which they responded "with all the zeal of their vigorous natures."

Women doctors today have no such violent stimuli to drive them onward. They are accepted, and what opposition to them remains is covert and localised. No vast intolerable social evils, no unbridgeable gulf between classes, stir up their chivalry. In school and university they have been given equal chances with their brothers. Yet the problems of the married woman doctor are in some respects harder of solution than those which faced the pioneers: it is seldom possible, nowadays, to hand over the management of home and nursery to well-trained and reliable deputies; there are financial complications, involving both rate of pay and taxation, when husband and wife are in practice together; and, as Dr. Mary Lennox said in a letter which we published last week, part-time employment is not as easily obtainable as it should be. Indeed, Dr. Gillie thinks that the problem of all married women's work, both inside and outside the home, is so large that it should provoke, in women, some of the energy of response shown by their forbears. Her address was a challenge to all who do not see that every gain should be a base for further effort.

NOMENCLATURE OF VIRUSES

Two main problems beset those who try to find the best method of naming viruses. The first is that of arranging viruses in their natural groups: this is fairly straightforward with, for example, pox viruses, where the relationship is clear, but it is extremely difficult with the many viruses which have still not been fully studied. The second and more intractable problem is whether viruses should be known by Linnæan binomials. There is still much debate as to whether they should be regarded as animalcules or as macro-molecules; recent researches on the mode of multiplication of bacterial viruses have revealed processes different from those of other micro-organisms. Most virologists would gladly have postponed the question of nomenclature until there was more fundamental information on the nature of viruses. Holmes,¹ however, introduced a system of Linnæan binomials which has thoroughly confused the situation; he classified them into genera mainly on such insubstantial grounds as their tissue affinities, and largely ignored their natural groupings. Nevertheless without an alternative system this classification might gradually infiltrate scientific literature and teaching.

Andrewes² has described the steps taken to meet this situation. At the International Congress of Microbiology in Rome last September it was officially decided to put forward non-Linnæan binomials to indicate the special character of viruses; such names could later be transferred to the Linnæan system under the International Code. The terms "genus" and "species" of the Linnaean system were deliberately avoided because they suggest taxonomic relationships, about which, so far as viruses

are concerned, we are still in the dark. The equivalents of generic names were formed by adding the suffix "-virus" to a suitable prefix. Thus, the virus of poliomyelitis would be styled *Poliiovirus hominis*; the viruses of smallpox and vaccinia, *Poxvirus variola* and *Poxvirus officinale*; and the viruses of the influenza group *Myxovirus*, to indicate the affinity of this group for mucins. This may prove a sound stepping-stone to a more firmly based classification.

AGRICULTURAL PROSPECT

F.A.O. continue to display clearly the problems before the farming communities of the world. In their latest report¹ predictions are given for food-production in 1956-57, if present national plans can be fulfilled. Many tables set out forecasts for the various crops in different regions, and some of the data may be summarised as follows:

*Predicted Food Production in 1956-57
(figures for 1934-38 = 100)*

World (excluding U.S.S.R., S.E. Europe, and China)	N.W. and S. Europe	America North	Latin America	Far East (excluding China)
Bread grains 128	107	148	126	124
Rice 128	—	—	—	123
Starchy roots 131	115	95	218	138
Milk .. 120	116	112	174	121
Meat 131	108	155	130	119
Population: 130	115	131	155	131

Most of the figures—especially in Asia—indicate an increase of food-production less than the corresponding increase of population, and no country can look forward with certainty or confidence to being able to do more than maintain present food-supplies. The figures for Western Europe certainly give no grounds for complacency, and they require emphasis in Great Britain at a time when rationing is virtually abolished and the activities of the Ministry of Food are being greatly curtailed. There are many cogent reasons which may justify these changes: that our problems of food-supply are solved is not one of them.

Most of the text of this report is taken up with discussions of details of regional agricultural developments. The need for more capital for investment in irrigation schemes, land reclamation, the prevention of soil erosion, and the supply of mechanical equipment is emphasised. Equally important is a supply of well-trained technicians and effective government services. Physical resources of power and machinery are valueless without the necessary will-power, knowledge, and enthusiasm wherewith to harness and drive them. It is suggested that, if sustained progress is to be achieved, far more attention may need to be given to investment in human resources. This means better education and health services.

1. The State of Food and Agriculture 1953. Part II: Longer Term Prospects. Rome: Food and Agriculture Organisation. 1954. Pp. 83. Obtainable from H.M. Stationery Office. 5s.

THE next session of the General Medical Council will open on Tuesday, May 25, at 2 P.M., when Sir DAVID CAMPBELL, the president, will deliver an address. The Medical Disciplinary Committee will meet on Wednesday, May 26, at NOON.

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The Wider World

OLD AND NEW IN NIGERIA CUSTOM, RELIGION, AND DISEASE

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Nigeria is more than four times the size of Great Britain and its 25 million inhabitants belong to many ethnic groups differing in customs and cultural background and in economic, political, and social development. The three main groups are the Yorubas and the Ibos in the Western and Eastern Provinces respectively of the south, and the Hausas in the north. With a population so diverse, the impact of western civilisation is bound to be varied, and the issue is further complicated by a variegated religious background.

Three Religions

The majority of the people of Nigeria are still pagans. In the north most of the inhabitants are Mohammedans, in the Western Provinces there are Mohammedans and pagans, and in the Eastern Provinces paganism is predominant. There are a few Christians throughout the country, but more are to be found in the Western and Eastern Provinces than in the north. Mohammedanism has made converts more easily than Christianity, for its tenets—especially its tolerance of polygamy—are more easily adapted to the African way of life.

PAGANISM

Pagans practise polygamy as a means of having a large number of children, but their moral code is strict and they strongly disapprove of fornication and adultery, as the following customs show :

Among the worshippers of Ogun god, it is believed that if a wife commits adultery and does not confess, the god would reveal her guilt by inflicting torturing bodily pains on her. A man of this sect, many of whom are hunters, will never commit adultery with the wife of one of his friends because if he did so his image and that of the paramour would be projected to the husband as a mating pair of deer. Should the husband shoot either animal, the guilty man or woman would die at once.

In some parts of Yoruba land, if a man sits on a seat just vacated by a married woman, or if he steps across the outstretched legs of a sitting woman, it is considered tantamount to adultery. There are parts of the country where it is unlawful to shake hands with a married woman; an offender would be sued for damages by the husband. The penalty for adultery varies from the sacrifice of animals to appease the local god, or payment of compensation, to forfeiture of liberty or life.

Pagans also value chastity, and a girl who is found to be unchaste on marriage loses caste.

One would imagine that with all these taboos promiscuity would be uncommon; but, despite them, concubinage is not unusual nor unrecognised, nor has polygamy prevented extramarital intercourse. The reason is not far to seek.

The usual custom is for each wife to sleep in turn with the husband for two to three nights. Sexual intercourse is expected on each of these nights. If the man fails, the wife feels that she is out of favour, or that she has done something wrong, or that one of the other wives is wielding evil influence against her. As a man grows older, he no longer finds it easy to satisfy the sexual needs of all his wives, particularly the younger ones. This often leads to unfaithfulness on the part of the wife especially if she is childless. The man himself becomes scared of impotence. He may experiment by having extramarital relations, feeling that a change might be helpful.

MOHAMMEDANISM

Mohammedanism permits up to four wives; but here again the moral code is strict.

The *Koran* says that if a woman is guilty of indecency, and four witnesses bear testimony against her, she is to be confined to the house for life or until she marries. The penalties for adultery are severe. Both guilty parties are flogged and are forbidden to have sexual relations with any but those who have been convicted of the same sin or with idolators. Mohammedan law protects the morals of female slaves, and sexual restraint and chastity are enjoined.

In the Northern Provinces, to prevent married women from coming in contact with strangers, houses are built with an entrance lodge, called *zore*, in which the owner or some other male member of the house sits. No-one can either enter or leave the house without his knowledge. Special quarters are set apart in the compound for the women, and no man is allowed near these apartments, unless accompanied by the owner of the house. On such occasions the wives are warned to stay in their rooms. Some of the wives are encouraged to take purdah and to accept the obligation never to go out during the day. Women are segregated from men during worship in the mosques and in day-to-day affairs.

But though Moslem law recognises adultery as a sin, yet it makes it difficult to punish miscreants because it requires four witnesses to render evidence valid.

Pagans and Mohammedans both regard polygamy as a means of curbing extramarital relations. And it must be remembered that according to their custom, coitus ceases with pregnancy, and no sexual approach should be made to a nursing mother until her child reaches the age of two or three years.

Another reason for polygamy is the arduous nature of household tasks, which includes the drawing and carrying of water often for long distances, the hewing of wood, and old-fashioned time-consuming methods of preparing maize and other staple foods. Often the housewife has to help on the farm. It is difficult for a nursing mother or a wife advanced in years to perform these duties; so, to lighten her tasks, she asks her husband to take another wife, and sometimes she actually carries out the negotiation herself to ensure that the new wife will be a help.

The urge to have many children to carry on the race and to help in the work of the farm is also strong among Africans. Without this urge it is doubtful whether the race would survive for infant mortality is high. In a rural district I lately found that a quarter of the children born to the women in the area died in infancy, and half died before the age of five years.

CHRISTIANITY

With colonisation came Christianity, and with Christianity the preaching of monogamy. The Christian belief in God was easily understood by the people because they already believed in God. But monogamy was foreign to them. To insist that, before he was baptised, a polygamist who adopted the Christian faith must cast out all his wives but one appeared contradictory to the Bible. Was Solomon with his thousand wives and concubines not a favourite of God? What of Abraham who, already married to Sarah, took his servant to wife? Practical difficulties arose. Should all wives be abandoned except one who was to be married according to English law? What was to become of the other wives and their children?

The insistence that a polygamous people should become monogamous has lowered their moral standard. Many converts who adopted monogamy in theory remained polygamous in practice. They kept mistresses, and this has introduced bastardy with all its attendant misery to a people to whom it was unknown.

Social Changes

Contact with Western civilisation has had profound effects on the customs and traditions of the people and on their social, economic, and political life. Education and travel are fast breaking old traditions and beliefs, yet nothing is being put in their place.

THE SLACKENING MARRIAGE TIE

The traditional respect for chastity is waning, though, as it is still important for a bride to be virtuous, promiscuity is commoner among married than unmarried women. Unhappiness in marriage, separation, or a childless marriage are causes of moral laxity among married women. Yet divorce is not encouraged. Whenever there are strained relations between husband and wife, every effort is made by the relatives on both sides to settle the disagreement.

The African woman believes that her primary duty in life is to bear children. As soon as she marries she expects to conceive during the first month. If after two or three months of marriage she is not pregnant, she becomes worried and her own and her husband's parents become anxious. If after a year or so she is still sterile, she thinks that maybe her infertility is due to incompatibility or that something is wrong with her husband. She is tempted to try another man. A similar train of thought passes through the mind of the husband and he tries another woman.

The greatest tragedy that can befall the African is to be childless. No matter how wealthy or important he may be, if he is childless he becomes an object of pity to his friends, and of ridicule to his detractors. Fear of remaining childless has been a constant source of conflict among those who adopt the English form of marriage, and there is sometimes a tendency to delay marriage until the woman is pregnant. Often, young people married according to English law have to be reassured that infertility a month or two after marriage is not a sign of permanent sterility.

THE DRIFT TO THE TOWNS

Commerce and trade have extended considerably and have brought together people hitherto widely separated. Improved transport has accelerated the drift into sea ports and large towns, with their clubs, dance halls, beer and palm-wine gardens. None of these facilities have improved morality, and the people are not shown how to use their leisure time. Few of them have hobbies. Libraries, night schools, and cultural centres are scarce; playing-grounds and other recreational centres are only to be found in a few large towns. The short twilight all the year round does not give much time for outdoor recreation. Most offices close at 5 P.M.; by 7 P.M. it is dark. Consequently, most recreation is indoors.

Apart from the temptations of urban life, the movement of people from their home town itself tends to encourage promiscuity, for it removes them from the restraint of their tribal law and customs. Urbanisation and industrialisation have thus indirectly encouraged the spread of venereal diseases, which are now so common as to be almost taken for granted.

Statistics of the incidence of venereal disease are difficult to obtain. The few that are available are not accurate, but they give a fair indication of its extent.

According to the *Nigeria Medical Report* for 1940 11.9% of hospital inpatients had venereal disease; more than double the number of cases of malaria admitted. The total number of cases of venereal disease treated in 1940 was 65,018. In 1949-50 the number of patients treated was 81,153. This figure does not include patients treated by general medical practitioners, nor the patients treated by medicine men, quacks, and those who deal in the illicit sale of sulphonamides. And also the fact that it is mainly male patients who report for treatment.

ECONOMIC CHANGES

Contact with the Western world has altered the simple life of the people. Previously their needs were few and easily met. The help of a wife on the farm was of value to her husband, and her petty trading earned enough to clothe and feed herself and her children, and sometimes the husband as well. The importance of a husband to

his wife, apart from procreation, was that he represented the family and performed accepted and defined duties on important occasions such as funerals, weddings, or fetish celebrations.

But since the advent of modern civilisation, clothes and adornments have become expensive. Traditional ceremonies which once could be carried out for a few shillings now cost pounds. Though there has been rapid rise in the cost of living, there has been no adaptation of age-old customs and ceremonies to offset these changes; indeed some of the ceremonies have become more elaborate and much more costly. The petty trading of the wife no longer meets her needs. Her husband, to whom she now turns and who is already finding things difficult, cannot help. Discontentment reigns in the home, so that the wife is tempted to look to another man for help.

This same problem faces young girls, particularly in the large towns. As employment for women is limited, girls—especially those who have received some education and been brought up to improved living conditions—find it difficult to support themselves. Parents who have already had a struggle to pay school fees—there are no free schools in Nigeria—are unable to meet the demands of a grown-up daughter while there may still be other younger brothers and sisters at school. The daughter may therefore marry precipitately or succumb to temptations.

DOWRY AND BRIDAL PRICE

In almost every part of the country it is customary for the man to pay a dowry for his future wife. The amount varies according to the wealth of the girl's parents, and the social status and beauty of the girl. Some twenty-five years ago the sum used to range from 50s. to £15. Today in some parts of the country a dowry amounts to from £100 to £200. The system has been commercialised. In some places, for example, the lighter the colour of the bride's skin the higher the bridal price. A higher dowry is asked for an educated girl than for an illiterate girl. Young men find it difficult to pay the high dowry prices and all sorts of subterfuges are resorted to which lead to immorality. At the moment public opinion is rising against high bridal prices, and many local authorities have either stepped in or have appointed committees of inquiry to stop this inflationary tendency.

Aids to True Civilisation

The only way to remove ignorance and superstition is to educate the people and to change undesirable customs. The old are set in their ways, and though there are a few night schools and attempts are being made at adult education, these changes are more likely to be achieved by the education of the younger generation. Yet few Nigerian children have the chance of going to school. There are about $6\frac{1}{2}$ million children in the 5-14 age-group and only about 1 million attend school. Of these only about 3% ever receive secondary education. There is no free education; fees have to be paid to the missionary schools, and in the few government schools. Thus young people are allowed to grow up in ignorance and superstition or are given an education which only leaves them bewildered, unable to fit into the old or the new pattern of life. They tend to drift to the towns.

The place of women in the community is still low, and very few of them receive any education. The proportion of girls to boys receiving education in the country is 1 : 4, and the proportion is even lower in the Muslim north.

The value of social services in combating social evils is undoubtedly, but in Nigeria only about 3s. a year is spent per head on social services compared with about £29 per head in Britain. An expansion of this form of Westernisation would offer Nigeria a more helpful view of the Western way of living.

Special Articles

REGIONAL HOSPITAL BOARDS AND BOARDS OF GOVERNORS OF TEACHING HOSPITALS

THE Minister of Health has appointed the following as chairmen of boards. Chairmen appointed for the first time are indicated by an asterisk.

South West Metropolitan Regional Hospital Board.—A. G. Linfield, O.B.E., J.P.

Oxford Regional Hospital Board.—Sir George Schuster, K.O.S.I., K.C.M.G., C.B.E., M.C.

Birmingham Regional Hospital Board.—V. M. Grosvenor, LL.B., J.P.

United Newcastle upon Tyne Hospitals.—Robert Muckle.

United Leeds Hospitals.—Sir George Martin, K.B.E., J.P.

United Sheffield Hospitals.—A. Ballard.

United Cambridge Hospitals.—Thomas Knox-Shaw, M.C., M.A.

United Oxford Hospitals.—Sir David Lindsay Keir, M.A., LL.D.

United Bristol Hospitals.—* Colonel H. Bland Stokes, M.B.E., B.A., J.P.

United Cardiff Hospitals.—* Alderman Thomas Evans.

United Birmingham Hospitals.—Evan A. Norton, M.A.

Royal Hospital of St. Bartholomew.—Sir George Aylwen, B.T.

London Hospital.—Sir John Mann, B.T.

Royal Free Hospital.—Geoffrey Bostock, F.C.A.

Eastman Dental Hospital.—* A. D. Page.

University College Hospital.—Sir Alexander Maxwell, K.C.M.G.

Middlesex Hospital.—Colonel J. J. Astor, M.B.E., D.LITT., J.P.

Charing Cross Hospital.—Lord Inman, P.C., J.P.

St. George's Hospital.—Sir Malcolm Trusram Eve, B.T., G.B.E., M.C., Q.C.

Westminster Hospital.—Lord Nathan, D.L.

St. Mary's Hospital.—Anthony G. de Rothschild.

Guy's Hospital.—Lord Cunliffe.

King's College Hospital.—The Marquess of Normanby, M.B.E.

St. Thomas's Hospital.—Sir Arthur Howard, K.B.E., C.V.O., D.L.

Hammermith, West London and St. Mark's Hospitals.—

Sir Desmond Morton, K.C.B., C.M.G., M.C.

National Hospital for Nervous Diseases.—Sir Ernest Gowers, G.B.E., K.C.B.

Royal National Throat, Nose and Ear Hospital.—Ernest E. Taylor.

Moorfields, Westminster and Central Eye Hospital.—

Lord Luke, D.L., J.P.

St. John's Hospital for Diseases of the Skin.—J. A. M. Ellison-Macartney.

Royal National Orthopaedic Hospital.—Sir H. R. Kincaid Floyd, B.T., C.B., C.B.E.

National Heart Hospital.—J. M. Oakey, M.C., D.L., J.P.

St. Peter's, St. Paul's and St. Philip's Hospitals.—Laurence Bevan.

Royal Cancer Hospital.—Sir Edward Cripps.

Queen Charlotte's and Chelsea Hospitals.—A. J. Espley, C.B.E.

MEMBERS OF BOARDS OF GOVERNORS

The following doctors have been appointed to boards. They will hold office till 1957. New appointments are indicated with an asterisk.

St. Bartholomew's Hospital.—George Graham, C. F. Harris, J. B. Hume, * E. G. Tuckwell.

London Hospital.—Victor Lack, Victor Dix.

Royal Free Hospital.—Gladys Hill, Katharine Lloyd-Williams, A. Margaret McPherson.

University College Hospital.—S. Phyllis Griffiths, Charles Wilcocks, * W. Bentley Purchase, * Wilson Smith.

Middlesex Hospital.—Alan Kekwick, R. W. Scarff, Philip Wiles, * H. L. Marriott.

Charing Cross Hospital.—Ernest Grundy, E. C. Warner, * D. H. Campbell, * C. Jennings Marshall, * A. G. Everard Williams.

St. George's Hospital.—P. J. Jory, * Rodney Smith, * C. Bowdler Henry.

Westminster Hospital.—A. Lawrence Abel, E. P. Brockman, H. E. Harding, R. J. V. Pulvertaft.

St. Mary's Hospital.—Sir Zachary Cope, A. G. Cross, Robert Cruickshank, L. H. Morris, S. L. Simpson, * G. B. Mitchell-Heggs.

Guy's Hospital.—J. M. H. Campbell, Sir William Kelsey Fry, O. Gayer Morgan.

King's College Hospital.—W. Ingleden Daggett, Brigadier H. L. Glynn-Hughes, Sir Cecil Wakeley.

St. Thomas's Hospital.—J. R. Dickinson, T. P. Kilner, Sir Max Page, * A. J. Wrigley.

Hammersmith, West London and St. Mark's Hospitals.—Sir Allen Daley, Cuthbert Dukes, Sir Francis Fraser, R. Cove-Smith, * G. B. Wood Walker, * Maurice Ewing.

The Hospital for Sick Children, Great Ormond Street.—Denis Browne, Sir Allen Daley, Eric Lloyd, George Newns, Bernard Schlesinger.

National Hospital for Nervous Diseases.—Sir Russell Brain, * J. St. Clair Elkington, * Michael Kremer.

Royal National Throat, Nose and Ear Hospital.—James Hogg, G. H. Howells, * S. E. Birdsall.

Moorfields, Westminster and Central Eye Hospital.—Frank Elliott.

Bethlem Royal and Maudsley Hospitals.—C. P. Blacker, * J. M. Mackintosh.

St. John's Hospital for Diseases of the Skin.—R. T. Brain, S. Cochrane Shanks, * Janet Aitken.

Hospital for Diseases of the Chest.—R. C. Brock, J. L. Livingstone, V. C. Thompson, * Kenneth Robson.

Royal National Orthopaedic Hospital.—C. H. Lack, J. R. Nassim.

National Heart Hospital.—H. A. Bulman, T. F. Cotton, Sir Francis Fraser, Basil Parsons-Smith.

St. Peter's, St. Paul's and St. Philip's Hospitals.—A. R. C. Higham, H. P. Winsbury-White.

Royal Cancer Hospital.—P. E. Thompson Hancock, J. H. Hunt.

Queen Charlotte's and Chelsea Hospitals.—A. Goodwin, Charles Newman.

Eastman Dental Hospital.—Brigadier R. A. Broderick, Sir William Kelsey Fry.

United Leeds Hospitals.—Digby Chamberlain.

United Sheffield Hospitals.—John Wilkie, * E. G. MacKie.

United Cambridge Hospitals.—Janet Bottomley, A. S. H. Walford.

United Oxford Hospitals.—A. D. Gardner, Gordon Scott, J. C. Scott, Janet Vaughan.

United Bristol Hospitals.—R. J. Brocklehurst, * L. E. Claremont, * G. L. Feneley, * T. F. Hewer.

United Cardiff Hospitals.—* Leonard Howells, A. G. Watkins.

United Birmingham Hospitals.—* Beatrice Wilmott Dobbie, * F. A. R. Stammers, * A. B. Taylor (until March 31, 1955).

United Manchester Hospitals.—F. C. R. Ferguson, W. I. C. Morris, Sir Harry Platt.

United Liverpool Hospitals.—W. M. Frazer, C. A. Wells, * J. Cosbie Ross, * H. H. Stones.

Medicine and the Law

An Unhappy Case

NOTWITHSTANDING what was justly praised as the magnanimity of the plaintiff, the recent action of Storie v. North East Metropolitan Regional Hospital Board and O'Malley¹ may suggest to the medical profession that the administration of justice can on occasion produce a singular result.

The plaintiff, Mrs. Storie, was claiming damages for the death of her husband, which she alleged to be due to the negligence of Mr. E. E. O'Malley, M.S., who at the material date was part-time senior surgical registrar at the Prince of Wales's Hospital, Tottenham. The deceased, who had been successfully treated for a varicose ulcer early in 1951, underwent an operation for a varicose vein on Feb. 11, 1952. No complaint was made against the surgeon who operated or against the nursing staff. The hospital board was dragged into the case on the ground of its vicarious responsibility in law for the actions of Mr. O'Malley. The plaintiff's counsel told the jury that,

1. *Times*, April 28, 29, and 30, and May 7, 1954.

after the operation in February, Mr. Storie was allowed to go home. He was examined by Mr. O'Malley at the hospital on Feb. 15 and again allowed to go home, with a direction to report on Feb. 18. He returned accordingly on the 18th, but he collapsed outside the hospital and died. The alleged negligence, on which the widow's case rested, was, according to her counsel's opening statement, this: a clot formed in the ligatured vein had been dislodged by sepsis and had travelled to the heart. The sepsis, according to the evidence of the pathologist who made a post-mortem examination, was so gross that it must have been readily discernible at the examination on the 15th. Counsel contended that Mr. O'Malley had examined the patient so carelessly on the 15th that he failed to observe the signs of sepsis.

Evidence in support of the claim was given by Dr. Alfred Piney, pathologist to the East Middlesex coroner. He described what he found at the necropsy—a little reddening of the skin round the stitches, and in the right groin some enlarged glands four or five times their normal size. The latter would have been palpable on Feb. 15. It was universal medical knowledge that, if sepsis was present, there was a risk of a clot coming loose and increasing in size. In cross-examination he agreed that the presence of a clot could be silent, almost symptomless and painless, and that its movement might be quite sudden; he accepted the authority of Mr. Harold Dodd for the view that glands were frequently found enlarged to four or five times their normal size after an operation; he agreed that, since the war, the greater proportion of surgeons were in favour of ambulatory treatment after most operations. In answer to Mr. Justice Stable he said that ambulatory treatment after this particular operation was a recognised practice; it would have been properly prescribed if there were no sepsis. Mr. O'Malley, giving evidence in his turn, said that on Feb. 15 he tested for the presence of a blood-clot and found no sign of one, nor was there any sign of sepsis; from his examination he considered that the patient was going on absolutely as expected; it would have been a bad thing to put him to bed. Captain J. E. Bridger, senior house-surgeon in the hospital casualty department at the time, gave evidence of having conducted the operation on the deceased and of having been present when Dr. Piney made the post-mortem examination. He said he had seen no sign of sepsis at the latter. As for the operation, it was a routine matter; nothing stood out in his memory about it. The learned judge brought out this point in a homely way:

"Is the effect of your evidence this, that you could not remember the sort of shave you had that morning, but, if you had cut off the end of your nose that day, you would have remembered it?"

"Yes, my lord," answered the witness.

Mr. Harold Dodd, another witness for the defence, was asked by the judge whether in the handling of the case by Mr. O'Malley there was anything which he himself would not have done, or anything he would himself have done which Mr. O'Malley omitted. He replied that the patient was well cared for. Patients under his own care were not seen for a week after the operation. The facts in evidence, he said, ranked as a good standard of supervision.

The learned judge, summing up to the jury, observed that the plaintiff's allegations depended simply and solely on the evidence of Dr. Piney. Mr. Dodd, he remarked, had "demolished Dr. Piney's evidence with one blow of the axe"; he had said he had no doubt that the glands had been swollen, because that was exactly what one would expect in the existing conditions, but that had absolutely nothing to do with the embolus which caused death; moreover Mr. Dodd had said that, in his own experience, where patients had died of an embolism there had never been any warning beforehand. The

abbreviated account of the summing up as reported in the daily press is necessarily incomplete, but it may appear somewhat surprising to the medical profession that the claim, in face of the evidence and the judge's view of it, was ever allowed to get to the jury. Get to the jury, however, it did, and with the unfortunate result that, after deliberation lasting for more than an hour, the foreman had to report that they disagreed and were unlikely to reach agreement. He regretted putting the court to such inconvenience. As the learned judge pointed out, it was not the court but the parties who would suffer.

A re-trial having inevitably been ordered, the case came on again a week later. There was then an unusual development. Mrs. Storie's counsel informed the court that, on the previous occasion, while waiting for the jury's verdict, she had expressed to him the hope that she would lose the case; having heard the evidence, she was satisfied that there was no ground at all for her complaint against Mr. O'Malley. He applied for leave to discontinue the action, which naturally was given. The judge complimented Mrs. Storie on a magnanimity unusual in a plaintiff, and added that Mr. O'Malley emerged from the case with his professional reputation not only unimpaired but enhanced. The court then made an order for the plaintiff's costs to be paid under the Legal Aid Act. If any other practitioner desires to have his reputation similarly enhanced, notwithstanding the disturbance to his professional work, the Act can provide the means; the State will pay an impecunious plaintiff's expenses and the lawyers and witnesses will do their best; if a patient has died, there is always the chance that a juror will find that it was somebody's fault. Should those comments sound too petulant, they are not very different from others which have been made on high judicial authority. If the position is unfair, what is the remedy?

Public Health

Statistics of Occupational Mortality

THE Registrar-General has published this week the first official statistics relating deaths to occupations for England and Wales since those prepared for the years 1930-32. The figures link men's occupations with the rates at which they, their wives, or their children die at various ages and from various causes. This volume¹ is the forerunner of a major study in the regular series produced after each census; the numbers in each occupation are based on the 1% sample results of the 1951 census, and the deaths and their causes are derived from the experience of the year 1950. To minimise sampling errors, figures are mainly restricted to the five "social classes" (I, professional; II, intermediate; III, skilled; IV, partly skilled; and V, unskilled). For some tables, however, these groups are sub-divided to show, for example, mineworkers, clerical workers, transport workers, agricultural workers, and others. The analysis includes infant and maternal mortality, still-births, and the mortality of occupied and retired men and married women, according to social class. Certain other factors, such as the type of area in which people live, have also been introduced in some of the tables.

In earlier years the mortality-rate among men under 65 rose from social class I to V, but the new figures show a low mortality in social classes II and IV. For some diseases, however, notably pneumonia, bronchitis, cancer of the stomach, and gastric ulcer, mortality increases steadily from social class I to V, while mortality from leukaemia, coronary heart-disease, and appendicitis falls from class I to class V. The decline of over 60% in infant mortality since 1921 is reflected to an almost equal extent in all social classes and the rising gradient of infant mortality from class I to class V has shown practically no change in the last 30 years.

1. The Registrar-General's Decennial Supplement, England and Wales, 1951, Occupational Mortality, Part I. H.M. Stationery Office. Pp. 75. 7s. 6d.

Some of the findings conform to the pattern of occupational mortality of 1930-32, but others show interesting changes which must await confirmation by a fuller analysis. But this volume will do much to make up for the gap of twenty years in our knowledge of these important statistics.

First Quarter in England and Wales

The Registrar-General's provisional figures¹ for England and Wales for the first quarter of 1954 show that for the first time since 1947 the number of births registered in the quarter is greater than the number registered in the corresponding quarter of the previous year. The total live births represented a rate of 16.0 per 1000 population, compared with 15.8 and 15.9 in the same quarters of 1953 and 1952 respectively. The infant-mortality rate was the lowest ever recorded in a March quarter—31.0 per 1000 related live births, compared with 33.8 in the first quarter of 1953. The stillbirth-rate increased from 22.5 per 1000 total births in the March quarter last year to 23.7 per 1000 in 1954. The death-rate was 14.1 per 1000 population, as against 15.8 in the first quarter of 1953, when influenza was widely prevalent.

1953 in Eire

The birth-rate in Eire decreased from 21.8 per 1000 population in 1952 to 21.1 per 1000 in 1953.² The infant-mortality rate last year was 39 per 1000 births registered—the lowest figure yet recorded. The death-rate of 11.8 per 1000 population was 0.1 less than the rate for 1952. The decline in the number of deaths from tuberculosis continues, and the total of 1190 deaths in 1953 was exactly half the figure for 1950.

Recognising Good Food

In British Columbia, health education is given an important place in the school curriculum, and a recent report³ tells of an effective method that is being used in many schools to emphasise to the children (and their parents) the importance of a good diet. Two pairs of rats are kept in school: the first pair are fed on a variety of food recommended in Canada's Food Rules; and the second pair have soft drinks, white bread, cake, and candies. After about 4 weeks the difference in weight, appearance, and disposition of the two pairs of rats is apparent.

1. Registrar-General's return for the week ended April 17, 1954. H.M. Stationery Office. Pp. 20. 1s.
2. Quarterly Return of the marriages, births, and deaths registered during the December quarter, 1953, and yearly summary, 1953. Government Publications Sale Office, G.P.O. Arcade, Dublin. Pp. 25. 6d.
3. Province of British Columbia. 40th and 41st Reports of the Medical Inspection of Schools for the years ended June 30, 1951, and June 30, 1952.

Infectious Diseases in England and Wales

Disease	Week ended April			
	3	10	17	24
Diphtheria	22	12	14	12
Dysentery	1642	1554	919	711
Encephalitis:				
Infective	2	5	1	2
Post-infective	4	2	1	1
Food-poisoning	178	107	89	85
Measles, excluding rubella	2330	2293	1914	2196
Meningococcal infection	39	43	24	34
Ophthalmia neonatorum	30	36	35	35
Paratyphoid fever	11	10	5	3
Pneumonia, primary or influenzal	529	518	452	478
Pollomylelitis:				
Paralytic	14	7	11	6
Non-paralytic	7	3	7	4
Puerperal pyrexia	245	275	185	232
Scarlet fever	1474	1375	1000	791
Smallpox
Tuberculosis:				
Respiratory	777	788	751	706
Meninges and C.N.S.	13	18	9	19
Other	90	95	102	94
Typhoid fever	1	6	1	1
Whooping-cough	2546	2474	1987	2135

In England Now

A Running Commentary by Peripatetic Correspondents

WE have had the builders in for some time now, hammering and bumping away, and we are beginning to show signs of what our French visitor calls "le Stress." The first thing to go was our internal telephone. It began insidiously, by doing little sums to itself, so that when we dialled 518 we got 629. Inspired by our statistician, we started doing our own little sums before we dialled, and for a time we had it baffled. But now when we lift the receiver we find ourselves in an echoing cavern populated by rattles and howls. We can occasionally identify the voices of our colleagues across the gulf, but our efforts to place ourselves in communication with them are vain. The other day the mad thought came to us that we would like to speak to Pharmacology, and we superimposed the appropriate number on the prevailing chaos. To our surprise there was immediate silence, and we could hear someone breathing heavily; "Hello," we said politely, "is that Pharmacology?" "Neither now nor at any time has it been Pharmacology," said a voice unpleasantly close to our ear, "this is the library basement. Why don't you get something done about your damned telephone?"

Nor is this all. Yesterday morning, just as we were passing the lecture-room, the rotary polisher broke away from the restraining hands of our industrious cleaner and made its way, lurching and growling, out of the lecture-room door to the hall, where it pinned the professor into one corner under the coat racks. Still kicking and buzzing spitefully, it was dragged off its prey by our resourceful secretary, and eventually silenced by cutting off the current, but not before a deep impression had been created.

Then there is the affair of the letter. We are used to receiving letters from overseas addressed to us at London, Oxford, or even London, Germany (we do not live in London), but until last week we had never had a letter addressed to us with the simple word "deceased" following our medical qualifications. It gave us quite a turn.

At last, however, we have an explanation of these occurrences. The builders have unearthed, from a cupboard scheduled for demolition, a small cardboard box labelled "Medieval teeth (St. Mildred's)." It is clear that St. Mildred is vexed with us for permitting all this banging, and we have put the box away carefully in the attic. It is too early to judge results, but the outlook is hopeful. One of our colleagues has just rung Anatomy and obtained the Post-mortem room, which is at least a near miss, and the epidiascope, after sulking for three weeks, is now working feverishly, and has set fire to a picture of Percival Pott.

* * *

I qualified at Durham, and I still remember the degree ceremony. Marshalled on a sunny July afternoon in the cool shadow of ancient cloisters, summoned ceremoniously into a chapter-house whose old wrought stones had watched ceremonies for nine hundred years, preached over in a vast nave dwarfed by pillars of primeval bulk, I felt at least that something obscurely significant was in progress.

Here in the great Metropolis (yes, I too have drifted from the mines) things are different. With much labour I have wrung from my new alma mater one of her lower doctorates, and she gave it to me the other evening. Some hundred-odd of us gathered in the middle of the square saucer that is the Beveridge Hall. Admiring relatives were terraced round us. The rainbow procession of dignitaries entered in all solemnity; but the bright efficient artificial light, the stern good taste of the furnishings, the air-conditioning, even the practised exactitude of the organisation, somehow spoilt the occasion for me. Only an incidental bishop seemed wholly happy in his fancy dress. There was much bobbing up and down of deans and doffing of caps to and by the vice-chancellor. We shuffled across in an endless belt, like pupils at a large school prize-giving.

It wasn't as bad as that really. Perhaps I was in the wrong mood. With a university as large as London,

something of the sausage-machine quality is inevitable, even in its higher-degree ceremonies. Why, of course, London University was ever allowed to reach its present ungainly incorporate bulk is another question.

* * *

What a rich language is our native tongue.

The other day while I was inspecting the underground medical equipment in one of the larger Yorkshire pits I met an old gentleman whose job it was, since an injury many years ago, to shovel the spilled coal back on to the conveyor-belt. Still wearing a leather spinal support he gave an energetic and dramatic reconstruction of his accident. With due solemnity, to impress the full gravity of his case, he told of his inability to take nourishment by mouth remarking: "They 'ad to feed me oop 'ill for fower days."

Early the next morning as I boarded a London train, I was approached by a transatlantic visitor holding a stamped addressed envelope in his hand. Plaintively he inquired of me the whereabouts of the "ledder dra-ap."

No wonder English-speaking men don't trouble to learn foreign languages.

* * *

Suffering, they say, is an ennobling experience. My illness was more of a humiliation, but it taught me a lesson more memorably than any textbook.

I was in a hot and sticky part of the Tropics, and one day, after lunch, I felt rather light-headed and staggered almost imperceptibly as I walked. My giddiness grew worse, and I lay down on my bed. In a little while I felt tired and unwell, my tongue stuck to my palate, and my eyes were blurred and heavy. Whenever I attempted to sit up gently, my dizziness became so acute that I was forced to flop back on to the pillow. My skin was dry and hot, and my limbs felt as if they were made of lead. I was barely able to take my temperature, which was 103·6°F, and my pulse was rapid.

During the rest of the afternoon and evening I slept fitfully. My thought processes were slow and confused; the only diagnosis compatible with blurred vision, staggering, and paralysis of the limbs was disseminated sclerosis, or so I argued. My future, so attractive in the morning, was a grim prospect by mid-afternoon, and I hoped I would have the stoicism to bear my disability with becoming fortitude. One of my friends who paid me a kindly visit suggested malaria, but I thought his diagnosis amateurish and said I'd see about blood films in the morning. However, he did give me some water for my parched mouth, for which I thanked him in a dysarthric voice.

During the night I slept well, and next morning I felt almost normal. I had postural hypotension when my feet touched the floor; my only other complaint was slight blurring of vision. Most welcome of all was the return of my normal powers of thought. I went down to the hospital and instilled eserine drops into each eye and my vision cleared in 7 minutes, confirming my hypothesis.

Before lunch on the day of my illness I had been dispensing a belladonna mixture, using the liquid extract; and, to assess how much flavouring agent to add, I had poured two small dashes of the extract on to the back of my hand and tasted them. I now have imprinted in my memory for all time the fact that the liquid extract of belladonna is 25 times as potent as the tincture.

* * *

The Old Lady of Threadneedle Street can be very old-ladyish. A friend of mine was invited to take part in a symposium in the United States, and, although his travelling expenses were being met, he naturally needed a few odd dollars for incidentals. He completed the necessary forms seeking permission to take some dollars with him and gave as the reason for his trip "To attend a Symposium." He received a strong negative from the Bank of England, and on making inquiries discovered that the word "symposium" was the stumbling-block. "Let's look it up in the dictionary," I suggested resourcefully. The first meaning given was "A drinking party."

* * *

Cause of Death

Surgeon: The patient died on the sixth day. He had had no operation or arteriogram performed. In other words death was spontaneous.

Letters to the Editor

PEPTIC ULCER IN UGANDA

SIR.—It would not be surprising if one could criticise on points of detail Professor Davidson's brief survey (March 20, p. 614) of so vast a field of inquiry as medicine in Africa. In drawing attention to one point I do not belittle the fairness of the whole presentation, but I do so because an important principle is involved.

Professor Davidson records that peptic ulcer, according to the information he culled in Africa, is relatively uncommon in Africans. In necropsies recently performed at Mulago Hospital, Kampala, Uganda, I have examined the stomach and duodenum of all cases with the following results:

In persons over the age of about ten, 42 (18%) out of 233 males and 3 out of 43 females had chronic peptic ulcers (38 duodenal and 7 gastric). Perforation had occurred in 2 duodenal ulcers. In spite of the lower average age at death of Mulago Hospital patients, this incidence is certainly not less than that recorded in necropsy series in more civilised countries.

Yet peptic ulcer is not commonly diagnosed here in life. The number diagnosed is increasing, but in only 4 of my cases was the presence of an ulcer suspected before death. There is no means of knowing whether Uganda is peculiar in this respect, but certainly the history given by an untutored African anywhere in the continent cannot be relied on to give even a pointer to many of his ailments. Thus, peptic ulcer may not be a *complaint* of Africans at present. But the morbid changes underlying the complaint may be widespread, and when advancement brings sophistication, leisure, wealth, and freedom from other diseases, the sufferers may indulge in their complaint and peptic ulcer may "increase."

In a similar way other benefits of civilisation are calculated to increase the apparent incidence of certain diseases in Africa. Increased expectation of life brings cancer and degenerative diseases in its train at one end of life, and congenital defects at the other. A mere increase in the number of doctors will bring other diseases into prominence, and so will the establishment of that hitherto rare activity, African domiciliary practice. Reliable vital statistics and universal certification of death will correct many misapprehensions about the incidence of disease.

Undoubtedly new disease patterns are introduced as a country changes its way of life. I am concerned here only to point out that these very changes will also reveal disease patterns already present but unsuspected, and to suggest that attempts to explain differences in disease incidence (whether geographical or temporal) should not be made on too narrow medical or genetical principles. Professor Davidson's article implies that he is fully aware of this possible fallacy.

Medical Laboratory,
Kampala, Uganda.

ALAN B. RAPER.

HAZARDS OF BROAD-SPECTRUM ANTIBIOTICS

SIR.—Your leader last week, commenting on the paper by Dr. Hay and Dr. McKenzie in the same issue, mentions that these workers reasonably said that broad-spectrum antibiotics should not be used for trivial and minor illnesses; and that we have to be more certain what is an appropriate case for their use.

This poses an almost moral problem for the dermatologist. Should these drugs ever be used topically in the treatment of the more easily curable cases of pyoderma, such as impetigo and superficial folliculitis barbae?

Wright and Tschan¹ and other workers have reported very favourably on the topical use of oxytetracycline

1. Wright, C. S., Tschan, D. N. *Arch. Derm. Syph., Chicago*, 1953, 67, 125.

OXYTETRACYCLINE IN PYOGENIC SKIN INFECTIONS

Type of infection and no. of cases	Infection clear within			Relapse after six months (no. of cases)
	7 days	14 days	Over 14 days	
Sycosis vulgaris (15) ..	3	3	5	4
Folliculitis barbae (21) ..	14	6	0	1
Impetigo (10) ..	13	3	0	0
Post-auricular dermatitis (12) ..	7	1	0	4.
Otitis externa (10) ..	3	2	0	5
Impetiginised seborrhoeic dermatitis (8) ..	6	2	0	0
Furunculosis (8) ..	4	3	0	1
Septic pompholyx (6) ..	3	3	0	0
Paronychia (5) ..	0	1	2	2
Infected atopic dermatitis (2) ..	2	0	0	0

Instruction was given that the ointment should be applied three times daily to all lesions; in sycosis, folliculitis, and furunculosis the ointment was applied to both nostrils twice daily for four weeks and to the skin lesions until completely healed.

(terramycin) in a wide variety of pyogenic skin infections. My experience is that oxytetracycline and aureomycin in ointment form are the most effective and rapid agents we possess in the treatment of this group of dermatoses, and like Peterkin² I have found oxytetracycline more certain in its effect than neomycin.

In the past fifteen months I have used an ointment of 3% oxytetracycline in a petrolatum base in a series of over 100 cases of pyogenic skin infection, and though a method of symmetrical paired comparison, with a control ointment, was not used it may be of interest to record my results, which are set out in the accompanying table.

Oxytetracycline achieved an excellent and swift response in 86 of these 103 cases, a proportion of which were unpromising seborrhoeic conditions. The one allergic flare-up occurred in a case of seborrhoeic otitis externa, a condition which is notoriously liable to reactions of this type.

Oxytetracycline and aureomycin, at present, work extremely well in most cases of pyoderma. Their employment will be widespread when they are generally released and the temptation to use them will be great. What guide should the practitioner be given, and what is the appropriate case for their use?

Hove, Sussex.

PATRICK HALL-SMITH.

THE BOMBS

SIR,—I do not think I misunderstood Dr. Alex Comfort. While accepting his right to describe himself as a medical sociologist if he personally considers that he possesses the necessary qualifications, I would nevertheless feel bound to question whether even a medical sociologist is entitled, still less obliged, to regard an attitude of neutrality the only possible one in the present tragic division of the world. Because we deplore the Cold War, we do not have to blind ourselves to the respective merits of the causes which divide the protagonists.

As long as the avowed object of international Communism remains the ultimate domination of the world, with the forcible destruction of all opposition by violence or treachery, it is hard to see how a member of a reasonably humane and liberal society, challenged by this particular form of tyranny, can conscientiously remain completely neutral. "Neutralism" is in this context a very favourable soil for the malignant, ruthless, and energetic efforts of Communist infiltration. We are therefore inevitably faced with the distasteful necessity of deciding on which side our principles demand that we stand. Dr. Comfort's own honesty of presentation compels him to reveal doubts as to whether Russian sociologists would be permitted to express opinions as critical of their own country's attitude towards atomic warfare, as those already publicly expressed by Lewis

2. Peterkin, G. A. G. *Brit. med. J.* Feb. 27, 1954, p. 522.

Mumford in the United States and quoted by Dr. Comfort in his letter. In fact, of course, Russian sociologists could not possibly express themselves publicly in any way contrary to the party line on this or any other matter. This is only one of the instances of the fundamental difference between tyranny and liberalism which it is the Communist's business sedulously to confuse.

Nevertheless there is no reason why Dr. Comfort should be confused by it; nor can I believe that he really is, although in his first letter he links McCarthy and Beria in a context which certainly implied this kind of confusion, possibly arising out of the determinedly neutral attitude at which he aimed. The essential difference, which once again exemplifies the fundamental contrast in attitude towards the value of human existence on the two sides, is surely this: McCarthy's aggressively intolerant and obnoxious behaviour has had to be displayed publicly and has inevitably led to a public inquiry, at which he has the right to call evidence and to defend his conduct, if he can, at the bar of American public opinion and constitutional procedure. Whatever the result of this inquiry, McCarthy neither stands to gain power of life and death over United States citizens comparable to that long exercised by Beria over the citizens of Soviet Russia; nor if discredited will he be executed or imprisoned for life. Beria on the other hand, for very many years held absolute power of life and death, including every measure of torture and intimidation between those two extremes which he or his organisation might choose. Moreover he exerted this over more than two hundred million people who had no hope of appeal to public opinion or independent judicial procedure. And this type of absolute despotism was, and remains, a normal part of Soviet political organisation. When it was Beria's own turn to disappear, his liquidation was as sudden, brutal, and entirely cynical as had been the fate of his innumerable victims.

For many of us who do not lack experience of psychology, criminology, nor of the other disciplines to whose authority Dr. Comfort appeals in expressing his own views, there is a necessary distinction to be made between the merits of the two "cultures in conflict" as he describes them. If Dr. Comfort himself is unable to choose between them, his dilemma is certainly an unfortunate one. But it is not one which inspires unbounded confidence in his sociological judgment.

Guy's Hospital,
London,
S.E.1.

D. STAFFORD-CLARK.

SIR,—I should like to support Dr. Comfort's opinion that, in respect of hydrogen-bomb hysteria, the present attitude-patterns of American society are more dangerous than those of Communist society; and I would go further and extend the American attitude-patterns in greater or less degree to the whole of the democratic West. This morbid condition, in accordance with the principles of psychiatry, may be attributed to an unresolved conflict within the collective mind arising from an attempt to live and think according to the incompatible philosophies of Christianity and secular humanism. The bombs have brought about something of a crisis in this unhappy relationship, since the Christian conscience repudiates the amoral materialism of which they are to date the latest product. On the other hand, the Christian notion of the bombs as instruments of divine judgment upon a sinful world is totally unacceptable to secular humanist presuppositions. Seeing little future in progress, but determined also not to fall on its knees, Western society finds itself in an impasse from which a complete smash-up may seem the only way out.

In Communist society, the conflict has been resolved, since the dominant party absorbs within itself the secular humanist tradition of which it may be a natural if not the inevitable fulfilment. All true Christians are at the

same time as explicitly, if silently, in opposition as when Tertullian contemptuously asked what Athens could expect to find in common with Jerusalem.

Dr. Comfort, if he remains true to the sentiments expressed in his broadcast talks in 1949, would presumably like to see a clear-cut rejection of Christianity by dominant opinion and a firm espousal of secular humanism as a means to mental health. I recommend the opposite course.

Darlington.

JOSEPH V. WALKER
Medical Officer of Health.

APPOINTMENT OF REGISTRARS

SIR.—In your issue of May 1, six senior registrar posts in various specialties are advertised by Guy's Hospital and the South East Metropolitan Regional Hospital Board. It is stated that preference will be given to applicants who have held a registrar post in the appropriate specialty in a teaching hospital.

In your journal, not very many issues ago, the question of junior staffing in peripheral hospitals was discussed and it was agreed that one of the causes of the dearth of applicants for such junior posts was just this tendency to select for the more senior teaching-hospital posts those doctors who were already working in teaching hospitals. Are we now to assume that the South East Metropolitan Regional Hospital Board desire to stimulate this drift from the "country"? One wonders how soon it will be before the other regions follow suit, if they have not already done so. It is also demoralising to speculate on the power of the "old school tie" philosophy in the regional boards, which blossoms forth in this type of prejudice against the non-teaching hospitals. What makes the position more depressing is the present policy of making all senior registrar posts on an exchange basis between the parent teaching hospital and a group of peripheral hospitals. This gives the teaching-hospital boards greater power than ever before to influence the appointments of all the senior-registrar posts in their region.

I suggest, Sir, that there is something dubious in this senior-registrar exchange scheme, and that it is made apparent by the prejudice expressed in these advertisements.

REGISTRAR.

TEXTBOOK ILLUSTRATIONS

SIR.—In his letter of May 8 Mr. Engel really raises two issues—namely, the supply of "opaque" photographs, which lend themselves immediately to textbook illustration; and sources of transparencies for teaching purposes. In relation to his suggested central library the two problems are slightly different in that the writing of textbooks generally represents individual effort, whereas teaching should have a common framework: these factors must influence the selection of material.

Even at the present time it is not difficult to view a reasonable supply of photographic prints of a given subject by contacting a number of photographic departments from which file copies are generally available. This is frequently done between departments informally, much to the surprise of medical staff who are unaware of this facility. Arrangements for specialised illustrative techniques may often be arranged on a similar basis.

As has been suggested by your correspondent, collections of miniature transparencies would be simple to establish and maintain. This has already been done in America by a commercial firm; slides being purchased from various departments after which they are duplicated and resold singly or in sets. The resulting turnover is reported to be in the region of 100,000 per year—obviously there is some demand for this service!

Westminster Hospital Medical School.
London, S.W.1. PETER HANSELL.

PROLONGED ANURIA

SIR.—We were interested in the discussion on the management of prolonged anuria by Prof. Scott Russell and his colleagues in your issue of May 1.

We have recently treated 3 similar cases on the same lines and by the infusion of hypertonic dextrose solution into the inferior vena cava via the saphenous vein at the groin. One of us has used this method of intravenous infusion for some years in all cases where difficulty in maintaining the infusion has been anticipated—for example, while operating with a steep Trendelenburg position.

In addition to the merits of this method of infusion mentioned in the article, we prefer it because it seems to us technically easier than infusion into the superior vena cava and also because it is appreciably more comfortable for the patient when infusion must be continued for some days. As regards technique, we do not consider it necessary to ligate the main tributaries at the upper end of the saphenous vein; we merely ligate the distal end. Similarly, we find that a gauze pad and 'Elastoplast' gives quite adequate pressure both during infusion and when the catheter is removed.

GAVIN SHAW
JAMES MAIR.

CLINICAL TESTS FOR KETONURIA

SIR.—We regret that Dr. Archer and Dr. Lehmann (May 1) were misled into thinking that we wished to deify the method of discovering ketonuria used hitherto. Our comments were directed towards the quantitative interpretation of essentially qualitative clinical tests. Our paper was not intended as a contribution to chemical pathology but rather to the use of these tests in clinical practice.

Dr. Archer and Dr. Lehmann do service to the historical aspect of the subject in drawing attention to the important papers by Kennaway and Hurtley. One of the latter's most important contributions to the Rothera test was his demonstration of the sensitivity of the test to aceto-acetic acid, which was unknown to Rothera. Hurtley's own test, however, is not used in clinical practice.

Although the concentrations of aceto-acetic acid and acetone in urine have been well known for many years, the numerous variations in technique in performing the clinical tests have, we believe, prevented a uniform interpretation in clinical practice and have made a standardised procedure desirable.

We set out to compare the two classical tests with the tablet test, we made it clear that our sensitivity tests corresponded to those of previous workers, and we referred readers to the review by Friedemann.

It is true that Kennaway's "slow-weak" reaction and similar reactions have been regarded as of no clinical importance by some clinicians. We considered this point and concluded that the significance of such results is still not clear. It is a dangerous assumption to regard them as of no clinical importance until more is known about the problem. A positive test for ketonuria should always be assessed in relation to the clinical state of the patient.

Our references to various textbooks were intended not so much as a criticism of the methods described as an illustration of the various descriptions which are current.

We agree that when Gerhardt's test is performed, as described by Harrison, it is usually adequate. We believe, however, that many nurses and clinicians throughout the country do not practise thorough boiling in a boiling-tube or open vessel. Indeed, we are certain that many of them possess neither a boiling-tube nor a beaker.

Dr. Archer and Dr. Lehmann conclude that because the tablet test is a "dehydrated," less sensitive Rothera test it has no advantages in the laboratory. We think that they should have more adequate reasons for what seems to us a hasty and illogical condemnation. We

agree that a rapid laboratory method for estimation of ketones is long overdue.

We fully agree with Dr. Kay (May 1) that dilution is often a useful procedure, which we have used from time to time. The use of a nitroprusside crystal is also convenient. We were concerned, however, to describe a standardised technique rather than to describe the many variations which can be usefully applied by those who prefer to develop a personal method.

Royal Free Hospital,
London, W.C.1.

JOHN NASH
JOHN LISTER
D. H. VOBES.

CONGENITAL PYLORIC STENOSIS

SIR.—The influence of heredity in pyloric stenosis is shown by those cases which occur in uniovular and binovular twins, and by family records such as that published by Dr. Carter and Dr. Powell in their article of April 10. In a pedigree which I described,¹ the disease

appeared in three generations of a family. Two males and two females were affected, and another female had otosclerosis (see accompanying figure). The diagnosis in all three generations was confirmed by operation.

One used to read in textbooks that the disease affected more males than females, in the ratio 9 : 1. Nowadays, it seems that more females are affected, and, in our experience, the ratio is 7 males to 3 females.

In very debilitated patients in whom medical treatment is given a trial, we do not persist with this treatment for more than 3 days. As a rule, we choose operation as the best and quickest means of treatment. We begin feeding the patients 6 hours after operation, and it is usually possible to send them home within 2 weeks.

Hilversum, Holland.

D. P. R. KEIZER.

JUVENILE SPRING ERUPTION

SIR.—The juvenile spring eruption affecting children's ears reported by Dr. Anderson and her colleagues in your issue of April 10, is not uncommon in that, as they mention, sporadic cases are seen by general practitioners and dermatologists in most years. Most practitioners usually seem to attribute it to a perniosis effect.

This "epidemic" in a holiday camp is similar to a minor one which I have just seen in a primary school at Windhill, Shipley.

At this school 25 boys were found to have such lesions on their ears. No girls were affected. The boys' ages were 8-11 years. All had developed the ear lesions between April 21 and 29, 1954. They were on Easter holiday over this period until April 29. The lesions varied in intensity from moderate (papules and vesicles) in 3 cases (12%) and mild (erythema and papules) in 14 (56%) to slight (erythema and scaling) in 8 (32%). Only 1 boy, aged 9, had had similar lesions on his ears each spring since he was 7 years old. Another boy thought the lesions might be due to his pet budgerigar playfully pecking his ears. None of these boys had lesions on the hands or elsewhere.

The weather during this period was cold and dry. Reports from the meteorological station at Lister Park, Bradford (2 miles away) showed that the winds were north-easterly from April 21 to 28, varying from light air to gentle breeze (2-9 knots). No rain fell during this time. The maximum thermometer reading was low for the time of year, varying from 45° to 56°F. The number of hours of sunshine per day was also low; it was zero on two of the days with much cloud, and the highest figure was 8.1 hours on April 28, when 7 (21%) of the cases developed.

Being on holiday, these boys had been out of doors most of the time. They had been bird-watching (modern term for bird-nesting), walking on the moors, playing football, cricket, or marbles, or out on bicycles. Many of them said that their mothers made them wear balaclava or leather helmets covering

the ears in cold winter weather, but they had worn no head-gear (or a cap only) during this spell. The district in which they live is well described by its name—Windhill.

I think this is an exposure dermatosis in which cold, in the form of prolonged exposure to cold winds, is a more important factor than the actinic rays suggested by Dr. Anderson and her colleagues. Moreover, apart from the protection afforded the girls by the long hair over their ears, they are more likely to stay indoors helping their mothers or to play in more sheltered places.

The reason for the age-incidence, 8-11 years, remains for conjecture; it may be that boys of this age have reached a stage of independence when they are more likely to remain outdoors longer than their younger brothers, but their ears are still more prone to perniotic influences than their older brothers.

I am indebted to Dr. G. Buckle, school medical officer Shipley, for calling my attention to this outbreak.

Royal Infirmary,
Bradford.

W. E. ALDERSON.

HASHIMOTO'S STRUMA LYMPHOMATOSA

SIR.—Dr. Cooke and Dr. Wilder, in their letter of May 8, say: "There is wide agreement about the histological changes in the thyroid—apart perhaps from how much fibrosis to allow before changing the name to Riedel's disease." This implies, though I doubt if that is what they intended, that the one condition can progress to the other. Clinically the distinction is clear, since Hashimoto's disease is confined to women of middle to late age and inevitably leads to hypothyroidism, while Riedel's disease occurs in both sexes, at all ages, and so far as I know never produces hypothyroidism. The degree of fibrosis in a section can do nothing to alter this distinction; and since in my experience neither condition is rare, I feel it is important to keep the separation clear. Diminution in size of the gland in Hashimoto's disease with oral thyroid medication does not seem to occur in later cases, presumably because of the increased fibrosis, and in these thyroidectomy in addition is still often called for:

London, W.1.

E. G. SLESINGER.

THE SAD TALE OF MRS. SMITH

SIR.—I am grateful to the Widdicombe File (May 1) for introducing me to "Our Rita" and her family. Her doctor says that she is a high-grade mental defective, but, if that is so, I do not think she has done such a bad job. Like Dr. Brewer I deprecate the fleas, the dirt, and the smell, though I doubt if these are directly attributable to the size of her family, for similar conditions may be found in quite small families. But Rita, on her allowance of £4 a week plus family allowances, keeps her family "surprisingly robust"—on the wrong kinds of food, of course. It must also be admitted that they wear ragged clothes, that they have no curtains, that their garden needs weeding, and that they have a television, but the garments are said to be adequate to keep them warm: nor are they unhappy. True, one of the children in the churchyard lies, but, when all has been said, there are no problem children or juvenile delinquents among the remainder.

Perhaps on £7 a week Rita and her husband should have had fewer children. As it is Rita leaves the Dutch cap and the spermicidal cream in the cupboard unused, and her husband, not too successfully it seems, still resorts to coitus interruptus. I fear I am like Rita: I cannot see that one method is very much worse than the other, though I repudiate both. At any rate, Rita and her husband do not appear to be heading for the divorce court. And there is still hope for her, because she is not going to be sterilised! I wonder how many children Rita should have had. Perhaps two. But if you told that to the five additional children who have

1. Keizer, D. P. R. *Pédiatrie*, 1952, 7, 1.

been born, I wonder what they would think of the Welfare State. I do not think they would be very pleased; and I for one would heartily agree with them.

Black Notley Hospital,
Braintree, Essex.

M. C. WILKINSON.

TUBERCULOSIS IN ADOLESCENCE

SIR.—In connection with this correspondence, the following figures may be of interest to your readers. Since January, 1952, all new boys in this public school (ages 13–14) have had a Mantoux test (1/1000). 418 boys have been tested. 140 gave a positive and 278 a negative reaction. In no case has evidence of an active tuberculous lesion been found.

Negative reactors are retested annually. Up to date 180 boys have been retested and only 3 of these have "converted."

SCHOOL MEDICAL OFFICER.

AVERTING POLIOMYELITIS

SIR.—The principles and sentiments expressed in Dr. Learoyd's letter of May 1 are admirable; but he is being over-optimistic to imagine that anyone is going to read such a long exhortation printed on a sheet of toilet paper.

Nobody—least of all school-children—will be bothered to read lengthy instructions. A short notice, printed in bold red letters, and fixed to the inside of the door so that it can be read in quiet contemplation would be far more effective, and cheaper.

Unless we all wear a kilt and no underpants I fail to see how we can comply with Dr. Learoyd's instructions, as they stand, and public decency!

Colchester.

D. W. BOATMAN.

LUPUS ERYTHEMATOSUS TREATED WITH PROGUANIL

SIR.—At a meeting of the Royal Society of Medicine,¹ the question was raised whether proguanil ("Paludrine") might be as effective as mepacrine in the treatment of lupus erythematosus.

A case of this disease was admitted to the Grove Hospital in October, 1952, and it was decided to try the effect of proguanil. The patient was a married woman of 45 years and gave a history of arthritis of hands and knees of 10 months' duration. She had the typical lesions of lupus erythematosus on face and hands, and the tips of some of the fingers were necrotic.

Lupus erythematosus cells were found in the blood, and the diagnosis was subsequently confirmed by the typical renal post-mortem findings.

Several days after the patient had been admitted and before the diagnosis had been established, sodium salicylate was given in large doses and the pyrexia subsided until the drug was discontinued, after a week, because of toxic effects. When the temperature had risen again to its previous evening level of 102°F, proguanil (0·1 g. t.d.s.) was administered. The general level of pyrexia subsided in three days, the evening temperature falling to approximately 100°; the proguanil was discontinued after a week and the evening temperature remained low, but it rose again four days later, falling again to normal the next day without treatment. A bout of pneumonia intervened and was treated with penicillin with good results, and a second attempt at treatment with proguanil was made in doses of 0·2 g. t.d.s. for four days with no response.

Mepacrine was also given to this patient for a few days with no effect, and she took her own discharge for Christmas. She was readmitted some days later and died shortly afterwards.

It was concluded that proguanil in normal doses had no effect on the course of the disease.

Grove Hospital,
London, S.W.17.

S. R. SIMS.

1. Hodgson, G. A. Proc. R. Soc. Med. 1952, 45, 713.

Parliament

N.H.S. Estimates

IN opening the debate on the National Health Service estimates on May 10 in the House of Commons, Mr. ARTHUR BLENKINSOP pointed out that though the Minister can truly say that his estimates this year provide for an increased capital allocation to hospitals of some 25% over the capital allocation last year, this percentage disguises a miserable total. It meant that on the £8 million allocation of last year there was an increase of some £2 million. But this modest increase did no more than partially redress the severe cuts made a year ago. It did not meet the real needs of the service.

Provision for revenue was even worse. The increase over last year was only about 3%. The extra provision in the estimates for the general running expenses of the hospitals was some £7½ million and the greater part of that would be swallowed by agreed salary and wage increases. He believed that we had reached the point when large expenditure on capital and maintenance would bring enormous economies. Many of our famous London teaching hospitals still worked in inadequate and outdated sanitary conditions. As places where capital grants were urgently needed he cited heating and laundry equipment. But he did not deny that there was room for economies as well as expenditure—for instance, by improving the system of hospital costing, reducing the employment of part-time specialists, and making fuller use of pay-beds.

In the future the chief need of the N.H.S., as Mr. Blenkinsop saw it, was for more effective co-operation within the service, and, with great respect to the Central Health Services Council, he did not believe that co-ordinating committees would get us far. "The danger is that we meet ourselves round the corner," he said, "for it is the same group of people, divided into twos, threes, fours or fives, which keeps meeting." Ideally, he felt, we needed a single health authority, but he believed we could make a start by linking the health executive councils and the local health authorities. Even more important was to improve actual physical contacts between the doctors in the different branches of the service. He believed that group practices could help a good deal, and he suggested that there should be some facilities for local-health-authority clinics to be held in the premises of group practices or at least that there should be some accommodation for health visitors or district nurses. But in working to achieve a new climate of co-operation within the service we must also think of the link between the service and the general public. We must encourage more and more people to understand the work which was being done. He believed that the service was capable of much more, not only by benefiting health, but also by encouraging a far greater understanding among the general public of how much we depend upon one another.

IS MORE ENOUGH?

MR. IAIN MACLEOD, the Minister of Health, pointed out that for the first time the true gross cost of the health service exceeded £500 million, at a total of £505 million. (The 1952–53 figures were distorted by the arrears of the Danckwerts award.) These figures showed a steady climb, since the first full year of the service, from a gross figure of £436 million and a net figure of £345 million.

Turning to the subheads which take this weight of expenditure, he explained that the increase of £1½ million in the general medical service reflected the increasing number of principals engaged. The pharmaceutical service remained more or less where it was. The general dental services showed an increase of £2½ million over the estimate for last year, but not more than £750,000 over the out-turn. An increase in the grants to local health authorities of some £1½ million was due in part, he was glad to see, to a genuine increase in the domiciliary services, particularly home helps and home nurses.

But the main issue of the estimates must be whether we were giving enough money to the hospitals and whether

the hospitals would be able to meet their main needs in the coming year. The estimate in the Votes came to £263 $\frac{1}{2}$ million, and there was available for allocation £265 $\frac{1}{2}$ million, taking the position of stocks into account. The estimate alone was £12 $\frac{1}{2}$ million above the out-turn for last year. He admitted that he had deliberately allocated less in proportion to the teaching hospitals than to the regional hospital boards. It might be a difficult year for many boards, but he felt that on the whole there was more scope for economy in the teaching hospitals and that, within the limits of what was available to him, it was right to be more generous to the regions. The outlook in the capital field was more encouraging than it had been for some time. On schemes up to the end of last year from the beginning of the health service, 20% of all moneys spent in the capital field went on ward accommodation; 17% on staff accommodation; 21% on special departments; 6% on outpatient departments; 4% on laundries and kitchens; 19% on engineering services; and 13% on other works. The policy of giving high priority to special departments had led to a greatly increased turnover of patients. For example, in 1952, 155,000 more patients were treated, which was a rise of 4·8%, although the number of beds available increased by no more than 1·4%.

Mr. Macleod was uneasy about making central allocations of capital expenditure. He was doing so in the mental-health field, and he was urged to do so for engineering. But the procedure if used too freely would take away from the autonomy of the regional hospital boards. Again, if he gave the impression that a fund was to be available for a particular service, such as the replacement of out-of-date and dangerous boilers, regional hospital authorities might come to think that they need not bother about financing any part of it out of their own budgets.

THE CHARGES

Disclaiming the title of "the apostle of charges in the health scheme" he gave on the whole a satisfactory account of their working. In the general dental service, the provision of dentures was running at about 2 $\frac{3}{4}$ million before the charges came in. They dropped almost at once to under 1 $\frac{1}{2}$ million, which was nearly half, and the figure had remained fairly constant since. In 1950-51 the number of applications for conservative treatment was less than 4 $\frac{1}{2}$ million; in 1951-52 it rose to nearly 5 million. In 1952-53, despite the introduction of charges, the number rose to over 5 million, and in 1953-54 to about 5 $\frac{1}{2}$ million. Within that increase, the number of children's courses, which was 170,000 in the last quarter of 1950, went up by 40% in the last quarter of 1951, 100% in the last quarter of 1952, and 150% in the last quarter of 1953. To complete the picture he added that school dentists had increased from 713 in 1951 to 945 in 1953.

Prescriptions dispensed were now about 213 million as against a peak of 225 million. The cost per prescription was down from the peak of 49d. to an estimated level of about 47 $\frac{1}{2}$ d. The cost to the Exchequer was £40 million as against a peak of £45 $\frac{1}{2}$ million, and the patients were paying about £6 $\frac{1}{2}$ million.

Turning to the Ministry's cost investigations, he said that they had selected four groups for investigation: the antibiotics, which were responsible for 20% of the total drugs and dressings bill; vitamins (5%); hormones (2%); and insulin (2%). The prices of penicillin and hormones had been reduced by the manufacturers themselves during the investigation—the cut in hormones was as much as 10%, which saved the Exchequer £50,000. He wanted to make clear, however, that he was conscious of the dangers of interfering with research, of the importance of the export trade, and even of the possibility that we might damage the structure of the industry itself. Of the 6000 proprietary preparations in categories 2, 3, and 4 of the Cohen report, the Ministry were investigating 91, which accounted for 30% of the total cost of proprietaries to the N.H.S., and 18% of the total drug bill. For each preparation, they were examining the profit margin and also the costs of production and sale. In one important group their investigations were now complete. They had not been able to reach agreement with the manufacturers on a reasonable level of profit, and they proposed shortly to advise the doctors

that satisfactory price arrangements had not been made and to ask them not to prescribe these preparations.

FAIR SHARES

His last main subject, he said, was the general-practitioner service. We had in the general-practitioner service 18,000 doctors of different ages and different outlooks, in different communities, with different backgrounds. It was impossible, and anyway wholly undesirable, to have uniformity. In anticipation of the financial arrangements coming into force on April 1, 1953, the number of doctors in partnership went up during 1952-53 by over 1000—an increase of 3·6%. A substantial share of the large number of doctors entering the service in 1952-53 went into the urban, under-doctored, designated areas, and the proportion of the urban population living in under-doctored areas had fallen from 60% in October, 1952, to 46% in July, 1953. The report of Sir Henry Cohen's Committee on General Practice was in his hands and it would be published shortly.

The estimate, Mr. Macleod thought, really raised two questions: was the sum too large or too little; and given the sum, was it being spent wisely? He thought criticism would centre on the first of these points. It was certainly true that the amount available was more than ever before. It was certain that if one took medical need alone as the criterion, we could justify expenditure vastly in excess of this estimate, vastly in excess of anything that any Chancellor could sanction or indeed that the country could bear. He had not tried to hide that it would be a difficult year for many hospitals, but the sum being spent was about £12 $\frac{1}{2}$ million more than the out-turn for last year. With that money we ought to be able to hold the line, to meet major needs, and to make some modest improvement, development, and advance.

SOME SUGGESTIONS

Mr. SOMERVILLE HASTINGS was grateful that the service had opened wide the gates of curative medicine to all the people, but had preventive medicine improved in the same proportion? Were not doctors more concerned with keeping people alive than with keeping them healthy? He also wondered whether the inpatient section of the hospitals had not been developing out of proportion to the outpatient facilities and home treatment. Many more people, especially old people and children, could be treated at home with advantage. As a possible money-saving device he suggested that consultants should no longer be paid travelling time and travelling expenses. At one small teaching hospital it was estimated that 18% of the consultants' fees were for travelling.

Sir HUGH LINSTEAD was dubious about the proposal to return the hospitals to local-authority control. It might be regarded as a betrayal of the old voluntary hospitals. Also the local-authority areas as redesigned would probably be so large that we would be in danger of getting away from real local control and interest.

Mr. HECTOR MCNEIL suggested that the apparent inclination of the public more and more to seek a remedy in the courts for alleged negligence in treatment led some general practitioners to shove a difficult patient off on to a consultant. The less the consultant found wrong with such a patient, the more likely he was to give him "all the works." These patients had the usual bacteriological and biochemical examinations, and a proportion of them found their way into beds badly needed for really sick people. He was not suggesting that it was improper for the public to find their remedy in a court, and above all he was not arguing that the medical profession should be given any particular protection; but he wondered if there could not be a neater and perhaps a quicker way—some form of tribunal, assisted perhaps by medical assessors as in the Ministry of Pensions—by which a remedy could be available to the public and about which the doctor would not feel so fussy or so nervous.

Commander T. D. GALBRAITH, joint under-secretary of State for Scotland, shared the general view that the service, although it might need tuning up here and there, was today doing a splendid job of work. One of the most important developments might well be group practice, and applications were being considered for grants from the £100,000 a year, set aside from the

national pool, for practitioners who wished to start a practice of this kind. The Government had no rigid preconceived notions of what constituted group practice : applications would be selected from those which held out most promise of improving the standard of service which the group of doctors would be able to offer. The health centres which had been set up were for experimental purposes, and he suggested that it would be wise to await development until it was seen how the present centres were serving the purposes for which they were intended.

He agreed with much that had been said in the debate on the importance of prevention. Local authorities were certainly not hindered by any limitations of their statutory powers, the scope of which, he felt, was too often underestimated by the authorities and their medical officers of health. For instance, a great deal could already be done for elderly people. In conclusion, he asked that in considering suggestions for administrative reforms it should be remembered that the structure of the service was called into being only six years ago, and that the task of the various boards and committees was one of great magnitude and complexity. It seemed to him that they were only now beginning to settle down. To suggest at this stage that they should be thrown overboard was short-sighted and precipitate.

QUESTION TIME

Hospital Board Changes

Mr. H. M. KING asked the Minister why he had not reappointed Dr. Stark Murray to the South West Metropolitan Hospital Board.—**Mr. IAIN MACLEOD** replied : In making this and other changes, I have followed the example of my predecessors in introducing new members at regular intervals to the boards, so as to widen the opportunity for service on them. **Mr. KING** : Is the Minister aware that this doctor has been one of the most capable and conscientious members of a very good hospital board ? Does he not agree that it would be a very bad thing if he determined the appointment of excellent men merely because they have been six years on the board ? Can the Minister assure the House that political considerations did not enter into this, since Dr. Stark Murray is a leading Socialist doctor and his successor is a leading anti-Socialist doctor ?—**Mr. MACLEOD** : If the hon. Member looks at not one instance, but at all the instances, and at other boards, he will know that there is no foundation for his suggestion.

Colonel MALCOLM STODDART-SCOTT : Can the Minister tell the House how many members of Parliament were originally appointed to hospital boards and to what political parties they belonged ?—**Mr. MACLEOD** : In the original appointments made to regional hospital boards, six members of Parliament were appointed. Subsequently the number was increased to nine, and, by a strange coincidence, all nine were Socialists.

Dr. EDITH SUMMERSKILL : Can the Minister tell us whether, before he made his decision, he was informed that this very able doctor was a founder member of the Socialist Medical Association ?—**Mr. MACLEOD** : I appoint people for medical and not for political reasons.

Mr. PETER SMITHERS : Can the Minister tell the House by whom Dr. Stark Murray was replaced, and what are his qualifications ?—**Mr. MACLEOD** : He was replaced by Mr. Lawrence Abel, one of the most distinguished surgeons in the country.

Unoccupied Pay-beds

Mr. SOMERVILLE HASTINGS asked the Minister what percentage of section v pay-beds were unoccupied.—**Mr. MACLEOD** replied : For the periods July to December, 1952, January to June, 1953, and July to December, 1953, the figures for non-mental hospitals are 34.5, 30.4, and 34.5 respectively.

Mr. HASTINGS : Does the Minister not agree that these figures show a terrible waste of beds ? Large numbers of waiting non-paying patients could quite well use these beds if the Minister would give instructions that they should be used, and such instructions were carried out.—**Mr. MACLEOD** : I did that in August last year, and the results of it are not apparent in these figures. I hope that they will substantially reduce the percentage of non-occupied beds.

Medical Rejections for National Service

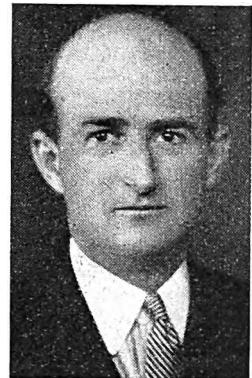
Replying to a question, Sir WALTER MONCKTON, Minister of Labour, said that the number for the first half of 1953 of National Servicemen medically rejected was 18,743.

Obituary

JOHN LOCKE LOVIBOND
T.D., B.A., M.D. Camb., F.R.C.P.

Dr. Lovibond, assistant physician to the Westminster Hospital, died on May 4 at the age of 47.

He was educated at Oundle School and Christ College, Cambridge, where he was an exhibitioner, and at the Middlesex Hospital. While at Cambridge he was president of the University Medical Society. He qualified in 1932 and later held resident appointments at the Middlesex, at Westminster Hospital, and at the Brompton Hospital. In 1934 he graduated M.B., and in the following year he obtained the M.R.C.P. With a whole-time grant from the Medical Research Council he returned to the Middlesex Hospital to work in the cardiographic department on the clinical value of chest leads, circulatory tests in left ventricular failure, and the problem of hydrothorax in cardiovascular disease which he chose as the subject of his M.D. thesis, in 1937. Later he held the post of medical registrar to Dr. Cockayne, and it was during this appointment that his gifts as a teacher became manifest.



[Lafayette]

Lovibond was a keen member of the Territorial Army, and at the outbreak of war he went to France as a regimental medical officer, and later served as medical specialist to a casualty-clearing station until the evacuation from Dunkirk. He was promoted officer-in-charge medical division of a general hospital, and for two years he had charge of the medical work in 35 B.G.H. in Iraq and Ceylon. In 1943 he was given command of that unit, and in the same year he was elected F.R.C.P. In 1944 he was in command of 38 B.G.H. in Burma, and later he acted as consulting physician 12th Army S.E.A.C. with the rank of colonel.

On his return to London after six years of Army service, Lovibond resumed his work with characteristic energy. For six months he was supernumerary registrar to Dr. Ward at the Middlesex Hospital, and he also held clinical assistantships at the Brompton and Middlesex Hospitals. In 1948 he had joined the staff of the King George Hospital, Ilford, and in 1946 he was appointed assistant cardiologist to the London Chest Hospital, Victoria Park. He was also physician to the Hostel of St. Luke for the Clergy.

At the beginning of 1948 Lovibond was elected assistant physician to Westminster Hospital, and he soon became a popular member of the staff. He was an excellent clinician with wide interests, but his special interest was cardiovascular disorders. His students will long remember his sound teaching and his interpretation of physical signs. He used his gift for drawing to illustrate his clinical findings, especially his X-ray screening observations. He wrote on many subjects, but one of his most important papers, published with Dr. Evan Bedford in the *British Heart Journal* in 1941, was on hydrothorax in heart-failure. He also published articles on clubbing of the fingers, picrotoxin in the treatment of barbiturate poisoning, and penicillin in cardiovascular disease.

Apart from his service to three hospitals, Lovibond found time for other interests. He continued to take an active part in the Territorial Army, and was M.O. to the 1st Regiment H.A.C. (R.H.A.). He was a keen horseman and rode in point-to-point meetings. On the morning of May 4 he paid his usual visit to the London Chest Hospital, and the news of his death came as a shock to his friends and colleagues, all of whom admired, and indeed envied, the energy with which he did his work. He will be greatly missed and he will always be remembered with affection.

Dr. Lovibond leaves a widow.

HARRISON STANFORD MARTLAND
M.D. Columbia

IN 1925 Dr. Harrison S. Martland, chief medical examiner of the City Hospital, Newark, New Jersey, published with his colleagues a paper in the *Journal of the American Medical Association* on Some Unrecognised Dangers in the Use and Handling of Radioactive Substances. In it they described some cases of profound blood dyscrasias, associated with necrosis of the jaw, in young women who had worked in the radium-dial painting industry during the first world war. The women had licked their brushes to point them and inevitably over the months ingested the radioactive paint in minute quantities. In 1929 Dr. Martland (together with Dr. R. E. Humphries) reported two osteogenic sarcomas occurring in young dial-painters, and in 1931 he published a longer discussion of the occurrence of malignancy in radioactive persons, again young dial-painters. These papers aroused great interest among haematologists, among those concerned with the experimental production of malignant tumours, and among those who had to provide protection against industrial hazards. Here was a physical agent, the alpha particle, capable of causing both blood dyscrasias and malignant tumours. The chances of exposure to such an agent were at that time slight. But in the early years of the late war those responsible for the Atomic Energy establishments were suddenly faced with the need to protect large groups of workers handling a wide variety of dangerous radioactive elements, often in considerable quantity. Few medical papers in the last few years can have been so often read and reread as those of Harrison Martland, and few can have had such a profound effect on governments and industry. In America Martland was naturally one of the men called in to plan protection for the U.S.A. Atomic Energy establishments.

The early effects of radiation on a population are now unfortunately known; the late effects are guessed, and the guesses are largely based on those early papers of Martland. Precise in description, vigorous in their warning of danger, exciting in their exploration of new scientific horizons, keen in their appreciation of the problems raised, they stand the test of time well. After the intensive study of the last ten years we can still add little to his description of the clinical effects and pathology of radiation injury as seen in the bone and marrow, and little has been added to his original concept of the pathogenesis of the disease. Words of warning written by him in 1925 and 1931 are echoed in current official manuals.

"From our experience it would appear that the intravenous injection of long-lived radioactive elements or the internal administration of radium . . . is not warranted in any medical condition. . . . This does not apply to the use of short-lived emanation."

"Some have thought that 10 µg. of radium deposited in the tissues of the body is probably just within the limits of tolerance. . . . My idea is that less than one-half of a microgram is dangerous."

The accepted permissible body burden of radium today is 0.1 µg.

He had lately completed his forty-sixth year as city pathologist for Newark, and in January the \$13 million municipal hospital which is now being built was named in his honour the Harrison S. Martland Medical Center. He died on May 1 at the age of 70.

WILLIAM LESLIE BURGESS

C.B.E., M.D. Edin., F.R.C.P.E., D.P.H., D.T.M. & H.

Dr. W. L. Burgess, professor of public health and social medicine at St. Andrews University, died at his home in Dundee on April 22 at the age of 68.

He was born in Aberdeen, and he took his medical course at Edinburgh, where he graduated M.B. with first-class honours in 1909. In 1911 he took the diplomas in tropical medicine and hygiene and in public health, and the following year he obtained the degree of M.D. with commendation. After holding public-health posts in Leith and in West Ham he went to Dundee in 1913 as chief tuberculosis officer. He was appointed medical

officer of health in 1918 and held this post until he retired from municipal work in 1951.

In 1917 he was appointed lecturer in public health in the University of St. Andrews at the Medical School in Dundee, and in 1930 he was advanced to a readership. About the time when he retired from his post as M.O.H. the university founded a chair in his subject, and he was appointed the first James Mackenzie professor of public health and social medicine. He retained a great interest in clinical work, and for many years he acted as physician in charge of the city's hospital for infectious diseases. One of his regrets was that the reorganisation brought about by the National Health Service largely isolated the public-health doctors from hospitals and sick people, and he strove for coöordination to allow of more interchange of work between the two services.

He was a member of the Eastern Regional Hospital Board and convener of its principal planning committee. His clinical experience and long acquaintance with the administration of hospitals and municipal medical services had given him clear ideas of what could be done, and how it could be best done, and with his help the board were particularly successful in extending the provisions in the region for the treatment of tuberculosis. He also served on a number of Government committees, including the Advisory Committee on Medical Research. He was appointed C.B.E. in 1944.

WILLIAM JAMES WILSON

B.A., M.D. R.U.I., LL.D. D.Sc. Belf., D.P.H.

Dr. W. J. Wilson, professor emeritus of public health in the Queen's University of Belfast, died at the age of 74 in his home in Belfast on May 6. He was a distinguished and devoted son of the university, with which he had been associated for over fifty years.

The son of Thomas Wilson of Strad Mills, co. Antrim, he was educated in Belfast at the Royal Academical Institution and the Royal University of Ireland—as it was then called. As an undergraduate he won many exhibitions and scholarships, and he graduated with first-class honours in arts and medicine and was awarded the gold medal for his M.D. thesis. After qualifying in 1905 he continued his studies in Berlin before returning to Queen's as Riddell demonstrator in pathology and joint lecturer in sanitary science.

He soon settled down to his life work in epidemiology and public-health bacteriology, and between 1906 and the first world war he published the results of numerous bacteriological studies. Even in those days he was interested principally in improvement of special culture and other diagnostic methods applicable to the endemic and epidemic disease of the Belfast of that period. Thus some of his earliest work was on improved culture methods for meningococci, and as early as 1907 he published his first paper on *Salmonella typhi*. He was active in work towards improving agglutination techniques, and in 1909-10 he reported the presence of heterologous antibodies in the sera of patients with meningitis and typhus fever. He demonstrated the power of the sera of typhus fever patients to agglutinate coliform organisms present in the urine of some typhus patients, thus anticipating the work of Weil and Felix by several years.

During the 1914-18 war, as a sanitary specialist in the R.A.M.C., he continued to work on bacteriological problems. He went on with his studies of cerebrospinal fever and typhus fever and he contributed much to the development of standard techniques appropriate to field conditions. His work on culture of anaerobic organisms contaminating wounds was particularly valuable.

Shortly after his return to Queen's he was given the title of professor of public health and he became bacteriologist to several public-health authorities. His appointment as director of water analysis to the Belfast Water Commissioners he held until shortly before his death. He was also consultant bacteriologist to the Government of Northern Ireland.

In 1921 he resumed his studies on the selective cultivation of intestinal organisms, and about this time he began with Dr. E. Maud Blair the work which led to the development of the Wilson-Blair bismuth sulphite typhoid medium, now a standard all over the world.

In his laboratories the *S. typhi* was first isolated from shellfish and sewage, and elsewhere other workers used the medium to demonstrate the organism in many substances such as seagull droppings. The first demonstration of the organism in drinking-water was made with its help, and Houston acknowledged that, although he and others had known that *S. typhi* must be in the water of the River Thames, he was able to prove his belief only after the work of Wilson and Blair.

His busy life in research did not prevent Professor Wilson from playing an important part in the administration of the university and in public affairs. He became a member of the senate and was an efficient and much loved dean of the faculty of medicine from 1928 to 1943. For twenty-three years he was a governor of his old school, and from 1942 to 1947 he was chairman of the board of governors. On his retirement in 1948 the university conferred on him the title of professor emeritus and in 1950 the honorary degree of doctor of laws.

Wilson was a shy and undemonstrative man, but his modesty of manner concealed a determined personality and strong convictions. He was extremely hardworking and persistent, and he loved bacteriology; so for many years he was consistently twelve and fourteen hours a day in his laboratory. But he always had time to give to students, and he was a friend to hundreds of the graduates of Queen's.

Professor Wilson is survived by his wife, a daughter, and three sons who are all doctors.

ERICH WELLISCH

M.D. Vienna, M.B.C.S., D.P.M.

Dr. Wellisch, director of the Crayford child-guidance clinic at Bexley Heath, has died at the age of 56.

After graduating at Vienna University in 1924, he worked at the Neurological Institute for a time, but though he maintained his interest in neurology he decided to specialise in physiotherapy, and he became chief physician to the institute of physical medicine at Margaretenbad.

He was one of the fifty Austrian doctors who were granted permission to qualify and practise in this country in 1938. After some years in general practice, Dr. Wellisch, at the age of 45, took up psychiatry, and during the war he was a medical officer at the Warwickshire and Coventry Mental Hospital. He was drawn to work among children, and he came to specialise in child guidance. Since 1947 he had been in charge of the Crayford child-guidance clinic.

E. S. and K. C. write: "Those who came to know Dr. Wellisch felt at once that here was a man with a sense of mission. He was serious, never casual, and always concerned to give of his best. This spirit permeated his clinic, where he was beloved by everybody. He was an excellent clinician and a scholar of great erudition. He had published a number of valuable articles on the problem of personality tests used in child guidance, especially the Rorschach test. In his theoretical orientation he was an independent who sought enlightenment from all schools. Lately he had given a great deal of thought to psychological study of biblical subjects, and in a posthumous book, shortly to be published, he set forth a highly original analysis of the story of the sacrifice of Isaac, which he viewed from the broad aspect of the parent-child relationship."

Dr. Wellisch leaves a widow and two children.

FRANK LLOYD HOPWOOD

M.A. Camb., D.Sc. Lond., F.Inst.P.

Professor Hopwood, consulting physicist to St. Bartholomew's Hospital, died on May 2 at the age of 70.

He was born in Cheshire, where his father William Hopwood was a mining engineer. He had a happy boyhood, but he was by no means pampered, and he often recalled how he used to walk several miles to school. From Hawarden Grammar School he went to the University College of North Wales at Bangor, and he continued his studies at the College of Science and at University College, London, where he was awarded the degree of D.Sc. Soon afterwards he was appointed assistant physicist to St. Bartholomew's Hospital. During the 1914-18 war his research for the Admiralty on detection of submarines, particularly on the vibration

caused by the propellers, meant hard and cold work on lakes, reservoirs, and the sea.

When he returned to Barts he was given charge of the physics department of the medical school, and appointed physicist to the hospital and a professor in the University of London. To his other duties he added those of vice-dean of the medical school, and in this capacity he migrated to Cambridge during the second world war, when the preliminary-science students were sent to Queens' College to continue their studies. While there in 1940 he was elected an honorary fellow of Queens'.

One of his special interests was radiology, particularly in connection with cancer, and he was a foundation member of the British Empire Cancer Campaign, and a member of its grand council as well as its honorary secretary. A former president of the British Institute of Radiology and the Röntgen Society, he received the Silvanus Thompson medal of the institute. For twenty-five years he was honorary secretary of the British Committee for Radiological Units. With Conti and Finlay he played a large part in the installation of the million-volt X-ray apparatus at Barts.

M. D. writes: "As a man, Hopwood was great in every way. Physically he was tall and broad-shouldered, with a resounding voice: mentally he was broad-minded and tolerant, and he had a great sense of humour. He had many friends and no enemies. He was ever ready to help anybody, be it the most junior student or the most senior consultant on the staff, and the British Empire Cancer Campaign owes much to his sound advice and zeal."

Professor Hopwood married in 1909 Helen Sproxton, of Wood Green, who survives him with one son.

MARGARET EVELINE PEAKER

M.R.C.S.

Dr. Margaret Peaker, an assistant medical officer in Middlesbrough school health service since 1947, died on April 27 at the age of 54. She was educated at Sydenham High School for Girls and at King's College Hospital where she qualified in 1928, and after holding resident posts at Sheffield Children's Hospital and the East Anglian Sanatorium she was appointed a school medical inspector for West Riding County Council in 1932. During the late war she served as a captain in the R.A.M.C. from 1942 to 1946.

A colleague writes: "Dr. Peaker was a very capable practitioner and particularly keen on the social side of her work. Her sunny disposition and interest in the individual ensured her popularity with patients and staff alike. During the last few years of her life she had frequent illnesses, but she worked on, with great fortitude, almost to the end. She leaves with her colleagues and her friends a pleasant memory of a real lover of children."

DR. H. P. JAMESON

T. C. H., who served with Dr. Jameson in Persia and Iraq, writes: "He was posted as a medical specialist to the Persia and Iraq forces in 1943, after having served for three years in India. He worked first at an Indian General Hospital at Kirkuk and later in the British General Hospital in Teheran, where he took a great interest in tropical eosinophilia and in the nutritional anaemias which he had studied in India. After his service in India he was anxious to be transferred to a more active theatre of war and serve in Europe. Instead he found himself again in Calcutta with a further spell of tropical work before him. He took this disappointment and further separation from home with calm philosophy and fortitude, and it was testimony to his fine spirit and sense of duty that he bore a genuine gratitude later to those above him who had used his tropical experience further. His work later earned him promotion to lieut.-colonel as o.c. medical division of a big general hospital. He set a splendid example of service and cheerfulness which showed at its best in Iraq and Persia where monotony and feelings of isolation and frustration were sometimes difficult to overcome. He enjoyed greatly the companionship of the Army, but it was the country and his family life at home which always took first place in his affections."

Notes and News

WORLD HEALTH ORGANISATION

In his opening address to the Seventh World Health Assembly at Geneva on May 4, Dr. M. G. Candau, the director-general, said that W.H.O. was now solidly established not only at headquarters but also in the regional branches, where it was engaged in the hand-to-hand struggle with disease. W.H.O. was continuing its policy of assisting each country to develop its own health services. Since its financial resources were limited, it could only stimulate health measures by means of demonstration projects, and coördinate international health work. Member countries could now depend more and more on W.H.O. for help in improving their epidemiological services. It was planned to continue the effort to develop rural health services and campaign for better sanitation and control of endemic disease. The time had come for W.H.O. to concentrate its efforts on long-term projects, but it could not embark on them if their fulfilment depended on financial resources which might not be forthcoming. Referring to the Asian Conference, with which the assembly is sharing the Palais des Nations, Dr. Candau said that, as doctors, they listened with anxiety to the reverberations, like an irregular heart-beat, of the deliberations affecting life or death, peace or war, for this world. He hoped that mankind would have the wisdom to decide once and for all that the only enemies worth fighting were ill health, poverty, and ignorance.

71 countries (68 member States and 3 associate members) are represented at the assembly, which is under the chairmanship of Dr. R. C. Bustamante, of El Salvador.

HEALTH CENTRES AT HARLOW

Most of the health centres hitherto built in this country, however instructive the lessons they may teach, are show places rather than likely prototypes; for the cost of reproduction in large numbers would be prohibitive. The Nuffield Provincial Hospitals Trust, once again allying an adventurous spirit with sober recognition of the feasible, is to sponsor the construction of three centres at the new town of Harlow, where it has already made possible the construction of a temporary centre, which was opened two years ago.¹

Strictly speaking, these new buildings will be, not health centres, but group-practice centres with clinics attached: in law a health centre must be owned by the county council and let to the local executive council, and ordinary N.H.S. general dental practice is not allowed; whereas in these three centres the doctors, dentists, and county council will be the tenants of the Nuffield Health and Social Services Fund, and a general dental service will be operated from them. The three centres, which will cost some £60,000, will differ from each other in minor respects, so that as much as possible may be learnt about design. Two of the three are to be one-storey buildings, while the third will have flats for health workers on upper floors. The centres will include accommodation for 2-4 general practitioners, local-authority clinics, health visitors, and district nurses; two centres will each accommodate two general dental practitioners, and in one of these there will also be a county dental unit for the treatment of children and expectant mothers. Since economy is an essential part of the scheme, the general practitioners and the county are to share waiting accommodation. One centre is to be immediately beside the site of the future Harlow Hospital, with the aim of providing a special link between all the general practitioners of the town and the hospital service. Harlow has two large industrial estates; and the Trust wishes eventually to secure the establishment, on an economical scale, of an industrial health service, in which the general practitioners shall play a full part. Thus Harlow may provide an example of a completely integrated health service.

In Harlow the Trust is assured of the coöperation of the general practitioners, the local executive council, the county council, and the development corporation (which is undertaking the building and management of the centres on behalf of the Nuffield Health and Social Services Fund). We should be grateful for such a realistic experiment; but only a small proportion of the population lives in new towns, and we should like to see the way made clear for further tests in other types of area.

1. See Taylor, S. *Lancet*, 1952, i, 253.

ADMINISTRATOR, DOCTOR, AND PATIENT

ADDRESSING the annual conference of the Institute of Hospital Administrators, held in Oxford last weekend, Lord Burden, the president, said that though doctors had a very important part to play in hospital administration it should be advisory and he did not think they should serve on executive boards and committees. Their training did not give them the art and science of administration, and as valued advisers they should be free from responsibility for the actual decisions.

Mr. P. H. Constable thought it inevitable that there should have been some change in the doctor-patient relationship under the National Health Service; but, though general relations had worsened somewhat, this was not permanent. In England (but not in Scotland) the doctor was the servant of the governing body; and Mr. Constable thought it might help if, in law and morally, the doctor was known to be fully answerable to the patient, whose servant he was, and not to the governing body. In America hospitals had a "chief of service" system: each branch (medicine, surgery, gynaecology, &c.) had a chief who convened meetings of all concerned with that branch at which the work done for the patient was discussed. British doctors showed less eagerness to undertake such discussions—and he was not saying that they should. "We are at fault as administrators," Mr. Constable said, "if we allow any meeting of the governing body to go by without some reference to the actual nursing needs of the patient." On no subject was it easier to arouse the interest and enthusiasm of administrators than in the welfare of the patient, and he felt a great deal of confidence in the future. Mr. A. F. Gray, who held that there is a place for doctors on administrative committees, said that the patient would not be happy if at the top there was antagonism in the trinity of secretary, matron, and senior medical staff. Mrs. Mary Ormerod believed profoundly in the lay administrator: the key lay in friendship between the lay administrative staff and the doctors. "You must do everything you can to give your young men and women the fullest education so that they can stand on an equality with the medical and nursing staff": their minds must be opened so that they had a sympathetic understanding of human problems.

Sir Allen Daley, speaking on coöperation between hospital and other services, said that the three branches of the N.H.S. are so interlocked, and the responsibilities are so arbitrarily divided, that the patient and the national health will inevitably suffer unless all concerned in its administration regard it as their first duty to ensure that no individual patient suffers. "Coöperation cannot be enforced by rule or regulation any more than agreement can be enforced by this method. Coöperation and agreement are personal factors and depend on the personalities and emotions of the people concerned. Personal contacts, professional and social, generally break down rivalries and antagonisms. People must meet, and, because of their joint responsibilities for the human needs of the patients, they will evolve, often by trial and error, the best methods of coping with the problems of the individual patients."

ROYAL DENTAL HOSPITAL

THE 37th annual clinical At Home of the Royal Dental Hospital was held last Saturday. The programme was as interesting and as varied as usual, and a Marconi closed-circuit television apparatus enabled large audiences to see the more important demonstrations in comfort.

A demonstration of great interest was that of the "air-abrasive" technique for cavity preparation. This method, first developed in the U.S.A., almost eliminates the use of the familiar—and dreaded—dental engine. No burr is used; instead a jet of aluminium oxide, with a particle size of 30 μ , is blown on to the tooth through a fine tungsten-carbide nozzle. The propellant is carbon dioxide, and a powerful electric suction fan withdraws the used abrasive from the cavity. The aluminium-oxide jet will not injure soft tissues, and the stream of carbon dioxide cools the tooth slightly and thus helps to avoid the thermal trauma to the dental pulp which sometimes occurs when a metal burr is used. The cutting process is reasonably fast, is free from noise and vibration, and is completely painless in at least 50% of patients; in only about 5% of cases is the pain really unpleasant. There are certain disadvantages—among them, the necessity for working with the cavity isolated by rubber dam and for using a conventional burr for the final stages. From the operator's point of view the feel of the handpiece is completely

different, but in practice this strangeness is soon overcome. Mr. G. E. Myers, who demonstrated the airbrasive method, said that all the patients on whom it had been used preferred it to the dental engine.

Dr. S. Blackman, the director of the X-ray department, gave a short talk on xeroradiography. This method, which is still in its infancy for medical and dental purposes but has been used in industry, especially in the U.S.A., for the last three or four years, obviously has a promising future. A metal plate, coated with amorphous selenium, is used instead of the usual film. This plate, protected by a cassette, is charged electrically in a special machine; it is exposed in the usual way, and the resulting electrostatic image is "developed" by sprinkling with a fine powder—one of the most successful, incidentally, is a well-known brand of baby powder. This electrostatic image persists for some six hours, and it must be recorded by direct photography if a permanent picture is needed. The whole process, including charging the plate (which may be used over and over again), takes less than two minutes, and the definition is that of a well-taken radiograph on the conventional silver-bromide emulsion. Dr. Blackman is now working on the problem of adapting xeroradiography to intra-oral work.

The only thing missing was the brains trust which has been such an entertaining and popular feature of the At Homes in the last few years. Perhaps this will return next year, when it would undoubtedly have a warm welcome.

HOSPITAL COOKING

Mr. Iain Macleod, the Minister of Health, addressing the Hotel and Catering Institute in London on May 3, said that he was looking to hospital authorities to give a lead in standards of cooking and kitchen hygiene. After paying a tribute to the high standards already achieved by many hospitals, despite "such tremendous problems as keeping food hot and fresh while it is transported over long distances through labyrinthine corridors to far-flung wards," he said that the national scheme recently approved for training apprentice cooks in hospitals was getting off to a good start. Some idea of the extent of catering in hospitals could be gained from the fact that in 1952-53 the cost of food in hospitals in England and Wales was over £30 million—or about an eighth of the total expenditure of the hospital authorities. In addition, the wages of catering officers, dietitians and other senior catering staff amounted to nearly £7 million. "We have recommended to hospital authorities," said the Minister, "that catering should be recognised as a separate department in the hospital's activities and should be in the charge of an officer suitably trained and of adequate status responsible to the chief officer of the hospital. My Ministry has on its staff dietitians on whom hospitals can call for advice on all aspects of catering. We also welcome the interest of the King Edward's Fund in this all-important subject."

University of Oxford

On April 29 the degree of B.M. was conferred on the following:

E. S. N. Hazel, D. R. Wright, M. P. Wright.

University of Cambridge

On May 1 the following degrees were conferred:

M.D.—E. K. Westlake.

M.B., B.Chir.—* P. O. Jones.

M.B.—R. J. Blow, J. P. Dickson, Betty Holt, Evelyn J. Mitchell,

* J. C. Newell Price.

* By proxy.

Royal College of Physicians of Edinburgh

At a meeting of the college held on May 4, with Dr. L. S. P. Davidson, the president, in the chair, the following were elected to the membership:

R. J. Peters, A. M. Fraser, I. Ahmad, T. P. Niyogi, A. J. Palwala, E. S. Shoucair, A. M. Jafar, K. Sengupta, R. Davies, J. L. Brando, G. V. Feldman, A. Z. Abd-El Massieh, F. J. C. Perera, G. L. Walton, R. M. Foster, A. J. Williams, K. M. Win, S. Loganadan, R. G. Loudon, P. C. Bhalla, V. Ramadas, J. A. R. Lenman, B. S. Hartnett, D. W. Beaven, J. M. Reid, F. Starer, D. D. Pottinger, H. J. Woodliff, M. Brando, L. J. P. Duncan.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on May 3, with Dr. Andrew Allison, the president, in the chair, S. G. McAlpine was admitted a fellow of the faculty *qua* physician.

University of Edinburgh

Dr. G. J. Romanes has been appointed to the chair of anatomy in succession to Prof. James Brash, who is retiring.

Dr. Romanes took his B.A. degree at Cambridge in 1938 and his Ph.D. in 1941 before coming to Edinburgh to graduate in medicine in 1944. He has held a Beit medical research fellowship and a Commonwealth Fund research fellowship in New York. He is at present senior lecturer in neuro-anatomy in the university. His published work includes papers on the motor apparatus of the spinal cord and the development of the nervous system.

Prof. G. L. Montgomery has been appointed to the chair of pathology in succession to Dr. A. Murray Drennan, who is retiring.

Professor Montgomery, who is 48, graduated M.B. at the University of Glasgow in 1928. He was appointed lecturer in chemical pathology at the University of St. Andrews in 1931, and in 1936 received the degree of Ph.D. of that university. In 1937 he returned to Glasgow University as lecturer in the pathology of disease in infancy and childhood. In 1937 he was elected F.R.F.P.S. During the late war he served, with the rank of colonel, A.M.S., on the directorate of pathology in the Central Mediterranean and in South East Asia. He was awarded the Bellahouston gold medal for his M.D. thesis in 1946. He was appointed to the St. Mungo (Notman) chair of pathology at Glasgow University in 1948. He took part in the Medical Research Council's streptomycin trials, and his other research includes work on renal function and non-tuberculous infection of the lung in children.

During the summer term, Dr. Douglas Guthrie will give six lectures on the Rise and Progress of Medical Education. The first lecture will be held in the physiology class-room at 5 p.m. on Monday, May 31.

Meeting of S.H.M.O.s

A general meeting of senior hospital medical officers of all regions will be held at B.M.A. House, London, W.C.1, on Saturday, May 29, at 3 p.m., to discuss the status and future of the grade and the new rate of remuneration.

Drummond Memorial Appeal

Some time ago a fund was opened to endow a fellowship for research into nutrition in memory of the late Sir Jack Drummond. The fund is still open, but the trustees are already able to announce that they hope to appoint the first fellow this summer.

The stipend of the fellowship is to be at the rate of £900 per annum, and the fellow would be expected to carry out his investigations in or associated with a university department or a research institute of similar standing. The appointment would, in the first instance, be for a year. Further particulars may be had from the chairman of the Drummond Trust, c/o The Provost, University College London, Gower Street, London, W.C.1.

Board of Registration of Medical Auxiliaries

The board held a dinner on May 4 at Apothecaries' Hall. Among the guests were Lord Horder, Sir Russell Brain, Sir Heneage Ogilvie, Sir Henry Souttar, Sir Zachary Cope, and Mr. J. W. Tudor Thomas, president of the B.M.A. Proposing the toast of The Board, Sir Russell observed that auxiliaries were now an integral part of medicine, and many of the advances in technique depended on their work. He commended the board for the energetic way in which it had fostered co-operation both among auxiliaries themselves and with the medical profession. In his reply, Mr. A. M. A. Moore, surgeon to the London Hospital and president of the board, outlined the origins and development of the board. In 1929 the B.M.A. had concluded that there was little immediate prospect of securing national legislation which would solve the problems of the auxiliaries, and a voluntary register seemed the most practicable proposition. This was established in 1930, and, after further deliberations, the board was incorporated in 1936, with Sir Henry Soutter as its first president. The founder members were the B.M.A., the Society of Apothecaries, the Chartered Society of Physiotherapists, and the Society of Radiographers. The two main objects of the board were, firstly, to maintain a register of persons who were competent to undertake auxiliary treatment, and, secondly, to promote the establishment of a statutory register. Sectional registers were published annually, and Mr. Moore hoped that before long a comprehensive register would be issued. As for statutory registration, the Minister of Health had lately declared that there was insufficient agreement to justify this step at present; but there were good hopes that a generally acceptable plan could be devised.

In a cheerful speech of welcome to the guests, Mr. John Hanby, president of the Society of Chiropractors, paid tribute to the splendid help which the auxiliaries had had from Sir Zachary Cope, notably during his long term as chairman of the committees that bear his name. Sir Heneage Ogilvie replied for the guests.

Royal Society of Arts

On Tuesday, May 25, at 5.15 p.m., at the house of this society, John Adam Street, London, W.C.2, Sir Leonard Rogers, F.R.S., will give a lecture on the Progress Towards the Eradication of Leprosy from the British Commonwealth.

Anglo-Austrian Holiday Exchange

The Anglo-Austrian Society is arranging exchange holidays for British and Austrian school-children during the coming summer. Last year over 850 boys and girls took part in a similar exchange. Applications can still be accepted from British children, for many applications have been received from children of Austrian doctors in the Tyrol, Salzburg, Carinthia, the Austrian Lake District, Styria, and Vienna. Children should be between 12 and 18 years of age. Particulars may be obtained from the Secretary, Anglo-Austrian Society, 139, Kensington High Street, London, W.8.

A New Hospital

On May 8 Mr. Iain Macleod, the Minister of Health, laid the foundation stone of the first large new hospital to be built in England and Wales since before the war and the biggest approved since the start of the health service. Greaves Hall, near Southport, is a project of the Liverpool Regional Hospital Board. It will cost some £3 million and will provide beds for over 1000 mental defectives. In his speech Mr. Macleod said that though nursing recruitment had made great strides, the mental and mental-deficiency hospitals had lagged behind the general advance, because it was not yet sufficiently well known that the atmosphere of the mental and mental-deficiency hospitals had been revolutionised by modern methods of care and treatment and that these branches of the nursing profession now offer a career with interesting work and excellent prospects. "I am sure," he added, "that if the general public really knew about the good work which is being done in our mental and mental-deficiency hospitals there would be no lack of recruits."

CORRIGENDUM: *Salicylates in Rheumatic Fever.*—The name of Dr. J. Lorber was mis-spelt in the first footnote of this leading article last week (p. 968).

Dr. Avois Donabedian, director of the health service at the American University, Beirut, Lebanon, with a British Council bursary, is studying university and school health schemes in Scotland.

Births, Marriages, and Deaths**BIRTHS**

BROWN.—On May 7, at King's College Hospital, to Jean, wife of Dr. R. J. K. Brown—a daughter.

MARRIAGES

BATTY SHAW—HECKELS.—On May 7, at Epsom, Anthony Batty Shaw, D.M., to Patricia Heckels.

DEATHS

LOVIBOND.—On May 4, in London, John Locke Lovibond, T.D., M.D. Camb., F.R.C.P., of 1, Montagu Square, London, W.1, beloved husband of Mary and son of the late Major J. L. Lovibond, T.D., and Mrs. Lovibond, of Underwood, Hexham, Northumberland, aged 47 years.

Appointments

CARROLL, J. D., M.B. Dubl., D.C.H., D.P.H.: asst. county M.O. for Nottinghamshire, and M.O.H., Mansfield, Woodhouse and Warsop urban district councils.

DURRAN, JOHN, M.B. Edin., F.R.C.S.E., D.O.: ophthalmologist (consultant), Perth Royal Infirmary and Bridge of Earn Hospital, regional clinics for the blind, and local authority clinics.

GLASS, ALAN, M.B. Manch., F.R.C.S.: consultant orthopaedic and accident surgeon, North Manchester Hospital Centre and Booth Hall Children's Hospital.

HEPPLESTON, J. D., M.B. Munc., DIP. BACT.: consultant group pathologist, South Cheshire hospitals.

MORRISON, S. L., M.B. St. And.: deputy borough M.O.H., deputy county divisional M.O., and deputy school M.O., Oldbury.

O'RIORDAN, J. P., M.B. N.U.I., D.P.H., D.C.H., Lieut.-colonel I.M.S. retd.: medical director, National Blood Transfusion Association, Dublin.

PATTINSON, J. N., M.B. Camb., F.F.R., D.M.R.D.: consultant radiologist, Hospital for Diseases of the Chest, Brompton, London.

RAMSAY, J. H. R., M.B. Glasg., F.R.C.P.S.: asst. physician (S.H.M.O.) in tuberculosis, Bangour Hospital, West Lothian.

East Anglian Regional Hospital Board: JENNINGS, J. H., M.B. Edin.: surgical registrar, Stamford and Rutland Hospital.

MERRITT, T. J. K., M.B. Lond.: registrar in psychiatry, St. Andrew's Mental Hospital, Norwich.

YORK-MOORE, M. E., M.B. Lond., D.O.B.S.T.: registrar in psychiatry, Hellesdon Mental Hospital.

Diary of the Week

MAY 16 TO 22

Monday, 17th

UNIVERSITY OF LONDON

5.30 P.M. (Guy's Hospital Medical School, London Bridge, S.E.1.) Dr. Bernard B. Brodie (Bethesda, U.S.A.): Biochemical and Clinical Implications of Studies in Drug Metabolism. (First of two lectures.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12

4 P.M. Dr. N. F. Coghill: Sigmoidoscopy in Medicine.

INSTITUTE OF SOCIAL PSYCHIATRY

8 P.M. (1, Wimpole Street, W.1.) Dr. J. L. Moreno (New York): Recent Advances in Sociometry.

Tuesday, 18th

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2

5 P.M. Dr. W. Hayes: Nature of Genetic Recombination in *Bacterium coli*.

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2

5.30 P.M. Dr. L. Forman: Lupus Erythematosus.

SOUTHWEST LONDON MEDICAL SOCIETY

8.30 P.M. (Bolingbroke Hospital, Wandsworth Common, S.W.11.) Dr. Paul Wood: The Physician's Approach to Cardiac Surgery.

Wednesday, 19th

UNIVERSITY OF LONDON

5.30 P.M. (Guy's Hospital Medical School.) Dr. Brodie: Biochemical and Clinical Implications of Studies in Drug Metabolism. (Second of two lectures.)

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. H. Haber: Histology of Some Skin Conditions in Children.

INSTITUTE OF LARYNGOLOGY AND OTOLGY, 330, Gray's Inn Road, W.C.1

5.30 P.M. Dr. I. Friedmann: Malignant Granuloma of Nose.

INSTITUTE OF OBSTETRICS AND GYNECOLOGY

3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Dr. Mary Barber: Investigation of Sepsis in a Maternity Unit.

MIDDLESEX COUNTY MEDICAL SOCIETY

3 P.M. (Clare Hall Hospital, South Mimms, Barnet.) Dr. J. S. Crowther: Spontaneous Pneumothorax. Dr. R. E. D. Harvey Samuel: Marital Tuberculosis.

WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY, Willesden General Hospital, Harlesden Road, N.W.10

8.45 P.M. Dr. R. Terry, Mr. F. W. M. Pratt: Medical and Surgical Aspects of Diseases of Gall-bladder and Liver.

UNIVERSITY OF OXFORD

5 P.M. (University Museum.) Prof. W. T. Astbury: Observations and Thoughts on Structure and Mobility of Flagella.

Thursday, 20th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2

3.45 P.M. Dr. F. Stansfield: Maxillary Air Sinus. (Arnott demonstration.)

5 P.M. Mr. V. E. Negus: Comparative Anatomy of the Nose and Paranasal Sinuses. (Hunterian lecture.)

GUY'S HOSPITAL MEDICAL SCHOOL

5 P.M. Prof. Michael De Bakey (Texas): Surgical Considerations of Diseases of Aorta. (Carbuncle lecture.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON

4 P.M. Dr. J. F. Goodwin: Pulmonary Hypertension.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1

7.30 P.M. Dr. J. Donald Ball (Uganda): Endomyocardial Fibrosis in Africa.

INSTITUTE OF CARDIOLOGY, National Heart Hospital, Westmoreland Street, W.1

9.30 A.M. Dr. J. H. Wright: Unilateral Renal Hypertension.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY

8.30 P.M. (11, Chandos Street, W.1.) Mr. Aleck Bourne, Mr. L. Courts, LL.M., Dr. H. J. Shorvon: Abortion.

UNIVERSITY OF OXFORD

5 P.M. (Radcliffe Infirmary.) Mr. Charles Read: Postmenopausal Haemorrhage.

UNIVERSITY OF ST. ANDREWS

5 P.M. (Medical School, Small's Wynd, Dundee.) Prof. Lawson Wilkins (Baltimore): Diagnosis and Treatment of Adrenogenital Syndrome.

Friday, 21st

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 58, Queen Anne Street, W.1

5 P.M. Mr. Ian Donald: Atelectasis Neonatorum. (Blair-Bell lecture.)

ROYAL COLLEGE OF SURGEONS

5 P.M. Prof. H. F. Humphreys: Value of Teeth as Evidence. (Webb-Johnson lecture.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON

2 P.M. Dr. D. A. K. Black: Disturbed Electrolyte Metabolism in Pyloric Stenosis.

4 P.M. Prof. John Squire: Metabolism in Renal Diseases, including the Nephrotic Syndrome.

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. R. T. Brain: Skin Diseases in Children.

FAULTY OF RADIOLOGISTS

2 P.M. (Royal College of Surgeons.) Group-Captain D. A. Wilson: Radiological Experiences of Atomic Explosion at Woomera. Dr. F. Baclesse (Paris): Radiotherapy in Cancer of Breast.

MAMMARY CANCER TREATED BY BILATERAL ADRENALECTOMY

L. N. PYRAH F. G. SMIDDY

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SENIOR SURGEON REGISTRAR

UNIVERSITY DEPARTMENT OF UROLOGY, LEEDS GENERAL
INFIRMARY AND ST. JAMES'S HOSPITAL, LEEDS

WE review here 22 cases of advanced mammary cancer, with metastases, submitted to bilateral adrenalectomy and bilateral oophorectomy between April and December, 1953.

It had previously been shown that some cancers of the breast and of the prostate gland can be influenced by the host's hormones. Surgical removal of the source of such hormones may cause regression of the growth; this has happened after oophorectomy for mammary carcinoma and, more often, after orchidectomy for prostatic carcinoma. Such neoplasms have been called dependent or conditioned; their cells may, however, ultimately change in character, cease to be hormonally controlled, and become autonomous. Huggins and his colleagues (Huggins and Bergenstal 1952, Huggins and Dao 1953) thought that, in the case of certain malignant growths of the breast and of the prostate in which a regression of the growth had been induced by hormonal deprivation or therapy and was followed by a relapse, there may have been a further build-up of a cancer-controlling substance within the adrenal glands. In cases of advanced mammary and prostatic cancer with metastases Huggins and his co-workers have done bilateral adrenalectomy (usually with gonadectomy), and in some of the cases so treated they have shown by clinical, radiological, and histological studies that a major remission of the cancer has been obtained. Conditioned and autonomous neoplasms have been reviewed by Furth (1953).

Mammary Carcinoma in Relation to Gonads

It is generally accepted that a relationship exists between the female breast and ovarian hormones, and between some mammary cancers and ovarian and testicular hormones.

MAMMARY CANCER AND OVARIES IN MICE

Lathrop and Loeb (1916) found that removal of the ovaries of female mice of different strains, some of which had a higher incidence of spontaneous mammary cancer than others, if done before the age of six months, led to a striking decrease in the incidence of breast cancer but did not entirely prevent it. In those oophorectomised mice in which cancer appeared it did so at a later age than in the non-oophorectomised mice of the same strain. These findings were confirmed by Cori (1927).

Lacassagne (1932) injected cestrin into 5 young mice (3 male and 2 female) belonging to a strain whose females had a high incidence of spontaneous mammary carcinoma, the males not being so affected. Cancer of the breast developed within six months in the male mice so treated, and in 1 of the females.

Burrows (1935) examined the effects of twice-weekly applications of a benzene solution of cestrin to the skin of male and female mice until they died. The earliest abnormality was dilatation of the ducts, and this was followed by hyperplasia of the epithelium lining the ducts; at this stage cysts sometimes appeared. In some cases adenomata developed and occasionally carcinomata. Bonser (1936) injected oestrone into male mice of a high cancer strain of which the females alone normally developed cancer. As a result the breasts showed acinar proliferation and dilatation of the ducts; and 3 of 23 mice so injected developed mammary cancer.

Fekete et al. (1941), who studied the accessory genital organs of spayed mice, found that, in spite of the absence of the ovaries, considerable amounts of oestrogen were produced during later life, probably from the adrenals, which were hypertrophied and contained yellowish nodules. Gardner (1941) found that adrenal tumours developed in 13 of 15 spayed mice aged 43–65 days, together with evidence of pronounced oestrogenic activity, such as changes in the vaginal and uterine epithelium.

A full account of the experimental work on this subject is given by Burrows and Horning (1952).

MAMMARY CANCER AND GONADAL HORMONES IN MAN *Oophorectomy*

The relation of the ovary to some cases of mammary cancer in women was first noted by Beatson (1896), who observed considerable clinical improvement in 2 of 3 cases of advanced breast cancer in which he had removed the ovaries. Similar cases were recorded by Power (1903), Waring (1905), and Clarke (1905). Lett (1905) collected 99 patients who had advanced breast cancer and had had their ovaries removed; in 23% of the patients there was much improvement, and there was some improvement in a further 13%. Raven (1950) reported a case of advanced breast cancer which was free from demonstrable disease twenty-two months after bilateral oophorectomy; he also reviewed the published reports. Probably the relatively low incidence of improvement and its uncertain duration explain why the operation has not passed into general use.

Farrow and Adair (1942) reported that a carcinoma of the male breast with metastases regressed after orchidectomy. Treves (1949) reported remission in 3 of 6 cancers of the male breast with metastases; relief of pain and healing of bone metastases were noted.

Irradiation of Ovaries

This treatment was first used by De Courmelles (1922) for the treatment of cancer of the breast. Dresser (1936) reported improvement in 43% of 59 patients with breast cancer and metastases who were treated by irradiation of the ovaries; relief of pain and regression of metastases lasted up to three years after the operation. Taylor (1939) concluded that this mode of treatment could be expected to produce temporary regression in a third of the cases with metastases.

Hormone Treatment

The administration of testosterone to neutralise oestrogens in cases of inoperable or metastasising breast cancer was used by Ulrich (1939). This form of therapy has been in common use for many years, with benefit in some cases.

Synthetic oestrogens given by mouth (stilboestrol, dienoestrol) have also been used for treating inoperable cases. Haddow et al. (1944) reported the results of treating 204 patients for periods of one to nine months, with improvement in 26·5%; but relapse eventually took place. Rae (1948) reported improvement in 8 of 12 cases similarly treated. Both testosterone and large doses of oestrogens depress the gonad-stimulating hormones of the pituitary (Furth 1953). However illogical the use of stilboestrol may appear, its use has produced a striking regression in some cases.

Effects of Adrenalectomy in Animals

Surgical removal of the adrenal glands can be done in some animals if sodium chloride is given. Such removal appears to have an opposite effect on different kinds of tumours.

DEPRESSION OF GROWTH-RATE IN SOME ADRENALECTOMISED ANIMALS

Joannovics (1916) found that transplanted sarcomas in mice in which the adrenals had been removed weighed

20% less than the controls—i.e., the rate of growth had been depressed. Roffo (1930) transplanted sarcoma and carcinoma in rats; adrenalectomy caused a decrease in the rate of growth of the transplanted tumour. Ingle and Baker (1951) found that the rate of growth of Walker carcinoma 256 in male rats was retarded after adrenalectomy. Talalay et al. (1952) examined the effects of adrenalectomy on the transplanted Walker tumour 256, standardised in respect of its rate of growth in well-nourished tube-fed albino rats; the rate of growth of the tumour was about 60% less than that in intact controls.

ACCELERATION OF GROWTH-RATE IN SOME ADRENALECTOMISED ANIMALS

Sometimes adrenalectomy appears to stimulate the growth of neoplasms. Murphy and Sturm (1943) found that adrenalectomy in the rat led to an increase in the number of successful grafts of a transplantable lymphatic leukaemia; the length of life of these rats was diminished. Law et al. (1947) showed that the incidence and the time of appearance of spontaneous lymphoid leukaemia in C58 mice was considerably increased after adrenalectomy.

Results of Adrenalectomy for Mammary Cancer in Man

Huggins and Dao (1953) reported 55 cases of breast cancer treated by adrenalectomy during 1951 and 1952 (2 men and 53 women). 3 women died within thirty days of the operation.

In 25 of the 50 women left for review bilateral adrenalectomy alone was done. The patients were aged 44–70, and it was thought that there was no significant ovarian function; some had undergone either X-ray sterilisation or oophorectomy at an earlier date, and more than half had been treated with testosterone. Of these 25 patients 9 died of cancer from one and a half to seven months after operation; 3 have advancing symptoms; in 10 the cancer has regressed considerably; and 3 have been operated on too recently for adequate assessment.

The remaining 25, aged 29–59, underwent adrenalectomy and oophorectomy. Of these 25 patients 8 died of cancer from sixteen to forty-seven months after operation; 3 have advancing cancer; in 10 the cancer has regressed considerably; and in 4 the operation was too recent to permit of assessment. Patients with metastases in the bones and pleura showed the best results, but extensive hepatic and intracranial metastases also showed improvement. In some cases bones which were the seat of osteolytic secondaries recalcified. Radiography showed that the intrathoracic deposits had apparently disappeared.

Of the whole series of 50 patients 14 have been under the observation of Huggins and Dao from one to two years after adrenalectomy with or without oophorectomy. 6 of them died; 1 was alive but not improved; and 7 were still in remission and appeared to be in good health at the time of writing, 2 having had adrenalectomy alone and 5 having had adrenalectomy and oophorectomy.

2 men with mammary cancer who had previously undergone orchidectomy were treated by bilateral adrenalectomy. In 1 patient, who had pulmonary and cerebral metastases, there was improvement in the pulmonary metastases, but the cerebral lesion progressed to a fatal termination seven months after the operation. The other man had extensive pleural metastases with effusion, necessitating repeated aspirations; after adrenalectomy there was great improvement, and no further aspirations were needed; and he was alive eleven months after the operation.

Pearson et al. (1953) reported the results of adrenalectomy in 12 patients with advanced mammary cancer. All had had oophorectomy at least six weeks before adrenalectomy. 5 of them had remissions lasting from

four to nine months; and 2 who did not respond showed objective evidence of regression of skin and bone metastases, with rapid growth of hepatic metastases.

Present Series

In the cases reported by Huggins and Dao (1953) the most favourable response was found in mammary carcinomata which had an alveolar or papillary microscopical structure, anaplastic growths usually showing little or no response. In spite of this we decided in this series to make no preliminary selection but to operate on all the cases referred to us because of widespread mammary cancer with metastases, provided that the patient was thought to be fit to undergo the operation. Only 2 patients, aged 70–80, have so far been rejected because of unfitness, which was due partly to malignancy and partly to senile changes. Most of the patients have been ill, some very ill, and in those the operation has carried risks. The first few patients underwent two operations. We prefer a one-stage operation whenever possible; but owing to the proportion of very ill patients in the series the operation was done in two stages in half the cases, an interval of about two weeks being allowed between the operations.

PREOPERATIVE MANAGEMENT

A search was made for metastases. Radiographs were made of the skeleton and of the chest. A blood-count was made, and acid and alkaline phosphatase, blood-sugar, and urinary 17-ketosteroids were estimated.

SUBSTITUTION THERAPY

Until cortisone was available for substitution therapy after bilateral adrenalectomy, the removal of both glands was hazardous and usually fatal; the administration of cortisone is essential to life after adrenalectomy. When the adrenalectomy is to be bilateral, the patient is given substitution therapy before and after operation; the dosage should be in excess of need preoperatively and gradually reduced postoperatively. Cortisone and deoxycortone acetate are adequate substitutes for the loss of the adrenocortical steroids. The routine recommended by Huggins and Bergenstal (1951), slightly modified, has been used and has proved satisfactory:

<i>Day Before Operation</i>	Cortisone acetate ..	50 mg.	6-hourly intramuscularly.
	Deoxycortone acetate ..	3 mg.	intramuscularly.
	Sodium chloride ..	3 g.	by mouth.
<i>Day of Operation</i>	Cortisone acetate ..	150 mg.	an hour before operation and 50 mg. 4-hourly intramuscularly.
	Deoxycortone acetate ..	5 mg.	intramuscularly.
<i>First Postoperative Day</i>	Cortisone acetate ..	50 mg.	6-hourly intramuscularly.
	Deoxycortone acetate ..	5 mg.	intramuscularly.
	Sodium chloride ..	3 g.	by mouth.
<i>Postoperative Days Two to Six</i>	Cortisone acetate ..	50 mg.	12-hourly by mouth.
	Deoxycortone acetate ..	3 mg.	intramuscularly.
	Sodium chloride ..	3 mg.	by mouth.
<i>After Sixth Postoperative Day</i>	Cortisone acetate ..	25 mg.	by mouth twice daily.
	Deoxycortone acetate ..	0·3 mg.	intramuscularly daily; alternatively 300 mg. implanted subcutaneously once every six months.
	Sodium chloride ..	3 g.	by mouth.

OPERATIVE TECHNIQUE

Anæsthesia

Before operation an intravenous drip of 5% glucose in physiological saline solution was set up and given. The skin to be incised was infiltrated with a local anæsthetic. Anæsthesia was induced with intravenous

thiopentone followed by intratracheal gas and oxygen, through a cuffed tube. Tubocurarine chloride was given as a relaxant. Careful watch was kept on the blood-pressure; and noradrenaline was available in case of severe hypotension, but was not needed in this series.

Adrenalectomy

The adrenals were removed through two separate incisions. The patient was placed on her side, the head and foot of the operating-table being lowered; this procedure may be undesirable in patients with spinal metastases. An oblique incision was made over the twelfth rib and carried forwards for some inches as for exposure of the kidney. The twelfth rib was resected, the incision was deepened through its bed, and the lumbar muscles were divided in the line of the incision. The upper pole of the kidney was exposed after incising Gerota's fascia and dissecting through the perinephric fat. The upper half of the kidney was freed sufficiently to enable it to be displaced downwards, when the suprarenal gland came into view; it was recognised by its bright yellow colour. The gland was dissected free from its surroundings with blunt-pointed scissors, sometimes assisted by the cautious use of the index finger. Haemostatic forceps may be applied as retractors to strands of adventitious tissue round the gland; but if they are applied to the gland itself this may tear owing to its great friability, and there may be some annoying haemorrhage. On the right side the upper pole of the gland is in relation to the posterior surface of the liver, from which it must be freed. Its deep surface is closely applied to the inferior vena cava, to which it is attached by areolar tissue and by the short stout adrenal vein. The adrenal is a vascular gland supplied by the adrenal artery, and there may be an accessory artery, arising from a branch of the renal artery, which will usually require separate ligation. The pedicle is dissected free and secured with long curved forceps, and the gland is removed; a hot gauze pack pressed into the cavity will check oozing. The left gland is easier to remove than the right. The lower pole may lie in close relation to the left renal vein, from which it has to be carefully dissected. The pedicle on the left side is longer and is easily exposed during the dissection.

In 8 cases one or both adrenals were found to be infiltrated by cancer. When such infiltration is early, the gland is firmer than normal and easier to remove. When the gland is grossly involved by cancer it may be three or four times its normal size and is firm in consistency; the tissues round the gland are then usually oedematous.

Oophorectomy

The ovaries were removed through a midline incision below the umbilicus; to save time no peritonisation of the stumps was attempted.

Evisceration of Testes

The testes were eviscerated through a single incision in the midline of the scrotum. An incision was made through each tunica albuginea; about half the tunica was removed, and all testicular tubular material was scraped away from the remaining part of the tunica albuginea with a sharp scalpel. A continuous stitch through the remnants of the tunica albuginea was used to arrest haemorrhage.

POSTOPERATIVE PERIOD

In 3 cases there was, after removal of the second adrenal, a sharp fall of blood-pressure, which lasted twenty-four hours and caused anxiety in 1 case. These falls took place, however, in advanced cases in feeble and ill patients and were not noted in the fitter patients. Where the operation was followed by major regression of the cancer, there was usually considerable subjective improvement, with a feeling of well-being in the

immediate postoperative period; and appetite was rapidly regained. In most such cases pain, which may have been previously severe, disappeared within forty-eight hours of operation. Where the operation was not followed by much regression of growth there was usually also a feeling of well-being, and pain was often relieved, but the changes were not so pronounced as in the first group. The operation wounds healed normally. Penicillin and streptomycin were administered in all the cases.

In early cases a watch was kept for excessive urinary excretion of salt, but there was no real worry about electrolytes. The maintenance of electrolyte and carbohydrate balance, without the onset of orthostatic hypotension, are the best criteria that the substitution therapy is adequate. One patient developed a troublesome degree of orthostatic hypotension which was not corrected by increasing the dosage of cortisone. Larger doses of cortisone are undesirable because the katabolic effect on the proteins then becomes excessive. At some convenient date after operation (in the later cases of the series at the end of the operation) 300 mg. of deoxycortone acetate in pellet form was inserted into the subcutaneous tissues through a small incision. The patients got out of bed early after operation unless bone metastases rendered such a procedure unwise, and normal mobility returned rapidly. Our patients did not experience in the postoperative period any collateral acute infections; but Huggins and Bergenstal (1952) recommended that, if such develop, the dosage of cortisone and of deoxycortone be increased.

Results

Our results were analysed as follows:

Cases Improved

Major remission ; patients alive and well ..	3
Major remission followed by (?) relapse ..	2
Moderate improvement, probable remission ..	1
Improving ; too early for final assessment (in 2 cases skin nodules have disappeared) ..	4

Alive and Well

Too early for assessment	3
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Cases Unimproved

Died of cancer without clinical improvement ..	6
Alive but not showing improvement	2
Postoperative death	1

Total	22
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The patients having been previously under the care of many different surgeons, there had been no uniformity in the earlier treatment as regards the use of hormones. Since many of the cases were very advanced, we decided not to await any possible response to hormone treatment but to proceed at once to adrenalectomy and oophorectomy. Of the 22 patients 7 have died of cancer (including 1 postoperative death) and 2 are alive but show no improvement.

10 cases in the series have shown improvement. In 2 of the cases (sixty-four days and forty-two days after operation) the skin nodules have disappeared; hence a major remission appears possible, but it is too early to claim this. There has been a major remission in 5 cases and a probable remission in 1. Details of these 6 cases is given below.

Case 1.—A woman, aged 36; had an adenocarcinoma of the left breast which was already inoperable when first diagnosed in April, 1952, and was treated by radiotherapy. Later she complained of severe pain in chest, spine, and ribs, and was treated with testosterone, which did not produce any relief. She was bedridden for six weeks before admission.

On admission on April 25, 1953, the left breast was hard and fixed, with enlarged glands in the right and left axilla and in the posterior triangle of the neck, and extensive skin nodules (fig. 1a) in the chest wall. The liver was palpable; there were extensive osteolytic metastases in the pelvis

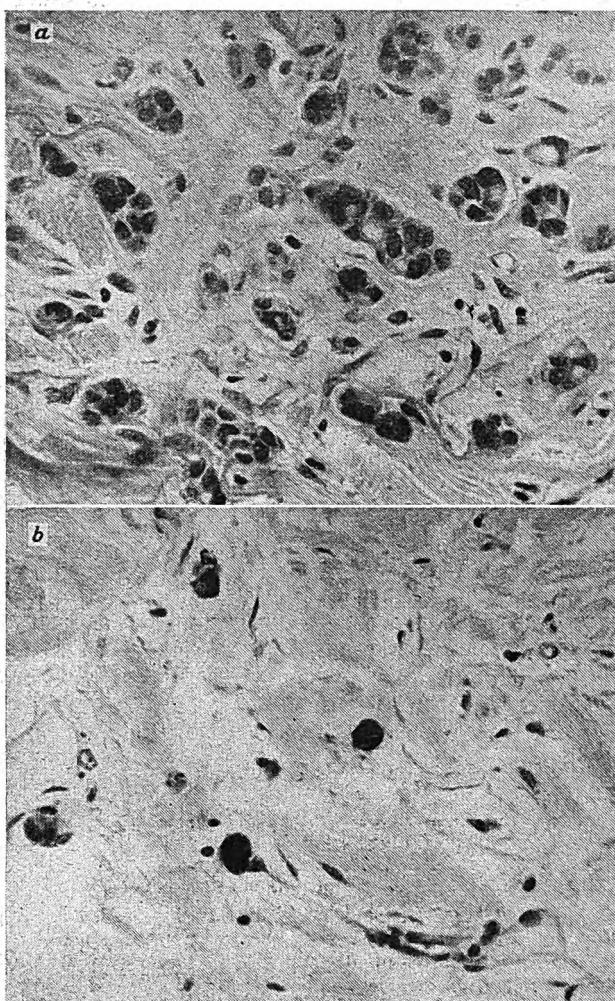


Fig. 1—Case 1 : a, skin nodule on April 14, 1953, five weeks before operation; b, remains of skin nodule on May 26, 1953, five days after completion of two-stage operation, showing disappearance of cells except a few degenerate ones.

and the spine ; and a chest radiograph showed lymphatic permeation of the lung fields.

Operation.—Bilateral adrenalectomy and oophorectomy (two-stage) were completed on May 21, 1953.

Result.—Complete relief of symptoms ; skin nodules have disappeared (fig. 1b) ; left breast has returned to a near-normal consistency ; chest radiograph normal ; recalcification of pelvic bones and vertebrae.

Follow-up.—The patient developed a left-sided pleural effusion following bronchitis at two hundred and twenty days ; it was treated by aspiration ; no malignant cells were seen in the pleural fluid, whose nature is still uncertain.

Case 2.—A woman, aged 43, had a spheroidal-celled carcinoma of the right breast, which was inoperable when first seen in January, 1952, and was treated with radiotherapy. Skin metastases were first noted in September, 1952. In January, 1953, stilboestrol was administered but produced no improvement.

On examination on April 1, 1953, the patient had been bedridden for three months ; both breasts were solid and shrunken ; there was extensive involvement of the axillary lymph-glands ; multiple widely spread skin nodules were present in the chest wall ; the liver was palpable ; free fluid was present in the abdomen ; and osteolytic metastases were found in ribs, spine, and pelvis.

Operation.—Bilateral adrenalectomy and oophorectomy (two-stage) were completed on May 21, 1953.

Result.—Slow improvement with gain in weight ; breasts have returned to more normal consistency. Some skin nodules remain but are much reduced in size and number ;

osseous metastases are regressing ; the patient is leading a normal life two hundred and twenty-five days after operation.

Case 3.—A man, aged 50, had a mixed spheroidal-celled carcinoma and adenocarcinoma of his right breast. He had first noticed a mass there in 1951. It was inoperable when first seen in 1953 and was treated palliatively by radiotherapy.

On examination on July 1, 1953, there was a fixed ulcerating growth 6 cm. in diameter in the right breast ; about a hundred skin metastases were present in trunk, neck, and arms (figs. 2a and 3a), and extensive dense secondaries in the lungs (fig. 4a).

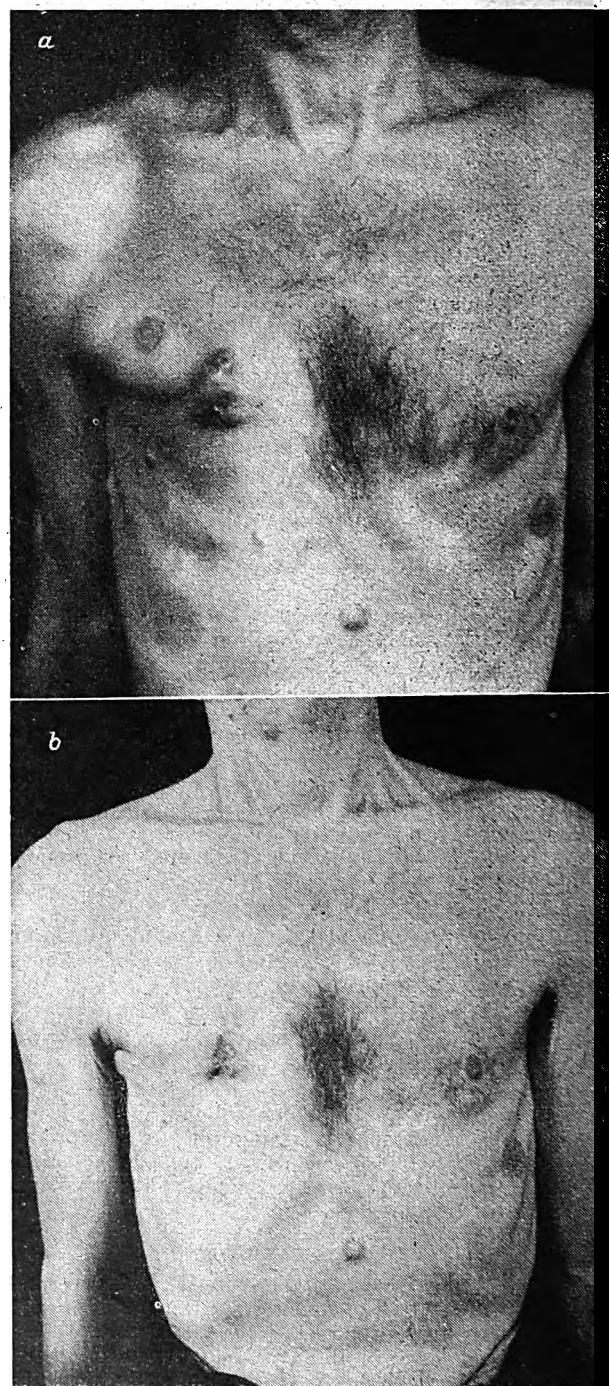


Fig. 2—Case 3 : a, inoperable carcinoma of right breast with numerous skin nodules on July 7, 1953, four days before operation ; b, carcinoma almost gone and nearly all nodules disappeared by Aug. 13, 1953, a month after operation.

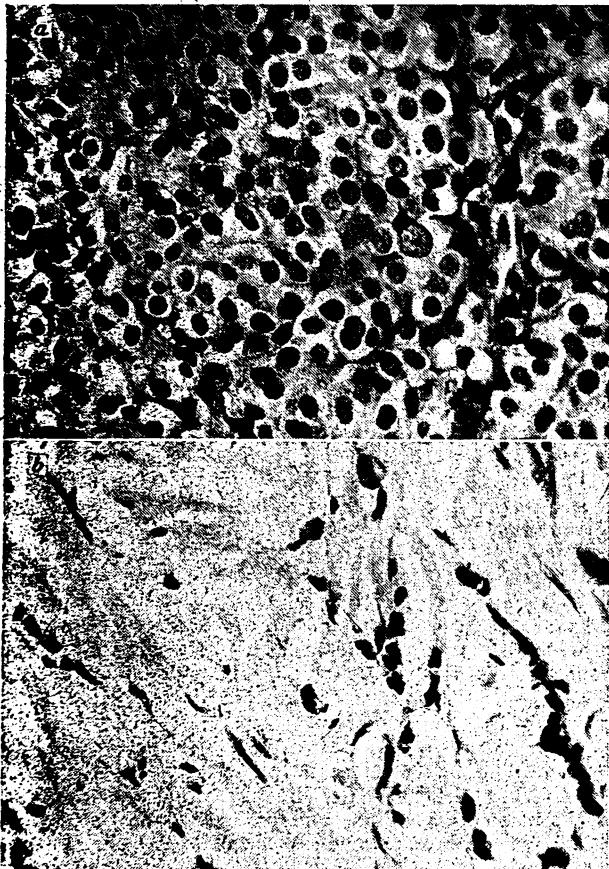


Fig. 3—Case 3: *a*, skin nodule on July 10, 1953, just before operation; *b*, remains of skin nodule, on Nov. 8, 1953, four months after operation, showing cancer cells disappeared or degenerate ($\times 250$).

Operation.—Bilateral adrenalectomy and orchidectomy (single-stage) were done on July 11, 1953. Adrenal metastases were found.

Result.—Disappearance of mass in right breast almost complete since operation; most skin nodules disappeared, and the few biggest ones were reduced in size (figs. 2b and 3b). Pulmonary deposits now radiotranslucent (fig. 4b). The patient is back at work a hundred and seventy-three days after operation.

Case 4.—A woman, aged 37, had a spheroidal-celled carcinoma of the left breast for which she had had radical mastectomy in January, 1950, followed by radiotherapy. In September, 1952, she had a recurrence in the upper chest wall and axilla and swelling of her left arm, for which she was treated by further radiotherapy followed by testosterone therapy.

On examination on May 10, 1953, she had been bedridden for some weeks and had generalised weakness and dyspnoea on exertion. There was massive lymphoedema of the left arm, which hung uselessly by her side, the circumference of the upper arm being 19 inches (fig. 5a). Multiple nodules were present in the skin over her chest, back, and left arm; there was a massive hard recurrence with ulceration over and round the mastectomy scar; there was a large left-sided pleural effusion (fig. 6c) which required multiple aspirations; and there were osteolytic metastases in spine and pelvis.

Operation.—Bilateral adrenalectomy and oophorectomy (two-stage) were completed on June 1, 1953.

Result.—The first improvement noted was a

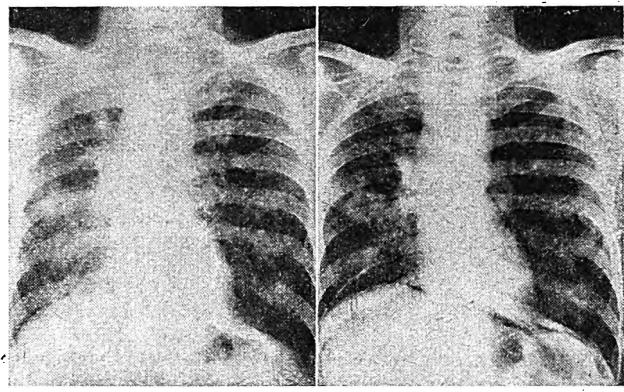


Fig. 4—Case 3: *a*, radiograph of chest on July 7, 1953, four days before operation; *b*, radiograph of chest on Aug. 13, 1953, a month after operation.

gradual shrinkage of the left arm, which is now a useful limb with full movement, though some swelling remains (fig. 5b); the pleural effusion has resolved (fig. 6b), no further aspirations having been needed; the osseous metastases are regressing; the skin nodules on the arm and chest wall have disappeared, and only a few remain on the back; and the patient is fully active two hundred and fourteen days after the operation.

Case 5.—A woman, aged 50, had a mixed spheroidal-celled carcinoma and adenocarcinoma of her left breast, for which she had undergone left simple mastectomy, with insertion of radium needles into the supraventricular fossa, in January, 1947. She had remained well until November, 1952, and then developed pain in the lumbosacral spine and right thigh; she had been treated by radiotherapy to the spine, and improved for three months. Testosterone had been given on deterioration of her condition.

On examination on June 20, 1953, she had been bedridden for a month before admission, mainly because of pain in the spine and right thigh; osteolytic secondaries were present in both femora and tibiae and the third lumbar vertebra.

Operation.—Bilateral adrenalectomy and oophorectomy (two-stage) were completed on July 28, 1953.

Result.—The operation produced partial relief of pain, and radiological improvement in bone secondaries. Interval, a hundred and fifty-five days.

Case 6.—A woman, aged 36, with spheroidal-celled carcinoma of the right breast, underwent right radical

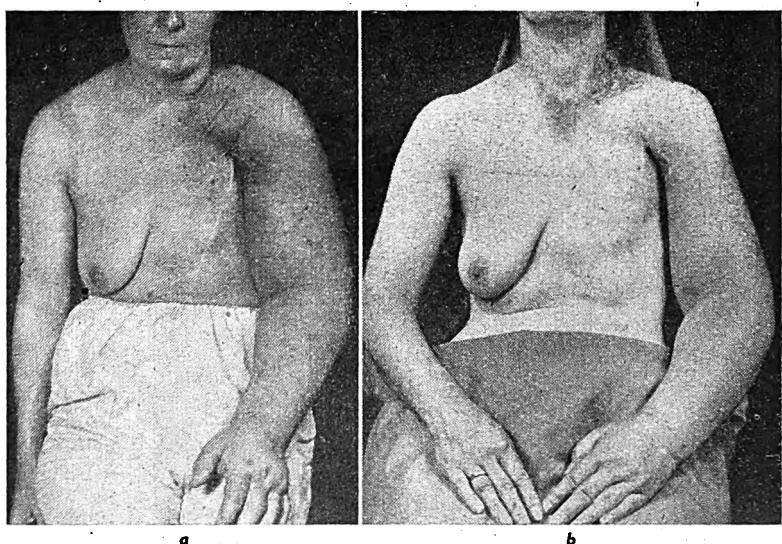


Fig. 5—Case 4: *a*, preoperative appearance of left arm, showing massive lymphoedema, many subcutaneous nodules of arm and forearm and chest wall near scar, and hard massive carcinoma above and below left clavicle; *b*, moderate postoperative reduction in size of left arm and disappearance of skin nodules on arm, a few nodules still on the chest wall, and much improvement in hard masses above and below clavicle.

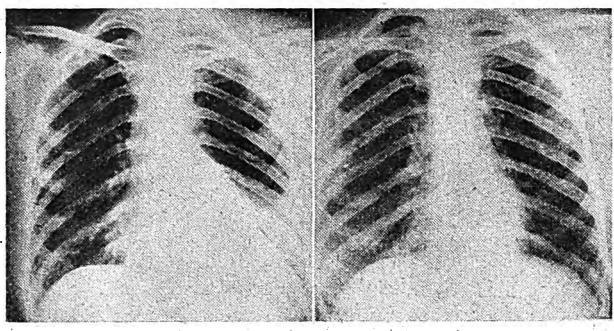


Fig. 6—Case 4: *a*, radiograph of chest showing left-sided pleural effusion before operation; *b*, radiograph six weeks later, showing resolution of pleural effusion. No aspirations were done postoperatively.

mastectomy in 1948. Recurrence in the spine and pelvis in 1952 were treated with stilboestrol and testosterone, which partially relieve the symptoms.

On examination on Aug. 1, 1953, the patient had pain in her right hip, right leg, and dorsal spine; she had lost weight, had no appetite, and was bedridden. There was lymphoedema of her right arm from the elbow downwards. She had an ulcerated sacral bedsore, and osteolytic secondary deposits in the ribs, the whole of the thoracic and lumbar spine, the pelvis, both femora (fig. 7*a*), and both tibiae.

Operation.—Bilateral adrenalectomy and oophorectomy (single-stage) were done on Aug. 7, 1953.

Result.—Major relief of pain was evident from the fourth postoperative day, but the patient still has intermittent aching in her limbs. No radiological improvement in the osteolytic secondaries was noted until forty-two days after operation, when the first signs of recalcification were seen (fig. 7*b* and *c*); improvement from this time has been fairly rapid. The patient's general health has improved, the bedsore is healed, the right arm has improved, and she is now fully mobile a hundred and eighteen days after the operation.

Discussion

Our findings confirm the work of Huggins and his co-workers in their claim that bilateral adrenalectomy with bilateral oophorectomy can bring about a major remission in some patients with advanced mammary carcinoma with metastases. About half the cases in the present series in which it has been possible to estimate the effect of the operation have improved.

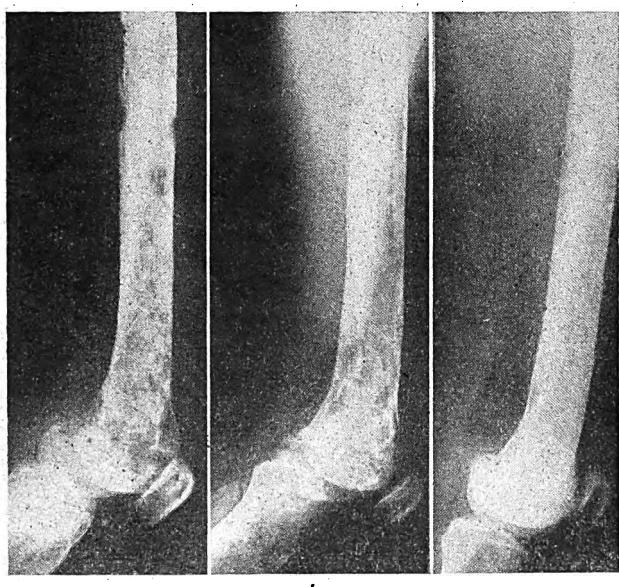


Fig. 7—Case 6: changes in appearance of femur: *a*, before operation; *b*, three weeks after operation; *c*, seven weeks after operation.

In 5 there has been a major remission, with great improvement in the general health and with demonstrable regression of the primary growth (if still present) and its visible metastases, and with well-marked radiographic improvement of osseous and thoracic cancerous deposits. The dramatic response in 4 of these patients in the short space of a few weeks to an indirect surgical attack on the origins of the cancer has been remarkable. That is not to say that these regressions are permanent, for indeed we do not know. Further observation of all the cases operated on and extension of the series are necessary before an accurate long-term estimate of the effect of bilateral adrenalectomy can be made.

Our findings agree with those of Huggins and his co-workers in that tumours having an alveolar or adenomatous structure have responded most favourably to adrenalectomy. It appears to be unwise to rely, however, on a single biopsy before rejecting a case as unsuitable for adrenalectomy. In 2 cases in our series biopsy specimens from different parts of the growth have been reported as showing spheroidal-celled carcinoma and alveolar carcinoma; and in 1 case with a favourable response the sole report that we have obtained so far has been that of spheroidal-celled carcinoma. In the selection of cases for adrenalectomy, therefore, though it seems that in cases showing an alveolar structure of the growth the prognosis is relatively favourable, if cases are rejected for operation on the evidence of a single biopsy an occasional case is missed in which a favourable response may be obtained.

Fig. 3 shows a high-power section from a skin nodule of spheroidal-celled carcinoma and a section of the remains of a neighbouring nodule which has almost disappeared, leaving only degenerate and partially strangulated cells in a stroma of fibrous tissue; whether these cells can grow we cannot say. The changes noted in the skin nodules in cases showing a response have been those of a slow gradual shrinkage rather than a massive necrosis with the formation of a slough. In 1 case a hard malignant recurrence in the chest wall gradually became softer but without ulceration. In 3 cases ulcers on the chest wall have healed and have gradually epithelised. Franks (1953), however, has recorded 1 instance of massive necrosis of widespread metastases following bilateral adrenalectomy for prostatic cancer.

How far the presence, and possibly the hypertrophy, of accessory adrenal tissue left untouched when the two adrenals are extirpated is responsible for relapse after a major regression is unknown. Graham (1953) found accessory adrenal cortical tissue round the celiac plexus in 32% of 100 necropsies, the accessory gland averaging $7 \times 4 \times 3$ mm. The degree of suppression of normal adrenal cortical tissue by the administration of cortisone is unknown. Pearson et al. (1953) have shown that in some cases the withdrawal of cortisone in adrenalectomised patients was followed by evidence of acute adrenal insufficiency. Whether these patients had accessory glands which proved insufficient to maintain life is unknown. This problem requires further study before a true opinion of the importance of accessory glands can be formed.

Theoretically, if the oestrogens in the adrenal gland are formed as a result of stimulation by the gonadotrophic hormone of the pituitary, removal of the pituitary gland may bring about a remission of some cancers of the breast and of the prostate. Luft and Olivecrona (1953) recorded some cases in which the pituitary gland was removed surgically in patients with extensive carcinoma of the prostate or of the breast. 1 case of carcinoma of the prostate and 9 cases of carcinoma of the breast were so-operated on without any postoperative death or serious complication. The case of prostatic carcinoma showed well-marked improvement following operation;

the pain disappeared within two weeks, and the patient could urinate without difficulty. Tests showed, however, that the removal of the pituitary had been incomplete. Difficulty of micturition recurred, and the patient died four months after the operation.

Of the 9 patients with carcinoma of the breast 5 were operated on recently, and it is too early to decide whether the removal of the pituitary has been complete. 2 patients are alive eight and five months after operation, but in both cases tests show that functioning pituitary tissue is still present. These patients showed no appreciable improvement. A 3rd patient died three months after operation without improvement. The 9th case was in a woman, aged 49, with very extensive ulcerating carcinoma of the breast. After operation there was a gradual improvement, with healing of the ulcerated surface. Tests indicated that removal of the pituitary gland had been complete. The growth was of adenocarcinomatous type.

Perrault (1952) reported improvement following hypophysectomy in a case of carcinoma of the breast with metastases in the lungs.

Summary

22 patients with advanced mammary carcinoma with metastases underwent bilateral adrenalectomy and bilateral oophorectomy.

1 died soon after the operation, and 8 have either died from cancer or have shown no improvement; 10 have improved and 5 of these have had a major remission.

The results confirm the work of Huggins and his co-workers that a favourable response sometimes follows bilateral adrenalectomy and bilateral oophorectomy.

We wish to thank the Medical Research Council for the cortisone which made these investigations possible; Dr. G. M. Bonser, of the cancer research department of the University of Leeds, for helpful criticism in the preparation of this paper; and Mr. J. Hainsworth for the photographs. We desire to thank the anaesthetists, Dr. G. Harrison and Dr. R. C. Lawrence.

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BIOPSY OF KIDNEY IN PRONE POSITION

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PHYSICIANS have always been rather envious of the opportunities of veterinary surgeons, who can hold the kidneys of cattle in their hand while doing a rectal examination. Now, at last, through the courage and foresight of P. Iversen (personal communication) one can outdo them and gain direct access to the kidney by biopsy through the back. Iversen and Brun (1951) and Brun (1954) have reported 164 attempts at aspiration withdrawal of renal biopsy specimens in 133 patients. Sufficient tissue for histological examination was obtained in 66 cases (50%). No complications referable to the biopsy developed, but transitory visible haematuria commonly appeared after the biopsy. Iversen and Brun do aspiration biopsies with the patient sitting up, and they cut the kidney tissue with a serrated needle 1.9 mm. broad and then apply suction to the needle to secure the cut tissue.

Our experience with Iversen's technique was unsatisfactory. The patients disliked the upright position; some felt faint, and others complained of pain. Moreover the mobility of the kidneys in this position made it difficult to secure tissue with any regularity. Parrish and Howe (1953) reported only 29 successful biopsies in 63 attempts with the Iversen techniques, and G. Kipnis (personal communication) and W. J. Dieckman (personal communication) have had similar experiences.

We therefore developed a completely new technique for kidney biopsy in the prone position, and obtained renal tissue 48 times in the first 50 attempts. Because kidney biopsy is a safe, painless, and extremely valuable clinical diagnostic method, we describe our technique in detail below.

Briefly, the patients lie prone on a sand-bag and are physically and mentally at rest during the operation. The weight of the body on the sand-bag and the slight elevation of the buttocks fix the kidney against the structures of the back. The surface of the kidney is first found with a fine exploring needle, and then tissue is punched and bitten from the kidney with a modified Vim-Silverman needle, which has been developed by Dr. Murray Franklin, of Cook County Hospital, and takes tissue cleanly without twisting the needle.*

Technique

PRE-BIOPSY STUDIES

To secure the safety of the patient, clinical, radiological and laboratory studies are made before the biopsies are done. These studies can usually be done in the outpatient department, but the patients are always admitted to hospital for the biopsy. At present the contra-indications to doing kidney biopsies are an uncooperative patient, a haemorrhagic diathesis, a perinephric abscess, an aneurysm of the renal artery, tumours and large cysts of the kidney; and a solitary kidney. We do not like to take tissue from the left kidney, because of the danger of hitting the spleen, but we have done so when necessary. The bleeding-time, clotting-time, the number of platelets, and the amount of prothrombin are estimated, and a tourniquet test and various tests of gross and discrete kidney function are made. Urine cultures are made, and one pint of

* The modified Vim-Silverman needle can be obtained from V. Mueller and Company, 330, S. Honore Street, Chicago 12, Illinois.

blood is set aside for the patient on the day of the biopsy. A plain radiograph of the abdomen is taken in the prone position, and a second film is taken fifteen minutes after the intravenous injection of 'Diodrast.'

KIDNEY BIOPSY

Biopsies are usually done in the early morning before breakfast. A mild sedative ('Seconal' gr. $1\frac{1}{2}$) is given to the patient thirty minutes before the biopsy. The patient empties his bladder and then lies on his abdomen on a firm-surfaced table or cart. A long sausage-shaped sand-bag 4-in. thick is placed under him and across the lower abdomen. The lateral border of the right kidney at either the twelfth or the eleventh rib is marked on the radiographs, and the distance from the vertebral spinous process to the lateral border of the right kidney is measured (x cm.). The surface markings of the vertebral spinous processes of the lower back, the right twelfth rib, and the right superior spinous process of the ilium are marked on the skin of the back with 1% aqueous solution of crystal violet. The lateral border of the right quadratus lumborum muscle is found and marked. The position of the lateral border of the kidney is marked by drawing a line on the skin of the back parallel to the line of the vertebral spinous processes and x cm. from it. These lines with the lower border of the twelfth rib, form a triangle in which the puncture is made, usually 1 in. medial to the lateral line and $\frac{1}{2}$ in. below the twelfth rib, or 1 in. below the eleventh rib if the twelfth rib is missing.

The patient is asked to take a deep breath. The kidney is then palpated from the back as it moves with respiration. Palpation confirms the position, mobility, and size of the kidney and indicates roughly its depth from the surface. Naturally the kidney cannot be felt in very obese patients.

1% procaine is injected into the skin at the puncture site, and a 7-in. long 20-gauge exploring needle is passed downwards and obliquely towards the kidney. The needle can be felt going through the back muscles, the deep lumbar fascia, the perinephric fat, and the kidney capsule.

The patient is next asked to take several deep breaths. If the exploring needle is in the kidney, a characteristic movement is seen: the hub of the needle swings through a wide arc, moving towards the head during inspiration and towards the buttocks during expiration. If the needle is not in the kidney tissue it is advanced slightly until it penetrates the capsule and moves smoothly on deep breathing. The depth of kidney below the skin is measured on the stem of the needle, and procaine is injected into the tissues of the back as the needle is withdrawn.

A small nick is made in the procainised skin with a bistoury scalpel. The modified Vim-Silverman needle and stylet are pushed through the nick in the skin and down the track of the infiltrating needle to the measured depth. Again one can feel the structures of the back being penetrated, and the kidney capsule is located exactly. The patient is again asked to take a deep breath. When the characteristic swing of the needle is seen, the cutting prongs are inserted to their full depth in the kidney tissue. The needle sheath is then advanced over the cutting prongs to make it bite tissue. While this is being done, the prongs must not be moved, lest they be pushed through the kidney. These manoeuvres secure a fragment of kidney 1-2 cm. long without twisting the needle. The prongs and needle sheath are now withdrawn, and the tissue is examined under a hand lens to make sure that both cortex and medulla have been taken. The tissue is immediately fixed, and the needle is swirled in a liquid medium for culture. Should extra tissue be required for the inoculation of laboratory animals, for additional histological

examinations (special tissue strains, radio-autographs, or enzyme studies), or for biochemical analysis, a fresh biopsy needle is reintroduced through the puncture site and down through the infiltrated tract; but the point of the needle is moved somewhat laterally before the second piece of tissue is taken.

The patient is asked to hold his breath, and should be quite still, whenever the needles or prongs are advanced into, or withdrawn from, the kidney. Moreover, the operator must not handle the needles while they are swinging during the deep-breathing manoeuvres. If these precautions are neglected the needles might tear the kidney.

POST-BIOPSY PROCEDURE

The puncture site is touched over with collodion, and a thick bandage is strapped down over the biopsy site. The pressure bandage from above and the sand-bag from below squeeze the kidney and prevent perinephric bleeding. The patient remains lying on the sand-bag for thirty minutes. This is sometimes uncomfortable but it is a necessary haemostatic device. The patient is kept in bed for twenty-four hours. His pulse and blood-pressure are measured at short intervals during the day, and his subjective sensations are charted on a board kept at the bedside. We make a point of questioning the patients about urgency, feelings of distension in the bladder, and pain in the back. Each sample of urine passed on the day of biopsy is examined by naked eye and microscopically. The specimen of urine taken two hours after the biopsy is cultured.

Discussion

The first 50 biopsies are analysed as follows:

Number of patients	47
Renal tissue obtained	48
Tissue inadequate	1
Tubules and vessels only	5
Clinical diagnosis changed	25
Clinical diagnosis confirmed	22
Gross haematuria	4
Microscopic haematuria	48
Transfusions	1
Pain on puncturing kidney	5
Positive cultures from kidney tissue	1

We did not get any tissue from a gross hydronephrotic kidney which we punctured, nor from a small and very mobile kidney in a thin woman. During the first few biopsies we pushed the needle too deeply into the kidney and at right-angles to the kidney surface. When this was done, only medullary tissue was taken. Now we try to place the tip of the needle just inside the kidney capsule, and aim the needle obliquely to the surface of the kidney. These refinements of technique and hand-lens inspection of the tissue fragments have been most useful in obtaining adequate tissue from both cortex and medulla.

It is surprising, in view of the loin pain and discomfort traditionally associated with kidney disease, that only 5 patients experienced pain, which was very mild, when the biopsy needle penetrated the kidney capsule. 6 patients also complained of aching pain in the back when the procaine anaesthesia wore off.

Although transitory microscopic haematuria always develops after biopsy of the kidney, gross haematuria is rare. In 4 patients we observed gross haematuria which lasted from six to twelve hours after the biopsies were done. One old gentleman with severe calcific atherosclerosis and essential haematuria passed bloody urine and clots of blood soon after the biopsy. He did not suffer shock, and his blood-pressure did not fall; but blood which had been set aside for him was given and he made an uneventful recovery. No other sequelae of biopsy were noted.

Biopsies have been repeated on 3 patients. 1 patient died four months after the biopsy; the only lesion found was a minute dimple on the surface of the right kidney. Patients who have had biopsies done by both

techniques much prefer having it done in the prone position.

We believe this operation to be safe if meticulous care is taken to protect the patient. All the patients should be brought into hospital for the biopsy, and the operation should be done only by those who are going to use the technique frequently as part of a programme for the study of patients with renal or related diseases. Indiscriminate use of the technique by untrained people will certainly lead to accidents. We suggest that those who plan to use the technique should practise on a piece of cheddar cheese with a Vim-Silverman needle before they take a renal biopsy specimen from a patient.

Summary

Kidney biopsies done with the patient in the prone position are safe and relatively painless. The technique is described in detail, and anybody with reasonable skill should be able to do a high percentage of successful biopsies with Franklin's modification of the Vim-Silverman needle.

Kidney biopsy is of great value and can either correct or confirm clinical diagnoses of renal disease, since by its use one can make exact pathological diagnoses. It is also useful in obtaining cultures of organisms from the kidney; in following the natural history of diseases involving the kidney; in assessing the effects of drugs on renal and cardiovascular disease; in studying renal cytology and cytochemistry; and in obtaining data which may clarify present concepts of the physiology and pathophysiology of the kidney.

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ENDOMYOCARDIAL FIBROSIS

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ENDOMYOCARDIAL fibrosis is a little-known form of heart-disease characterised in its advanced stages by endocardial fibrosis, especially at the apex of the ventricles, often with thrombus upon part of the damaged area, and with variable necrosis or degeneration of sub-endocardial muscle. Since endomyocardial fibrosis in West and East Africans was first recorded by Bedford and Konstam (1946), and independently in Uganda by one of us (Davies 1948a, b, and c) shortly afterwards, it has become increasingly clear that this distinctive form of myocardial injury is responsible for many otherwise unexplained cases of heart-failure in the part of Africa where we work.

From other parts of the world isolated or small groups of cases have been published in which the clinical course and the terminal morbid anatomy seem to correspond closely to those we describe (Smith and Furth 1943, Edge 1946, Gray 1951, Fienberg and Holzman 1951, McKusick and Cochran 1952). In these 10 cases there was old-standing endocardial fibrosis which in some

cases involved the structures of the auriculoventricular valves, and mural thrombus was a feature in several. Hughes and Smith (1953) report a case from Aberdeen with all these features but also with gross coronary atheroma, diffuse fibrosis, and old and recent infarcts. In 5 cases reported by Löffler (1936), Mumme (1940), Egger (1944), and Roulet (1944) eosinophilia was present at some time; 2 examples of a possibly earlier stage are described by Büchler (1941-42) and Lennox (1948).

Our object is twofold: to draw attention to what is a major cause of heart-disease of obscure aetiology in this area and possibly elsewhere in Africa and deserves to be fully explored; and to present a more comprehensive account of its clinical features than has so far been attempted. The significance of the clinical patterns to be described will be clearer if a brief summary of the morbid anatomy of the heart is given first.

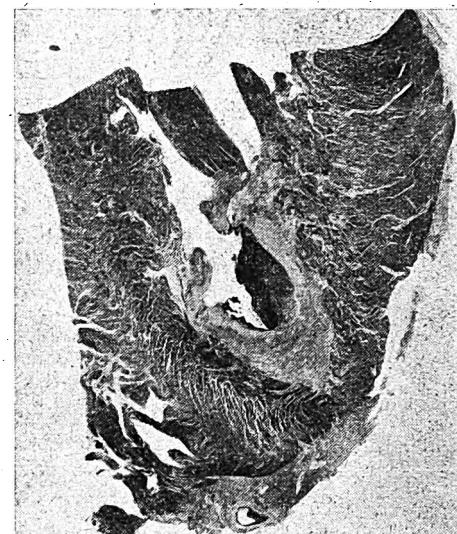


Fig. 1.—Section of left ventricle and part of right apex, showing endomyocardial fibrosis of apex of left ventricle, covered in part by thrombus. Fibrosis involves myocardium to a considerable depth and is spreading upwards from apex to involve papillary muscles. (Masson-Goldner. $\times \frac{1}{2}$.)

Morbid Anatomy

Macroscopically there is usually moderate hypertrophy. Some hearts are greatly dilated. There may be a hydropericardium, but the pericardium and epicardial muscle are healthy. Endocardial fibrosis may be confined to small patches, or may involve nearly the whole of one or both ventricles. Where it is not concealed by mural thrombus (often partly organised) it is covered by smooth endocardium, giving a pearly white appearance, with sometimes a rugose surface. The fibrous layer may be several millimetres thick, and strands may extend as far as two-thirds of its thickness into the myocardium (fig. 1). The coronary arteries are healthy, and the fibrosis has not the distribution of an infarct. The site of election is the apex of the left ventricle (table 1). The tendency is for the lesion to extend from the apex upward on to the posterior wall and the septum. The papillary muscles may become surrounded by, and later buried in, fibrous tissue, and the chordæ thickened, fused, and shortened. The cusps may become thickened and attached

TABLE I.—INCIDENCE OF ENDOMYOCARDIAL FIBROSIS IN THE DIFFERENT REGIONS OF 32 HEARTS

Region	Number	%	Subdivisions
Left ventricle	30	94	Mild 7 Moderate 11 Severe 13
Right ventricle	31	97	Mild 16 Moderate 6 Severe 9
Mitral valve	24	75	—
Tricuspid valve	23	72	—
Left auricle	6	19	—
Right auricle	7	22	—

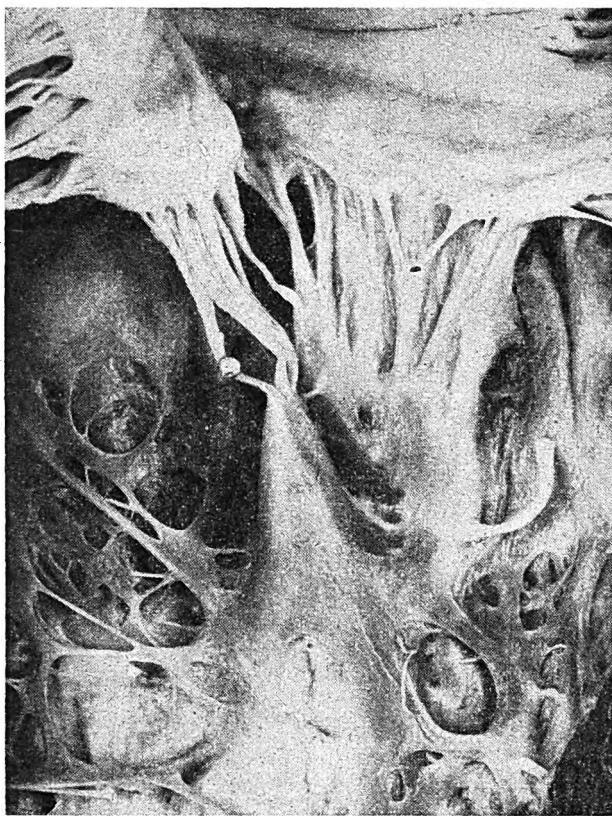


Fig. 2.—Mitral valve lesion (case 20) : anterior cusp on left shows only slight thickening ; posterior cusp is firmly adherent to the posterior wall of ventricle, and chordæ are embedded in gelatinous white fibrous tissue ; below mid-point of cusp, white fibrosis is covered with brownish deposit of organising thrombus. Upper part of apical lesion is seen at bottom of figure.

to adjacent structures ; the short posterior mitral cusp is particularly liable to be involved in this process and may become fixed to the posterior wall in a fibrous plaque or organising thrombus (fig. 2). When present these changes combine to produce various degrees of mitral or of tricuspid incompetence. Calcification may develop in the fibrous tissue, especially at the apex. Bacterial endocarditis is a rare complication. The commonest lesion in the auricles is ante-mortem thrombus in the appendages, more often the right ; this may be completely organised into white fibrous tissue. The pulmonary and aortic valves are not affected. Embolic lesions have not been common in our cases.

Histological section shows a superficial (endocardial) layer of hyaline avascular fibrous tissue and a deeper layer with dilated blood-vessels (fig. 3). Increase of elastic fibres is sometimes seen but is neither extensive nor uniform. The muscle-fibres in many parts of the heart may show hydropic, hyaline, or waxy degeneration, often with enlarged hyperchromatic square-ended nuclei.

Age, Sex, Race, and Geographical Distribution

The published cases cited above include both Negroes and Whites. Among the latter are persons known to have lived in the tropics (West Africa, Pacific) and others of whom nothing was stated about residence outside Europe or North America. The African patients of Bedford and Konstam (1946) were young adult males, from many tribes of West Africa and from some East African tribes, serving in the Middle East war theatre. Our Uganda cases, drawn from a civilian population, naturally have a different age and sex incidence. All were Africans. Records at Mulago Hospital show that no age-group is exempt from endomyocardial fibrosis. The sexes appear

to be equally affected. Representatives of many East and Central African tribes are included, the heaviest incidence being among the immigrant labourers from Belgian Ruanda-Urundi. We have no knowledge of the incidence of endomyocardial fibrosis in that country, but it can be said that in Uganda, where they come to find work, these people belong generally to the poorest stratum of society.

Clinical Patterns

The following observations relate to 20 patients, studied clinically between 1950 and 1953, in whom the diagnosis was proved post mortem. From what has been said about the situation, area, and depth of endocardial fibrosis and the variable involvement of right and left sides, septum, and structures of the auriculoventricular valves, it will be natural to expect variation in the clinical picture. This expectation is fully borne out in this small series.

The cases fall into two main groups (table II) : a small group with heart-failure only and a larger group in which signs of incompetence of one or both of the auriculoventricular valves accompany those of heart-failure. Cases with "obliterative" endomyocardial fibrosis of the right ventricle, or with a large pericardial effusion, fall into neither group. The salient clinical and anatomical features of the 20 cases are set out in table III. These patients form a consistent group, clinically, at least in the negative sense that accepted forms of heart-disease are absent, and that the semilunar valves are always spared. In most of our patients heart-failure is already severe when we first see them. So far we have no criteria for recognising or suspecting endomyocardial fibrosis, in the absence of tricuspid or mitral incompetence, before the onset of failure.

HEART-FAILURE WITHOUT OTHER DISTINGUISHING FEATURES

Of the 20 cases only 6 were without evidence of mitral and/or tricuspid incompetence both clinical and post mortem : 2 of these proved to be examples of the "obliterative" type ; the remaining 4 had bilateral heart-failure without other distinguishing features.

The histories of 3 of these 4 patients were relatively short, being three, three, and eight months from first



Fig. 3.—Heart, showing superficial thrombus ; grossly thickened endocardium with vascular channels but without inflammatory cells ; atrophic myocardial fibres underneath. (Haematoxylin and eosin $\times 16$.)

TABLE II.—CLINICAL GROUPS IN 20 CASES OF ENDOMYOCARDIAL FIBROSIS PROVED BY NECROPSY

Group	No.
<i>Heart-failure without other distinguishing features :</i>	
Isolated left or right heart-failure	0
Bilateral heart-failure	4
<i>Heart-failure with incompetence of auriculoventricular valves :</i>	
Mitral only	10
Tricuspid only	2
Mitral and tricuspid	2
<i>Other categories :</i>	
Obliterative endomyocardial fibrosis of right ventricle	2*
Large pericardial effusion	1*

* 1 patient belongs to both groups.

symptoms until death. The 4th patient had had retrosternal pain for more than two years but dyspnoea and oedema for only a few months. In each case dyspnoea and oedema had started at about the same time. On examination the signs of right heart-failure—raised jugular venous pressure, hepatic engorgement, ascites, and oedema—were very obvious. The orthopnoea and pulmonary crepitations of left heart-failure were equally evident in 3 of these patients, but less pronounced in the 4th. Only 1 had a significantly loud apical systolic murmur; in this case necropsy revealed that the left ventricle was two-thirds filled with ante-mortem thrombus. Possibly some mitral incompetence was present, but unfortunately this specimen is not available for further study.

At necropsy all the hearts were found to be enlarged, 3 greatly so. Characteristic endocardial fibrosis was present in both ventricles in 3, and in the left ventricle alone in 1. Ante-mortem thrombus was present in both ventricles in 2 and in the left ventricle alone in the other 2. The valves were normal in every case. Although we have not yet seen a patient presenting the signs of pure left-sided failure, it seems reasonable from consideration of the pathology to anticipate that such cases will be observed from time to time. Two cases presenting pure right-sided failure have been classified under "obliterative" endomyocardial fibrosis for the reasons given.

MITRAL INCOMPETENCE

There were 10 cases in which mitral incompetence was present alone, and 2 others with tricuspid incompetence in addition. The duration of symptoms in the 10 with mitral incompetence alone ranged from two to twenty-four months, starting in 3 with dyspnoea and in 3 with oedema and ascites; in the remaining 4 the histories suggest that symptoms of right and left heart-failure appeared together. 5 patients had noticed palpitations as one of the earliest symptoms, and 6 complained of anorexia. 8 patients had advanced bilateral heart-failure, as in the first group. All had a loud apical systolic murmur, in some palpable as a thrill. Special note of the pitch of this murmur was made in 6 cases; it was recorded as high-pitched in 4 and medium in 2. An apical diastolic murmur was heard in 5 cases, but it was faint, short, or transient in 4. A short early diastolic murmur was present in 13 of Brigden and Leathem's (1953) 30 cases of mitral incompetence. Triple rhythm was present in 8 of our cases.

Enlargement of the heart was shown in all 7 patients who were radiographed; the cardiothoracic ratio varied from 0.57 to 0.73. The amplitude of pulsation of the left ventricle was greatly diminished in 3 cases in which this feature was looked for. The left auricle was slightly or moderately enlarged in 4 cases in which oblique radiography was recorded; 3 of these were examined carefully for pulsation of the oesophagus, but only 1 showed definite systolic expansion of the left auricle. In several recent cases not verified at necropsy, which were subjected to

more thorough radiography, rapid expansile movement of the left auricle in systole, backwards in the right oblique, and to the right in the anteroposterior position was observed. In these 10 cases the suspicion of organic mitral incompetence arose during life from (1) a loud apical systolic murmur, in the absence of hypertension, aortic-valve disease, anaemia, or any other apparent cause, for a systolic murmur, and (2) moderate enlargement of the left auricle, with or without systolic expansion, in the absence of the diastolic murmur, loud first sound, or opening snap of mitral stenosis.

The structural changes demonstrated post mortem included embedding of the papillary muscles in dense white fibrous tissue (fig. 4) or their replacement by the latter; fibrosis and thickening of the free margins of the cusps, particularly of the posterior cusp; and adherence of the posterior cusp to the wall of the ventricle (fig. 2). In our experience mitral incompetence is present in at least half the clinically recognisable cases of endomyocardial fibrosis and provides the clearest criterion, when other causes can be excluded, for clinical diagnosis in the later stages of the disease. Thus organic mitral incompetence stands in much the same relation to endomyocardial fibrosis as does mitral stenosis to rheumatic heart-disease.

TRICUSPID INCOMPETENCE

There were 4 cases with clinical and post-mortem evidence of tricuspid incompetence; in 2 of these mitral incompetence was present also.

Both patients with isolated tricuspid lesions had predominant right heart-failure, but both had some dyspnoea also. Factors contributing to the dyspnoea included hydrothorax in 1 patient, bronchitis in 1, and elevation of the diaphragm in both. Both had a high jugular venous pressure with prominent C waves. Ascites and dependent oedema were gross. The liver was enlarged in both patients, but expansile pulsation was not recorded; 1 patient was slightly jaundiced. In 1 patient a systolic

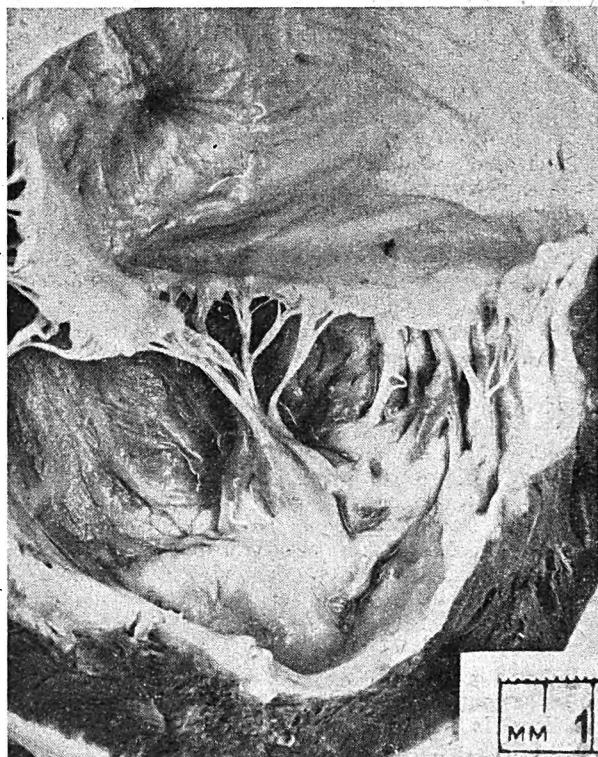


Fig. 4.—Lesion at apex of left ventricle (case 16): disc of firm white fibrosis 2-3 mm. thick occupies entire apex, and strands spread up on posterior wall to reach but not involve posterior cusp.

murmur at the lower left sternal edge was heard. Radiography showed a very large and globular heart in both cases; in neither was the oesophagus displaced.

At necropsy endomyocardial fibrosis restricted to the right heart was found in both cases, extending from the apex to involve the papillary muscles and the tricuspid chordæ. In 1 case the entire apex and most of the wall were coated with thick white fibrous tissue and the ventricle resembled those described below as "obliterative" endomyocardial fibrosis. The right auricle in both cases was dilated and hypertrophied, one being enormous, with much ante-mortem thrombus upon the wall.

OBLITERATIVE ENDOCARDIAL FIBROSIS

In 2 other patients the clinical picture was very similar to that of isolated tricuspid incompetence; it bore an even closer resemblance to that of constrictive pericarditis. One had been troubled for seven years, the other for nearly three, by gross ascites and oedema but without dyspnoea or other evidence of left heart-failure. Both patients had high jugular venous pressures without conspicuous pulsation. In both the liver, though enlarged, did not show expansile pulsation. Murmurs were absent.

These features raised the possibility of constrictive pericarditis. In 1 case this was excluded during life because a massive low-tension pericardial effusion was present and radiography after the substitution of air showed a thin ballooned pericardium. This patient had a very loud third sound, maximal over the lower sternum, and persistent auricular fibrillation—two signs which strengthened the resemblance to constrictive pericarditis.

At necropsy in both cases the pericardium was normal, but there was extensive endocardial fibrosis of the right ventricle, with extraordinary distortion of the cavity, almost obliterating the inflow tract; little but infundibulum remained, and the apex had disappeared. Some of the tricuspid-valve chordæ and papillary muscles were completely buried in this mass of fibrous tissue, and the tricuspid ring was enormously dilated. The myocardium was greatly thickened at the apex, giving the impression that the opposing walls of the ventricle had fused in this region, obliterating the cavity between them. This impression of obliteration has been reinforced by the condition of other hearts, at an earlier stage of the lesion, which are not included in this series.

Thus these cases have close clinical and haemodynamic affinities with constrictive pericarditis. 2 remarkably similar cases (Fienberg and Holzman 1951, McKusick and Cochran 1952) have been reported from the United States, and 1 (Egger 1944) from Switzerland. The designation "constrictive endocarditis" used by McKusick and Cochran is appropriate in so far as it emphasises the clinical resemblance to constrictive pericarditis. Egger's expression "endocarditis obliterans" describes more exactly the appearance of the affected ventricle and its greatly reduced capacity. Since either term might be taken to imply inflammation, which in the present state of our knowledge cannot be assumed, both terms are perhaps best avoided.

The close resemblance between cases in this group and those with isolated tricuspid incompetence has already been remarked. In fact there is probably some incompetence in the former, if one can judge by the size of the tricuspid ring and the distortion of the valve components.

HYDROPERICARDIUM

In 5 of our 20 cases a small pericardial effusion (100–200 ml.) was found post mortem. 1 other patient, already mentioned in the section on obliterative endocardial fibrosis had more than 2 litres of clear yellow fluid in an enormous thin-walled sac which, in spite of aspirations, persisted with little change for eighteen months. At one sitting 1500 ml. was removed. The fluid was not under tension,

and even after the substitution of air the pericardium still appeared half-full. The protein content varied between 2.1 and 3.2 g. per 100 ml., and the cells, chiefly lymphocytes, from 1 to 50 per c.mm. Inoculation of the fluid into guinea-pigs gave negative results on two occasions, and no evidence of tuberculosis was found post mortem.

Factors important in the production of these pericardial effusions probably include a high central venous pressure, a low plasma-albumin level, and a small heart. The plasma-albumin level in this last case varied between 1.3 and 2.0 g. per 100 ml. Hydropericardium is to be expected in occasional cases of endomyocardial fibrosis when there is a combination of factors favourable to its accumulation.

Electrocardiography

Fourteen electrocardiograms recorded from 11 patients do not reveal any consistent pattern, but all are abnormal in some respect.

A low voltage of QRS in the limb leads was almost the rule, as might be expected in a group of patients in severe heart-failure nearly all having much oedema and ascites and some pleural or pericardial effusion. Low or flat T waves in many (especially the limb) leads was common, sometimes but not always in association with very low QRS.

Correlation of electrocardiograms with the clinical or anatomical evidence of auricular or ventricular hypertrophy was consistent in some cases but not in others. The similarities in the electrocardiographic patterns in ventricular hypertrophy and incomplete bundle-branch block (Rosenman et al. 1950) complicate assessment of these factors in life. Electrocardiograms are seen suggesting right or left ventricular "strain," with QRS splintered and relatively broad but not exceeding 0.1 sec., and lacking the high-voltage R and S of ventricular hypertrophy. Incomplete bundle-branch block was considered a factor in 3 patients with electrocardiograms of this pattern. In 2 of these (cases 11 and 15, table III) the corresponding surface of the septum was involved, with deep invasion of the septal muscle in case 11. In the other (case 7) the changes were attributable to digitalis; both ventricles were involved in this case, and injury to conducting tissue as an additional factor cannot be excluded. Extensive subendocardial fibrosis of the septum and apex, without evidence of conduction defect, is also seen.

Delayed atrioventricular conduction was observed in 3 cases and auricular fibrillation in 1.

Significant deviation of ST not attributable to digitalis was not found in this series. If a phase of acute muscle injury precedes endomyocardial fibrosis it is probably past by the time we see our patients. The injured muscle is dead and is being replaced by fibrous tissue. There can be no "current of injury," and ST deviation from this cause is not to be expected at this stage of the disease.

Thus we have found the electrocardiogram of little assistance in the diagnosis of endomyocardial fibrosis or as an aid to localisation of its main lesion in the heart. All that can be said from the study of these cases is that a physiological electrocardiogram would be fairly strong evidence against extensive endomyocardial disease in its later stages; that "injury" effect is not seen in the late stages of endomyocardial fibrosis; and that unequivocal conduction defects are not more common in this disease than in severe heart-failure from other causes. Finally, as with the clinical signs and symptoms, we have no knowledge of the changes in the electrocardiogram at the time of the initial lesion which precedes endocardial fibrosis.

Prognosis

5 patients died within a few days of admission to hospital, but most patients lingered for weeks or months

in a waterlogged condition unhelped by treatment. In some of these patients intercurrent infection—e.g., bacterial endocarditis, miliary tuberculosis, and whooping-cough—contributed to death. Our longest period of observation was twenty months; this patient had a history of recurrent attacks of oedema for two or three years previously. Another patient had had symptoms for seven years. These were the longest histories among the 20, and both patients had endomyocardial fibrosis of the obliterative type with gross fibrosis, which appeared to be of long standing. Evidently some patients can survive the initial injury for many years, fibrosis proceeding to a point where cardiac disability becomes stationary or only very slowly progressive, as in rheumatic heart-disease. A few cases have been seen at necropsy with localised patches of superficial endocardial fibrosis at the apex of one or other ventricle. In them the cause of death was not attributable to this lesion and there was

no reason, from the clinical evidence available, to suspect any impairment of cardiac function during life.

The response to treatment of heart-failure by rest in bed with digitalis, mercurial diuretics, and aspiration of fluid was disappointing. Temporary improvement was observed in a few cases, but all relapsed quickly. It seems that, once heart-failure is established in endomyocardial fibrosis, there is little chance of remission or of controlling failure sufficiently to restore any useful capacity for sedentary activity. A selected series of necropsies is not representative, but in other patients where heart-failure has been attributed to endomyocardial fibrosis we have never seen a prolonged remission.

Clearly then the period of survival after heart-failure is established varies considerably, but the ultimate prognosis is the same. What we do not know is how long elapses between the initial injury and the onset of heart-failure and how extensive an endomyocardial lesion

TABLE III.—SUMMARY OF CLINICAL AND NECROPSY FINDINGS IN 20 CASES OF ENDOMYOCARDIAL FIBROSIS

Case no.	Sex	Age (yr.)	Duration of symptoms (mos.)	History of heart-failure	Systolic murmur at apex	Blood-pressure on admission (mm. Hg)	Radiographic findings		Chief electrocardiographic findings	Heart weight (g.)	Chambers affected (in order of severity)	Site of ante-mortem thrombus	Valves involved	Clinical group
							Loudness	Pitch						
1	M	35	2	B	L	105/80	410	L.V. L.A. R.A.	R.A.	M	M.I.
2	M	35	12	L → B	L	Too low to record	340	L.V.	L.V.	M	M.I.
3	M	55	6	R → B	O	145/95	0.65	538	R.V.	O	T	T.I.
4	M	45	32	B	F	115/85	T flat limb leads L.V. "strain"	510	L.V. R.V. R.A.	L.V. R.V. R.A.	O	H.F.
5	M	20	21	L → B	L	110/75	0.61	+	..	454	L.V. R.V.	O	? M	M.I.
6	M	35	11	B	+	80/60	0.67	524	L.V. R.V.	O	M	M.I.
7	M	30	8	B	F	100/90	0.72	?	A.V.C.D., I.V.C.D., with coupling; digitalis effect	"Big"	L.V. R.V.	L.V. R.V.	O	H.F.
8	M	40	15	B	L	H.P.	100/85	0.57	..	368	L.V.	O	M.	M.I.
9	F	35	3	R → B	L	Too low to record	325	L.V.	L.V.	? O	H.F.
10	M	18	2	B	III*	H.P.	95/75	..	QRS < 0.5 mV†	295	L.V. R.V.	L.V.	M + T	M.I. + T.I.
11	F	40	13½	R → B	O	O	90/60	0.79	O	368	R.V. R.A.	R.A.	T	T.I.
12	F	29	11	R → B	II*	H.P.	110/80	0.66	O	210	R.V. L.V. R.A. L.A.	R.A.	M + T	T.I. + M.I.
13	M	30	6	R → B	III*	M.P.	105/90	0.70	++	640	L.V. L.A. R.A. R.V.	O	M	M.I.
14	M	24	2½	O	III*	H.P.	Too low to record	L.V.	L.V.	M	M.I.
15	M	30	3	B	O	O	100/60	Obscured	..	680	R.V. L.V. L.A. R.A.	O	H.F.	
16	M	35	33	R	O	O	115/95	Obscured	Obscured	400	R.V. L.V. R.A. L.A.	R.A.	T	O. (R.V.)
17	F	8	24	L → B	III*	H.P.	90/70	0.73	++	378	L.V.	O	M	M.I.
18	M	25	84	R	O	O	85/75	325	R.V. L.V. R.A.	R.A.	T	O. (R.V.)
19	F	5	12	R → B	IV*	H.P.	125/90	0.66	++	210	L.V. R.V.	O	M	M.I.
20	M	30	5	R → B	IV*	M.P.	100/80	0.62	..	320	L.V. R.V.	L.V.	M	M.I.

* Levine classification: +, present; O, absent; .., not recorded.

† Tallest R or S in limb leads less than 0.5 mV.

A.V.C.D., auriculoventricular conduction delay or defect.

B, bilateral heart-failure.

F, faint.

H.P., heart-failure without other distinguishing features.

H.P., high pitch.

I.V.C.D., intraventricular conduction delay or defect.

L, Loud.

L → B, left progressing to bilateral heart-failure.

L.B., left bundle-branch.

M, mitral valve.

M.I., mitral incompetence.

M.P., medium pitch.

O. (R.V.), obliterative endomyocardial fibrosis of right ventricle.

R, right.

R → B, right progressing to bilateral heart-failure.

R.B., right bundle-branch.

T, tricuspid valve.

T.I., tricuspid incompetence.

has to be to produce heart-failure. Nor do we know whether or how far the initial lesion is reversible, and whether recovery in the earliest stage may take place without any permanent endomyocardial damage whatever. We do know that an arrested lesion, limited in extent, is compatible with unimpaired cardiac function.

Diagnosis

In this part of Africa, where its high incidence is established beyond doubt on post-mortem evidence, endomyocardial fibrosis must always be suspected in any case of heart-failure without obvious other cause. Clinical diagnosis rests on careful exclusion of other forms of heart-disease, a process facilitated in Uganda Africans to the extent that coronary, thyrotoxic, and pulmonary heart-disease and beriberi are absent or extremely rare. The most common problems in differential diagnosis arise in connection with rheumatic heart-disease and tuberculous pericarditis. Differentiation between a much dilated heart and a pericardial effusion may be impossible without paracentesis, for neither clinical nor radiological signs have proved altogether reliable; the resemblance between obliterative endomyocardial fibrosis and constrictive pericarditis has been shown.

In our experience the following criteria are of value in the diagnosis:

- (1) A loud apical systolic murmur, especially if high-pitched or associated with a thrill in the absence of hypertension, aortic-valve disease, mitral stenosis, bacterial endocarditis, and severe anaemia.
- (2) Enlargement of the left auricle in the absence of mitral stenosis.
- (3) Evidence of auricular hypertrophy in the electrocardiogram in the absence of mitral stenosis.
- (4) Expansile systolic pulsation of the left auricle, visible radiographically in the right oblique and at least one other view.
- (5) Tricuspid incompetence in the absence of bacterial and rheumatic heart-disease.
- (6) Signs suggesting constrictive pericarditis but with a larger heart than is usual in that disease and without calcification of the pericardium.
- (7) A large hydropericardium of unexplained cause.
- (8) Diminished pulsation of the heart seen radiographically in the absence of pericardial fluid.
- (9) Bilateral heart-failure without valvular disease in the absence of other adequate cause.
- (10) Auricular fibrillation in the absence of rheumatism, hypertension, and thyrotoxicosis.
- (11) Electrocardiographic evidence of intraventricular conduction defect in the absence of syphilis, rheumatism, coronary disease, and hypertension.

Discussion

Much heart-failure is observed in African hospitals which cannot be explained in terms of recognised aetiology. In our experience in Uganda much of this is attributable to endomyocardial fibrosis.

We are concerned here primarily with the clinical aspects of endomyocardial fibrosis. The clinical picture we have presented is far from complete but may serve to aid recognition and observation of this disease in other areas where it may occur, particularly where facilities for necropsy are restricted.

Important papers bearing on our subject have recently appeared from two sources in southern Africa. The clinical picture and course of "nutritional heart-disease" (Gillanders 1951, Higginson et al. 1952) are similar in many respects to those of endomyocardial fibrosis, but in the former endocardial fibrosis is very slight and found only beneath a thrombus, and there is also a constant association with hepatic cirrhosis, which is lacking in endomyocardial fibrosis seen by us in Uganda. Becker et al. (1953) have developed their conception of "cardio-vascular collagenosis" from a study of cases in which parietal endocardial thrombus was found at necropsy. Certain findings common to endomyocardial fibrosis,

including involvement of the papillary muscles, are noted, but we feel that this is a heterogeneous group; it may well include some cases of the type we see in Uganda but is not representative of it. In neither of these series is gross deformity or fixation of the auriculoventricular cusps described, nor is anything resembling the obliterative type reported.

Certain resemblances between endomyocardial fibrosis and rheumatic heart-disease are sufficiently close to merit comment. Not only is clinical diagnosis between them sometimes difficult but also some of the gross changes which may take place are similar in the two diseases. However, the incidence of these changes in either disease is very different, and the difficulty which may arise over a single case disappears when series of cases of the two diseases are compared.

We do not discuss the aetiology here, because we have insufficient evidence to offer. The negative evidence and the more likely possibilities are discussed elsewhere (Williams et al. 1954). Nor, it must be emphasised, have we any certain knowledge of the pathology or the symptoms of the earliest stages of endomyocardial fibrosis. Wider recognition of this disease will, it is hoped, provide information of its incidence and distribution and so make possible study of its aetiology and prevention.

Summary

A brief account is given of the pathology of endomyocardial fibrosis.

Large areas of firm white fibrous tissue are seen on the endocardial surface of the ventricles, commonly involving the structures of the auriculoventricular valves, particularly the posterior mitral cusp and chordæ, with resulting mitral incompetence. In some cases an obliterative effect is produced, reducing the capacity of the right ventricle. Parietal thrombus is common.

The signs and symptoms produced by these different lesions are described from observations on 20 cases proved at necropsy.

Knowledge of the earlier stages is wanting, and the cause is not known.

It is suggested that endomyocardial fibrosis is the cause of much of the heart-disease of obscure aetiology in Africa.

We are grateful to our clinical colleagues for permission to study their cases and for access to their records, particularly to Dr. H. C. Trowell and Dr. P. W. Hutton; to Dr. A. B. Raper and Dr. B. G. T. Elmes for the use of necropsy material and records; to Dr. J. Scott Brown and Dr. A. G. M. Davies for assistance in radiology; to all these for their interest and helpful criticism, and to Dr. Phillip Evans, of Guy's Hospital, for his advice in the preparation of this paper; to Mr. T. N. Salthouse for preparing the photographs; to Dr. A. A. Alderdice, medical superintendent of Mulago Hospital, for his interest; and to the Research Committee of the University College of East Africa for a grant towards expenses in connection with this work.

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PROPHYLAXIS OF SUMMER HAY-FEVER AND ASTHMA

A CONTROLLED TRIAL COMPARING CRUDE GRASS-POLLEN EXTRACTS WITH THE ISOLATED MAIN PROTEIN COMPONENT

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PRESEASONAL injection therapy is the method of choice for prophylaxis in patients with seasonal hay-fever when sufficient relief is not obtained with palliative anti-histamine drugs. Using large doses Frankland (1954) has shown that equally good results are obtained with four different types of grass-pollen extracts. We therefore investigated which part of the crude grass-pollen extracts is responsible for the beneficial results of the injections. Much of the material shown by skin tests to be inactive can be removed by dialysis (Augustin Friedmann 1952), and the active components have been shown to consist of protein complexes of average molecular weight 14,000 (Augustin 1953a). Accordingly we concentrated the active material by ultrafiltration through a collodion membrane, and thus separated the active protein from the bulk of the cutaneously inactive components of molecular weight <10,000.

Materials

'Pollaccine,' the material used in our standard treatment, is a mixture of crude extracts of pollen of timothy and cocksfoot grasses containing 100,000 Noon units per ml.—i.e., after being defatted with acetone, 100 g. quantities of dry pollen were extracted with 1000 ml. of slightly alkaline saline buffer (Evans 1922).

The *ultrafiltrate* of pollaccine was shown by paper chromatography to contain pigments, carbohydrates, amino-acids, and peptides (Augustin 1953a). Its volume was equivalent to that of the original extract. It was used for treating some patients because it could conceivably have contained some clinically important factor not revealed by skin tests.

Purified Pollen Protein.—The material left behind on ultrafiltration consists of the pollen-protein concentrate and was fractionated according to a scheme already published (Augustin 1953b). The main component common to the two grasses (Augustin 1953c) was used alone in this trial. It was almost colourless, contained only 2% of combined carbohydrate, and proved on a weigh-for-weight basis somewhat more active than the other protein components. Purified pollen protein 0.05 g. was dissolved in 100 ml. of a solution containing 5.0 g. of glucose, 5.0 g. of glycine, 2.5 g. of sodium chloride, 0.363 g. of KH_2PO_4 , and 1.43 g. of $Na_2HPO_4 \cdot 12H_2O$ in 1 litre of distilled water; 1 : 10,000 thiomersalate was used as a preservative. Equivalent dilutions of this solution of purified pollen protein were compared on corresponding sites of the forearms with those of the original 100,000 Noon unit solution of pollaccine. The sizes of the weals for each of the equivalent dilutions were the same.

Phenol saline solution consisted of physiological saline solution containing 0.4% phenol and was coloured slightly yellow with burnt sugar.

All the solutions were sterilised by Seitz filtration, and all were used as if containing 100,000 Noon units per ml. (Noon 1911). Equivalent dilutions of all four solutions were made in phenol saline solution. From previous

experimental findings in the trial of 1952 (Frankland 1954) it seemed that an injection course going up to 20,000 units gave as good results as a larger dosage up to 100,000 units. The lower dosage was therefore used in the present trial.

Scheme of Trial

During the summer of 1953, 200 patients were put in the trial: 100 received grass-pollen injections—50 the standard pollaccine and the other 50 purified pollen protein—and the remaining 100 were also divided into two equal groups, one receiving ultrafiltrate (shown by skin tests to be practically inactive) and the other phenol saline solution.

The patients chosen for the trial were those with summer hay-fever with or without an associated summer asthma. Only patients who had had no previous injection treatment and no symptoms other than those due to grass pollen were put in the trial. Randomisation and follow-up of the patients were similar to those in previous trials (Frankland and Gorrill 1953, Frankland 1954).

Method of Assessment

After the course of treatment was completed, the patients were reviewed and the results were recorded in ignorance of the kind of treatment which the patient had received. There was thus no possibility of asking biased questions when reviewing the patients. As in previous trials, the patients kept daily record charts of their symptoms, and at the end of the trial were asked for their over-all impression of the result of treatment.

Results of Treatment

Table I shows that the four groups are comparable as regards sex, age, age at onset of hay-fever, and follow-up.

TABLE I—THE FOUR GROUPS OF CASES

	Pollaccine	Purified pollen protein	Phenol saline solution	Ultra-filtrate
<i>Sex :</i>				
Male ..	30	31	34	30
female ..	20	19	16	20
<i>Age (yr.) :</i>				
0-9 ..	8	3	10	8
10-19 ..	17	20	24	24
20-29 ..	19	18	9	13
30-39 ..	5	6	5	5
40-49 ..	1	3	2	..
50 or more
<i>Age at onset (yr.) :</i>				
0-9 ..	9	6	8	7
10-19 ..	17	18	22	25
20-29 ..	16	16	14	12
30-39 ..	8	8	5	5
40 or more	2	1	1
<i>Follow-up :</i>				
Attended interview ..	48	45	48	47
Replied by letter ..	2	4	2	2
Defaulted ..	0	1	0	1

Table II shows the results of treatment in the four groups:

"Excellent" means that the patient was completely free from symptoms.

"Good" means that the patient considered the treatment had been well worth while, though some mild symptoms were present on occasions.

"Moderate" means that the patient considered that some improvement had taken place, but that some undesirable although not serious symptoms had occurred. This group includes any patient who was in any way disappointed with the result.

"Poor" means that no benefit was derived from the treatment.

Table II shows that 78 (79%) of the hay-fever patients had either good or excellent results following pollen treatment—26 (27%) said they had been completely

* In receipt of a full-time grant from the Asthma Research Council.

TABLE II—RESULTS OF DIFFERENT TREATMENTS OF SEASONAL HAY-FEVER IN 200 PATIENTS

Results	Pollaccine	Purified pollen protein	Phenol saline solution	Ultra-filtrate
Excellent ..	13	13	1	0
Good ..	27	25	14	18
Moderate ..	4	6	11	4
Poor ..	6	5	24	27

free from hay-fever—compared with 33 (33%) who had either good or excellent results when treated with either phenol saline solution or the ultrafiltrate (only 1 of these claimed a summer completely free from hay-fever). 21 (21%) had poor results following pollen treatment, compared with 66 (67%) of the controls.

The patients in the four groups who had an associated asthma with their hay-fever are compared similarly in table III. 29 (94%) of those who had received either the ordinary whole mixed pollen (pollaccine) or the purified pollen protein had either good or excellent results, and only 2 (6%) either moderate or poor results, compared with 8 (30%) who had either good or excellent results and 18 (70%) who had either moderate or poor results on treatment with either phenol saline solution or the ultrafiltrate.

Table II shows that the results obtained in the patients treated with phenol saline solution are very like, and as poor as, those of the patients treated with the ultrafiltrate. Comparison of the results obtained with the total pollen extracts (pollaccine) and those of the purified pollen protein shows that again the results are very similar and equally good. For purposes of analysis the results "excellent" and "good" can be considered "good,"

TABLE III—RESULTS OF 4 DIFFERENT TREATMENTS OF SEASONAL POLLEN ASTHMA

Results	Pollaccine	Purified pollen protein	Phenol saline solution	Ultra-filtrate
Excellent ..	15	8	4	3
Good ..	1	5	0	1
Moderate ..	0	0	2	1
Poor ..	1	1	6	9

and the "moderate" and "poor" can be considered "poor." The results of treatment with phenol saline solution and with the ultrafiltrate were pooled and compared statistically with the pooled results of treatment with pollaccine and with purified pollen protein: $\chi^2=39$, and $P=0.001$ —i.e., the probability that the differences between the two groups are due to chance is less than 1 in 1000.

Reactions to Injection Treatment

3 patients developed asthma in 1953 for the first time: 2 of them had been treated with phenol saline solution and 1 with the ultrafiltrate. 9 patients, including the 3 who developed asthma, claimed that the year had been the worst they had known as regards hay-fever. Since only 1 of the 9 had had pollen (pollaccine) injections, these statements were not surprising.

No patient who had injections of phenol saline solution had any local reactions, but 1 stopped the injections because vomiting developed immediately after the tenth injection and the patient thought that the vomiting was caused by the injection. 2 patients who received the ultrafiltrate stopped the injections because of alleged local reactions; 1 other patient developed epilepsy during the course of injections, and 2 others said they had felt tired and irritable. In contrast to this, 18 of the 50 patients on the mixed pollen extract and 12 of the 50 patients on the purified pollen protein had general reactions.

The size of the skin weals was noted before, during, and at the end of treatment. The weal at the end of treatment was much smaller than the pre-treatment weal in all the patients who received either pollaccine or purified pollen protein. The patients who had received either phenol saline solution or the ultra-filtrate usually showed no change in size of the weal.

Discussion

Preseasonal injection therapy in the treatment of hay-fever and asthma is a time-honoured procedure and has been in general use for the past forty years (Noon 1911); yet we do not know of any published report of a single clinical trial properly controlled according to modern standards. The earlier reports were reviewed by Fitzgerald and Sherman (1949).

The present investigation was prompted by the fact that the crude extracts used in conventional treatment must contain much clinically useless material which could have been responsible for some of the untoward reactions of the treatment. We wanted to find out which part of these extracts was responsible for the success of preseasional injection therapy; whether the therapeutically important components were identical with those responsible for the skin-test reactions; whether there was more than one sensitising fraction; and if there were several, whether they can be used interchangeably in the treatment.

An unfractionated pollen-protein concentrate obtained from giant-ragweed extracts by dialysis has been used as an immunising agent in hay-fever patients (Stevens et al. 1951). It proved active, but unfortunately this was not a strictly controlled trial.

Service (1937) used an antigenic polysaccharide from pollen (not timothy-grass) and had the impression that some attacks in man were lessened by this carbohydrate.

No active uncombined polysaccharide has so far been isolated from grass pollens, but several protein complexes have been isolated (Augustin 1953a and b) which differ in carbohydrate content, pigment content, electrophoretic mobility, and iso-electric point. All these fractions are active according to skin tests. In the present clinical investigation only one of these fractions, the principal component, was assessed. It is not known whether all the different protein fractions are contaminated with small amounts of one and the same hypothetical active component. If further investigations confirm that there is no such hypothetical contaminant, it still remains to be seen whether the different protein components can take the place of each other therapeutically.

In the present investigation no difference was found between the results of treatment obtained with the conventional crude extracts and those obtained with their principal protein component. Other protein components thus appear to have played little part in the treatment. This may be merely because there is less of them. On the other hand, their manner of action may be identical, and it may clinically be impossible to show finer quantitative differences. Moreover the non-protein factors of the extracts seem to have neither a beneficial nor an obnoxious effect.

However, 32% of the patients treated with either the ultrafiltrate of pollaccine or phenol saline solution had good or excellent results (compared with 78% of the patients treated with either pollaccine or purified pollen protein). This may be considered an unexpectedly high figure; one reason for this may be that grass-pollen incidence in 1953 (if counts at Cardiff may be taken as a guide) was relatively low (H. A. Hyde, personal communication).

Summary

In preseasional injection therapy the results obtained with the conventional crude pollen extracts (pollaccine)

and with the purified main protein component of such extracts were compared with those obtained with the combined non-protein constituents of pollaccine shown by skin tests to be inactive and with control phenol saline solution on 200 patients with summer hay-fever.

The results obtained with purified pollen protein were very similar to those obtained with pollaccine.

The ultrafiltrate of pollaccine, consisting of the components other than the pollen protein, gave results similar to those obtained with phenol saline solution.

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ISLET-CELL ADENOMA OF THE PANCREAS IN A CHILD AGED SEVEN YEARS

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CHRONIC hypoglycæmia caused by a functioning islet-cell adenoma of the pancreas is extremely rare in children aged less than 12 years. Only 6 cases in this age-group have been published hitherto. Of these children 3 were cured by removal of the adenoma (Harnapp 1936, Wangensteen 1937, Wilder 1940), and 3 died, the adenoma being discovered at necropsy (Wolf et al. 1933, Rabino-vitch and Achs 1945, Sherman 1947). On the other hand, about 400 cases have been described in adults (Howard et al. 1950).

In the present case the neurological signs were rather unusual, and there was a satisfactory response to corticotrophin therapy before surgical exploration.

Case-history

A girl, aged 5½ years, was referred to the hospital in October, 1951, because of the recent onset of major fits and periods of stupor. She had been quite well until July, 1951, when her parents began to notice a change in her behaviour : she became irritable, tired, and troublesome. She was sleeping on much later in the mornings than usual. In October, 1951, she had her first major fit at 8 A.M. and was very drowsy for some hours afterwards. She was admitted to the Westminster Children's Hospital a few days later for investigation. At that time there were no abnormal signs between attacks. The signs in the nervous system during and after the fits were those found in any epileptic child. The fits usually occurred in the morning, and the period of stupor which followed lasted several hours. Since, after investigation, no cause for the fits was found, she was discharged home taking phenobarbitone, which had seemed to have a slightly beneficial effect in hospital. During the next few months she gradually developed constant ataxia of the arms and legs and fine tremor of the hands ; meanwhile the fits and periodic stupor occurred as before, and she often remained "asleep" in bed at home till midday. She lost weight, and vomited occasionally.

On readmission in January, 1952, motor incoordination of the arms and legs was found. The muscles were generally hypotonic, but the tendon-reflexes were present, though usually sluggish. She was very irritable and difficult to manage. She was emotionally unstable and liable to burst into tears. There was no evidence of a rise in intracranial pressure, but ventriculography was done by Mr. J. E. A. O'Connell to exclude cerebral tumour ; the result was normal. The child now developed slurring and scanning of her speech. The cerebrospinal fluid was normal and contained 58 mg. of glucose per 100 ml.

In March, 1952, she was readmitted for further observation because the fits and ataxia were becoming more severe. Her condition still could not be diagnosed, and she was treated with sedatives. During the summer of that year she was relatively free from serious attacks, but it became necessary for her to attend a special school because her mental powers were deteriorating. Her reeling gait by then strongly suggested cerebellar ataxia.

In the autumn of 1952 the symptoms again increased, and on one day in November, after a fit at home, she remained unconscious for five days.

In April, 1953, while in hospital, it was noticed that she had some wasting of the thenar eminences and of the first dorsal interossei muscles of both hands ; that she woke up from her drowsy state if given a drink containing sugar ; and that, if food was deliberately withheld in the morning, she would almost certainly have a fit. By that time the child was thin, pale, underweight, and seriously incapacitated by her condition. Her fasting blood-sugar level was

Fig. 1—Glucose tolerance with patient on normal diet.

estimated on April 30, 1953, when

it was 43 mg. per 100 ml. On May 4 the level was the same. The Wassermann reaction and Kahn test of the blood

were negative, the serum-potassium level was normal during an attack, and the urine was normal throughout.

Further blood-sugar investigations.—Fasting blood-sugar levels during the morning of May 15, 1953, were 55 mg. per 100 ml. at 9.40 A.M., 43 mg. per 100 ml. at 10.20 A.M., and 49 mg. per 100 ml. at 11 A.M. There was no detectable rise in the blood-sugar level after an injection of 3 minims of adrenaline 1 : 1000. A glucose-tolerance test (preceded by normal diet) showed a high and sustained level after an initial hypoglycæmia, without glycosuria (fig. 1), and the level remained high at 2½ hours. A glucose-tolerance test (after three days' diet containing at least 200 g. of carbohydrate) showed a slight rise from a hypoglycæmic level after the ingestion of glucose, and a return to a low level soon afterwards (fig. 2). Fasting blood-sugar levels after an injection of 40 mg. of corticotrophin showed a slow rise from 75 mg. per 100 ml. to 100 mg. per 100 ml. after 2½ hours. A glucose-tolerance test after two weeks' corticotrophin therapy and a high-carbohydrate diet

showed a virtually normal curve, with a fasting level of 92 mg. per 100 ml.

Treatment and progress.—The diagnosis was now obviously organic hyperinsulinism ; so the child was treated with a high-carbohydrate diet and corticotrophin for two months (50 mg. of 'Acthar gel' daily) while awaiting surgical exploration of the pancreas. There was a striking change in a few days ; the convulsions disappeared, and no further drowsiness was observed. After only two weeks'

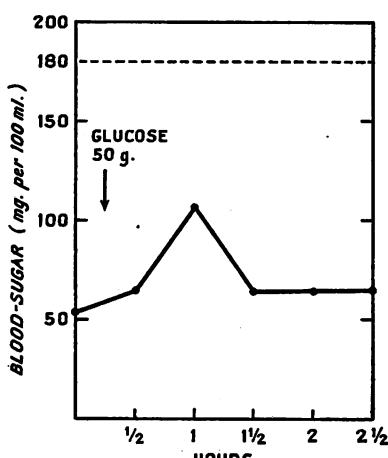


Fig. 2—Glucose tolerance with patient on high-carbohydrate diet.

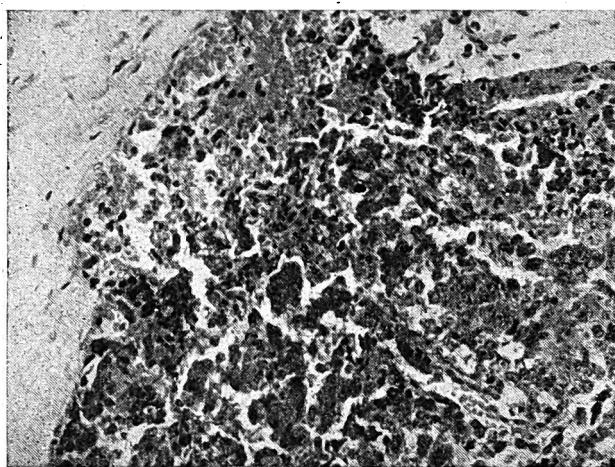


Fig. 3.—Islet-cell tumour of pancreas.

treatment the ataxia became almost unnoticeable, the tremor vanished, and for the first few weeks the child's mentality and behaviour improved remarkably. Slight glycosuria was occasionally observed. At the end of two months' corticotrophin therapy she had gained 6 lb. in weight, was symptom-free, and walked normally. She was, however, still rather troublesome and often had temper tantrums. She was sent home taking a high-carbohydrate diet and no sedatives, and remained well for four weeks after the corticotrophin injections had been stopped. Then, after an initial fit, the original symptoms returned, and she was readmitted in August, 1953, and again treated with corticotrophin with good effect in a few days. This treatment was continued until the day of operation.

Operation.—On Oct. 20, 1953, the pancreas was explored by Mr. David Levi and Mr. Rupert Corbett at the Westminster Children's Hospital. A glucose-saline intravenous infusion was running before, during, and after the operation. The adenoma was not found until the duodenum and the head of the pancreas had been mobilised and drawn forward to expose the posterior pancreatic surface. The tumour, about 1·3 cm. in diameter, was lying in the lower part of the head of the pancreas. It was easily dissected out, being encapsulated. It was red and roughly spherical and had a slightly lobulated surface; it was firm and homogeneous.

Postoperatively the child progressed well. A glucose-tolerance test done three weeks later gave a normal curve, and the fasting blood-sugar levels were normal. The child has been free from untoward symptoms and has gained weight well. Four weeks after the operation it was impossible to detect any ataxia in arms or legs; and the muscular hypotonia had much diminished. Mentally the child was still rather "silly" and immature for her age, but her mother said that she was improving every day and was a different child from what she had been six months previously.

Discussion

Hypoglycaemia is seldom discovered to be the cause of fits and neurological disorders in childhood. In the present case the clinical picture was not at all typical of hypoglycaemia in diabetic children. There were four main features in the neurological picture: major fits, periodic stupor and coma, a severe and constant ataxia, and mental deterioration.

A study of the published cases has not brought to light any chronic hypoglycaemia associated with the type of ataxia seen in the present case. However, anterior-horn cell degeneration in patients with islet-cell adenoma has been described (Silfverskiöld 1946, Lidz et al. 1949, Tom and Richardson 1951, Barris 1953); these patients had previously been diagnosed as having progressive muscular atrophy, and were cured by removal of the pancreatic adenoma.

The anti-insulin effect of corticotrophin was most impressive. Cortisone and corticotrophin have been recognised for some years as agents for raising the blood-sugar level and have been used in hyperinsulinism

with good effect in some cases (McQuarrie 1951, Brown 1951, Brown et al. 1952, Smith and Cochran 1952, Steiner 1953, Mason 1953). These hormones probably act by promoting gluconeogenesis, by inhibiting the peripheral action of insulin, and possibly by decreasing the peripheral utilisation of glucose in the tissues.

The beneficial effect of corticotrophin persisted in this girl for four weeks after the injections had been stopped, which was longer than has been reported in most other cases. The hormone was given in the form of acthar gel once daily.

Diagnosis

Although most reported cases of organic hyperinsulinism have had blood-sugar levels of 50 mg. or less per 100 ml., this is not an absolute diagnostic sine qua non, as has been shown by the cases of Duras (1951) and Webster and Blades (1952), where higher levels were recorded, even in coma. The glucose-tolerance test may be very misleading in diagnosis. It is essential to have the patient fully saturated with carbohydrate for some days before the test; otherwise starvation or diabetic types of curve may be obtained. Morley (1952) has suggested that more reliable readings will be obtained if the patient is kept walking about while the test is proceeding.

It is not suggested that either corticotrophin or cortisone should be used in organic hyperinsulinism except as a palliative preoperative treatment in selected cases and in the treatment of cases where no adenoma can be found or where the adenoma is malignant.

Morbid Histology

Histological sections showed a proliferating tumour consisting of spheroidal cells with darkly staining nuclei (fig. 3). These cells occasionally group themselves to form acini, but in many areas form diffuse sheets. They are of the same general type as islet-cells, and show no specific histological evidence of malignancy.

Summary and Conclusions

A case of functioning islet-cell adenoma of the pancreas is described in a girl aged 7½ years, who for two years had had hypoglycaemic symptoms—namely, fits, coma, ataxia, and mental deterioration.

Hypoglycaemia was suggested by the rapid response of the patient to the ingestion of sugar when she was stuporous.

Corticotrophin produced a complete but temporary remission of all the symptoms and most of the signs. This remission lasted four weeks after the treatment had been discontinued.

A small benign islet-cell adenoma was removed from the posterior aspect of the head of the pancreas. After the operation the girl has made a rapid recovery.

I am grateful to Dr. C. F. Harris for permission to publish this case and to Dr. H. Miller for the numerous blood-sugar estimations and for the histological sections.

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DIASTOLIC ARTERIAL HYPERTENSION AND ULCER OF THE LEG MARTORELL'S SYNDROME

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IN some patients with diastolic arterial hypertension painful ulcers appear on the anterolateral aspect of the leg. These are called hypertensive ulcers and the condition is termed Martorell's syndrome because he described the first four published cases (Martorell 1945).

Valls Serra (1946) reported the first male case. Hines and Farber (1946), of the Mayo Clinic, confirmed the existence of these ulcers and published additional clinical cases. Oller Crosiet (1947) devoted a paper to this syndrome, and Wright (1948) described the second male case. Recently several papers have confirmed the existence, aetiology, and clinical characteristics of hypertensive ulcer. I reported one case myself (Alonso 1951).

The ulcer is due to ischaemia caused by obliterating lesions of the small arterioles. These lesions are similar to those found in other localities in essential hypertension. The most common changes are an increase in the thickness of the arteriolar wall and a decrease in the diameter of the lumen. The lesions are specific to hypertensive disease, with subendothelial hyalinosis in some cases, or thickness and an increased number of nuclei in the media in others (Martorell 1945, Hines and Farber 1946).

The lesion may have been initiated as the result of slight local trauma or even without it. Usually the first symptom is a painful red patch in the skin, which soon becomes blue and purpuric. Afterwards superficial necrosis develops, and finally ulceration appears, which is often bilateral and symmetrical. The ulcer is located on the anterolateral aspect of the leg at the union of the lower and middle thirds (see figure). There may be an ulcer on one side and a simple pigmented spot on the other side. The ulcer becomes sensitive and painful; and the pain is not relieved by rest in bed. There is no history of thrombophlebitis, and there are no varicose veins. The dorsalis pedis arteries are palpable.

The diagnosis of hypertensive ulcer is made when ulceration such as is described above coincides with diastolic arterial hypertension in the arms and arterial hypertension in the legs, without any arterial occlusion or disturbance of the venous circulation.

ILLUSTRATIVE CASE-REPORT

A woman, aged 46, came to the clinic in July, 1953, with an ulcer proximal to the lateral malleolus on her left leg; it had appeared after a slight trauma. There was nothing relevant in her family history. She had hyperten-

sion, for which she had first been treated six years before. There was no history of thrombophlebitis. The lesion started as a small, bluish-red, flat spot in the skin. A haemorrhagic bleb developed soon and broke down into a superficial ulcer, which gradually became bigger and very painful.

Examination showed a superficial ulcer on the anterolateral aspect of the leg at the union of the lower and middle thirds (see figure). The blood-pressure was 210 mm. Hg systolic and 130 mm. Hg diastolic. The heart was enlarged. There was no evidence of varicose veins or of chronic venous insufficiency. Peripheral arterial pulsations were all normal.

Treatment.—Under local treatment with brilliant-green and general treatment with vasodilator drugs ('Esplenormon') the ulcer healed in seven weeks.

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TRAVERSING WOUND OF THE HEAD

B. H. DAWSON

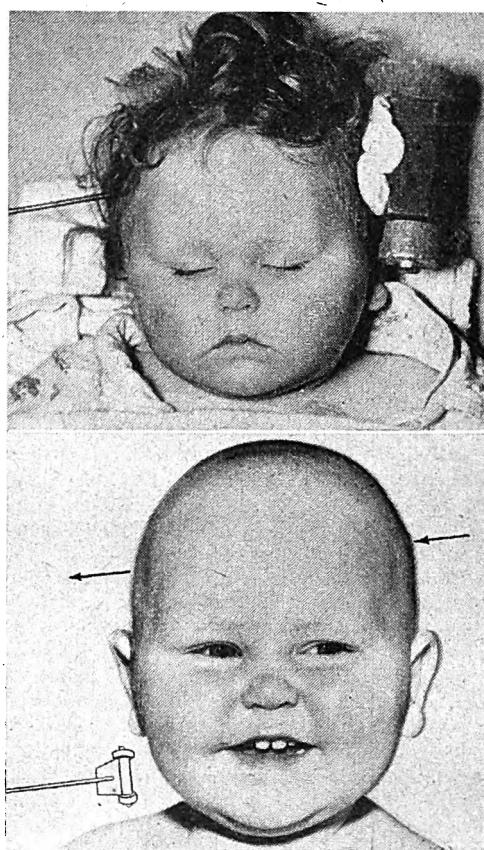
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THE following case is reported because of its rare and bizarre character and to illustrate how little, if any, disability can follow a serious-looking transfixing injury of both cerebral hemispheres.



Hypertensive ulcer of the leg in typical site at junction of middle and lower thirds of the lower leg in a patient with blood-pressure 210/130 mm. Hg.



Above: metal spike in situ before operation. Below: child on seventh postoperative day.

CASE-REPORT

An infant, aged 15 months, fell out of bed and struck the left side of her head against the projecting metal rod of a toy lying on the floor. She did not lose consciousness but picked herself up and walked with the toy attached to her head.

On examination at the hospital fifteen minutes later it was found that the rod, 20.0 cm. long and 0.4 cm. in diameter, had penetrated the left parietal bone just above the pterion, plunged across the brain, and emerged from the right side at a site almost opposite the entrance wound (see figure). The rod was arrested at the point of entry by the base plate and wooden wheels of the toy. The baby was pale and drowsy but responded rapidly and irritably to normal stimuli. There was no surface bleeding, the rod being gripped firmly on either side by the surrounding scalp. Nothing abnormal was found in the nervous system apart from very slight relative weakness of the right arm.

Treatment.—Antitetanus serum 750 units was given, and the rod was cleansed and withdrawn (Mr. Murray Falconer). Anesthesia was not required. Skull radiography after the removal of the rod showed a small flake of bone driven in at the point of entry on the left side, and an elevated flake of bone at the point of exit on the right side. No deeply situated foreign bodies were seen.

Operation.—The head was shaved and cleansed under general anesthesia and both scalp wounds were excised. From the left side a depressed fragment of bone 0.5 cm. in diameter was removed, together with a wisp of hair 5.0 cm. long, which had been driven in by the impact of the metal rod. The edges of the punctured dura mater were trimmed, but no brain tissue was sacrificed, because the exposed cerebral cortex, apart from the puncture site, looked normal. A similar surgical toilet was done on the everted compound fracture on the right side. Both scalp wounds were closed without drainage.

Postoperative Treatment.—After the operation prophylactic systemic and intrathecal injections of penicillin were given for six days. The lumbar cerebrospinal fluid was examined daily for seven days; it contained 300 leucocytes per c.m.m. on the first day, and 1400 per c.m.m. on the second day, whereafter it fell steadily to normal. The slight hemiparesis observed on admission cleared within forty-eight hours, and thereafter the child made a complete recovery. An electroencephalogram (Dr. Denis Hill) just before her return home was normal for her age; she was discharged fourteen days after the injury. Phenobarbitone gr. $\frac{1}{4}$, twice daily was prescribed for six months to reduce the risks of epilepsy.

Follow-up.—Six months after the accident the child appears normal in every way.

COMMENTS

The injury was alarming but it was little more than a transverse puncture of the head by a metal rod 4 mm. in diameter.

The mode of entry was in favour of a good prognosis, because missiles which penetrate the skull at right angles cause relatively little damage to bone compared to tangential injuries.

The course taken by the rod lay above the vulnerable basal midline structures and passed through a part of the cerebral cortex not highly charged with function. Major cerebral blood-vessels escaped puncture, and there was no serious intracranial bleeding.

Deep brain infection and septic meningitis (serious hazards in a penetrating head wound) need not have been greatly feared in this case, because it was possible at the operation to remove the in-driven bone and hair. Further, with the advent of the antibiotics the mortality from sepsis in head wounds has greatly diminished.

Post-traumatic epilepsy remains a possible late sequel to this injury. The facts that fits were not observed in the early days after the injury, that all foreign material was removed at operation, and that there was no extensive pulping of brain tissue, greatly reduce the likelihood of this delayed complication.

Preliminary Communication

ACTION OF

I-ADRENALINE, *I*-NORADRENALINE, AND DIHYDRO-ERGOTAMINE ON THE HUMAN UTERUS

ADRENALINE B.P. (epinephrine, U.S.P.) is usually prepared from certain mammalian adrenal glands and thus, according to the manufacturers, contains 15–20% noradrenaline. Since much of the previous work on the human uterus has been done with this preparation, there is clearly room for more detailed study with the pure substances *I*-adrenaline and *I*-noradrenaline.

Adrenaline and Noradrenaline

In vitro, using strips of human myometrium suspended in oxygenated Locke's solution at 37°C, I have found that both *I*-adrenaline (as the hydrochloride) and *I*-noradrenaline (as the bitartrate) stimulate the myometrium to contract. This reaction is obtained with material from both pregnant and non-pregnant uteri, and the minimal effective dose of adrenaline is about three and a half times as great as that of noradrenaline.

In vivo, by recording uterine contractions in late pregnancy and in labour with an intra-uterine hydrostatic bag, I have found that adrenaline during its administration consistently inhibits the large coöordinated uterine contractions, whereas noradrenaline consistently stimulates them. The doses have been about 5–15 µg. a minute given by slow intravenous infusion over twenty minutes. This agrees with the work of Kaiser,¹ who obtained similar records by external hysteroscopy.

Dihydro-ergotamine

Gill and Farrar² and others have reported favourably on the use of dihydro-ergotamine in incoördinate uterine action. From the results in experiments on animals it has been claimed that dihydro-ergotamine acts by its powerful sympatholytic properties opposing the influence of adrenaline.

In vitro, I have confirmed, with strips of human myometrium, that this takes place: after the addition of dihydro-ergotamine to the bath of Locke's solution adrenaline and noradrenaline no longer have their usual stimulating action, and may even inhibit contraction.

In vivo, dihydro-ergotamine given to healthy women in late pregnancy or in labour, in the doses recommended by its advocates, modified neither the inhibitory action of adrenaline nor the stimulating action of noradrenaline. Perhaps it would do so in larger doses, but these approach oxytocic levels, as can be demonstrated by tracings from the puerperal uterus, and are thus unsafe.

Comments

From these observations it is clear that, without further elucidation of the seemingly contradictory responses of excised tissue and of the intact uterus, it is unjustifiable to draw conclusions from experiments *in vitro*, or from other animal species, and to apply the resultant theories to the human pregnant or parturient uterus. On such evidence has the theory of the action of dihydro-ergotamine hitherto been based.

The practical point is that the clinical response undoubtedly observed with dihydro-ergotamine in incoördinate uterine action may well be solely due to its action as a dilute oxytocic substance rather than to a sympatholytic effect.

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New Inventions

A JET-PROPELLED DUODENAL TUBE

IN 1943 I described a new type of duodenal tube,¹ and in 1951 I published details of an improved version.² The interest which it has aroused and the successful results that have been achieved have encouraged me to give this short account.

Many kinds of duodenal tube have been devised; most of them do not differ greatly from Max Einhorn's sound,³ which consists of a flexible tube with a perforated tip or nozzle to allow passage of liquids both ways. A tube of this type depends largely on peristalsis for its passage through the stomach, and its movements are often irregular. It occurred to me that it might be possible to design a nozzle in which the escape of liquid injected down the tube forced the nozzle forward—by jet propulsion, as it were. To do this, the liquid must leave the nozzle in the direction opposite to that in which the tube is

being passed. A simple experiment shows that when water is passed at moderate pressure through an Einhorn tube, or one similar, the tube tends to move backwards; my aim was to reverse this movement and to use it to simplify the passage of the tube into the duodenum. I therefore designed the tip shown in fig. 1. This looks the same as the Einhorn tip, but the central canal divides and the two branches turn back to leave the tip near its neck. The escape of liquid from these jets propels the tube forward, as can be shown by repeating the experiment. In the stomach the tube moves progressively towards the duodenum under the combined action of the jets and gastric peristalsis (fig. 2). For

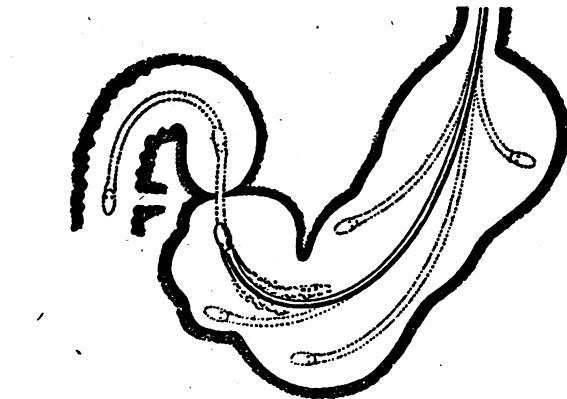


Fig. 1.—The tip of the tube.

satisfactory propulsion, I use water and air jets. I fill the syringe partly with water and partly with air, and hold it vertically during the injection so that the air follows the water down the tube.

The results with this tube have been excellent. I find that the time necessary for duodenal intubation has been much reduced, which is as welcome to the patient as to the doctor.

I have also designed a more complicated tip which works on the same principle but produces thinner and stronger propulsive jets. But the simple tube I have described is easier to make.

Laboratorio de
Pesquisas Clínicas,
Juiz de Fora, Brazil.

CLOVIS DE PAIVA AGUIAR
Médico, Minas Gerais

1. Aguiar, C. P. *Hospital, Rio de J.* 1943, 24, 81.
2. Aguiar, C. P. *Med. Cirurg. Farm.* 1951, 188, 637.
3. Einhorn, M. *Le tube duodenale.* Translated by Gustave Monot. Paris, 1927.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Hæmorrhage After Tonsillectomy

THE section of laryngology met on May 7, with Mr. C. P. WILSON, the president, in the chair, to discuss Hæmorrhage after Tonsillectomy.

Mr. D. WALKER ASHCROFT, whose paper was read on his behalf by the President, had heard within the past few weeks of no fewer than six deaths from this cause. Hæmorrhage after tonsillectomy was terrifying to the patient. It might be equally alarming to a doctor inexperienced in dealing with it: more skill was needed to control hæmorrhage than to do the tonsillectomy. Successful treatment depended on an understanding of the causes.

Three types of hæmorrhage could be distinguished: (1) reactionary bleeding within the first 24 hours after operation; (2) the bleeding of convalescence, occurring usually on the 5th or 6th day, from the separation of ligatures or sloughs, sometimes with a slight rise of temperature; and (3) true secondary hæmorrhage, associated with damage to the muscular tissues of the tonsil bed, occurring any time between the 3rd and 14th days and accompanied often by a raised temperature due to the local inflammation.

The factors responsible for postoperative hæmorrhage could be classified according to the stage at which they came into operation. Among preoperative factors were the type of patient, any hæmorrhagic diathesis, local acute inflammatory conditions, jaundice, menstruation, toxic conditions, pyrexia, or heat-wave weather conditions. Hypertensive or plethoric people tended to bleed freely, as did heavy smokers, chronic alcoholics, highly excitable persons, red-haired females, and sandy-haired freckled children. Operation should be postponed for some weeks after acute tonsillitis, sinusitis, or quinsy. Jaundice lowered the fibrinogen content of the liver and was a contra-indication to operation. Thyrotoxicosis, nephritis, rheumatism, diphtheria, and diabetes might cause operative complications, and such cases should be discussed fully with a competent physician before tonsillectomy.

Skill and care in doing tonsillectomy could certainly reduce the incidence of postoperative hæmorrhage. Aberrant or abnormally large blood-vessels should be seen or felt, and a fatality should never occur owing to their severance. The tonsillar fosse must be dry before the patient left the theatre. The blood-pressure should not be lowered by deep anaesthesia or hypotensive drugs, and the cough reflex should return immediately the operation was over. If a longitudinal vein were completely severed it should be ligatured at both ends; but ligatures might slip if they contained an excess of tissue, or cause necrosis which would be followed by sloughing and secondary hæmorrhage. Vasoconstrictor agents were not recommended since their application might be followed by reactionary vasodilatation; but coagulants, such as friar's balsam or thrombin, were devoid of this risk.

On completion of the operation, all blood-clot should be removed from the nose and nasopharynx as well as from the tonsillar fosse. Normal rhythmic respiration must be achieved, the patient placed on his side, and the tongue prevented from falling backwards. If cyanosis occurred without laryngospasm or the tongue having fallen back, bronchoscopic aspiration of blood or blood-clot must be begun forthwith. The risks of hæmorrhage from postoperative factors could be minimised by laying the patient on his side when he was returned to bed; besides permitting free respiration and reducing congestion, this allowed any blood to run out of the mouth and reduced the risks of inhalation. The anaesthetic

airway could be removed as soon as the patient discarded it, provided that the cough reflex had returned. Sedatives should be given if required, and the patient kept in bed for the first day. Hot baths should be forbidden for a week and, for a further week, strenuous exercise, tobacco, and alcohol. Upper respiratory infections should be avoided if possible. There had been much discussion as to whether salicylates could cause a severe enough hypoprothrombinæmia to encourage postoperative bleeding. Mr. Ashcroft had no personal evidence that they did.

One might expect slight oozing for the first hour after operation; but if, after this, there was still bleeding or if freshly swallowed blood were vomited, the case should be treated as one of reactionary haemorrhage. A sedative should be given; in the adult morphine was the most effective, and a child could be given subcutaneous 'Nepenthe.' After 20 minutes the throat reflexes would be reduced and anxiety allayed, and the throat should then be re-examined; good illumination was essential. If blood was still present, a tumblerful of cold water should be drunk; this was followed by further inspection. If there was no active bleeding nothing further need be done. If there was, all blood-clot should be removed and another mouth-wash given. If this still did not stop the bleeding, cotton-wool soaked in hydrogen peroxide and wrung out should be held with forceps in the fossa for 1 minute. If this method failed after three trials, thrombin should be substituted for the hydrogen peroxide. These methods would usually control the haemorrhage, but if it continued, or if the pulse-rate continued to rise, the patient should be returned to the theatre without delay. It was much better to give a second anaesthetic while the general condition was still good than to wait until it had deteriorated. Chloroform should never be given since it lowered the blood-pressure and concealed the signs of haemorrhage. Bleeding points were identified and ligatured or under-run. If bleeding continued, the faecal pillars should be stitched together over a gauze swab.

Haemorrhage during convalescence usually was not severe and ceased within an hour or so. Gargling with weak peroxide solution would usually stop it; but, if severe, it must be treated in the same way as reactionary haemorrhage. This was seldom necessary.

True secondary haemorrhage was fortunately less common. There was often a warning haemorrhage. Since the infected tissues were friable, simple ligature was often difficult or impossible, and suturing of the faecal pillars over a swab might be required. Ligature of the external carotid artery was of doubtful value because of its rich anastomoses. Transfusions might be necessary.

Postoperative haemorrhage could be largely avoided by careful selection of cases, competent operative technique, efficient haemostasis, and the maintenance of a free airway until the patient regained complete consciousness.

Dr. J. W. STEWART confined himself to defects responsible for severe postoperative bleeding that are demonstrable by laboratory tests. For normal clotting platelets, antihaemophilic globulin, calcium, prothrombin, fibrinogen, factors V and VII, and the Christmas factor must all be present. Several tests were available for detecting deficiency of these. Coagulation-time, clot-retraction, bleeding-time, Hess's test for capillary fragility, prothrombin-consumption time, and the thrombin-generation test were all useful. The importance of clot-retraction lay in the fact of its occurrence rather than its extent. Gross deficiency or excess of platelets were associated with bleeding; the bleeding-time was a very crude test, but it could be determined simply, and an abnormal increase indicated capillary disease. Hess's test measured the extent of the vascular defect and was also very simple. The prothrombin-consumption time measured the amount of prothrombin consumed during the process of clotting and normally nearly all of it was

absorbed. The thrombin-generation test was a very useful screening test. It exactly measured the amount of thrombin formed and the time taken for it to form during the process of clotting. Other laboratory tests would identify the deficiency in most cases of bleeding disorders and indicate the appropriate treatment. Dr. Stewart concluded that while a patient might die from the effects of haemorrhage, such as inhalation of blood into a bronchus, no patient should die of anaemia since blood was nowadays always available in hospitals.

Mr. W. STIRK ADAMS cited figures from the Children's Hospital in Birmingham which showed a higher incidence of bleeding in the winter months, which coincided with a greater incidence of upper respiratory infections. These infections, he felt, might interfere with the clotting-time, even when local symptoms were absent. It was important to group blood in advance for any patient who might be expected to need it, and to carry out cross-matching in the early stage of any continued postoperative haemorrhage.

Mr. S. MAWSON felt that, apart from stopping the bleeding, the replacement of blood-volume was the vital factor in saving life during haemorrhage in the reactionary period. The volume of blood that could be safely lost without replacement depended on the age of the patient: it should not exceed one-tenth of his total blood-volume. This in a child aged two years amounted to only half a teacupful (100 ml.) whereas an adult could safely lose a whole bottleful (500 ml.). Replacement was essential if the blood-loss reached three-tenths of the total volume. Since blood-grouping took so long, Mr. Mawson thought that one should always be prepared to give substitute transfusions. Dextran, for example, would adequately replace the lost volume in an acute haemorrhage.

Mr. R. S. STRANG said that he had given up all medical treatment in postoperative haemorrhage, and favoured an immediate return to the theatre. Many subsequent speakers agreed with this view.

Mr. A. BOWEN-DAVIES advised that none other than an experienced surgeon and an experienced anaesthetist should deal with postoperative haemorrhage when a second operation was necessary.

AMERICAN ASSOCIATION FOR CANCER RESEARCH

The forty-fifth annual meeting of the association was held in Atlantic City from April 10 to 12.

Cigarette-smoke

Two groups of workers reported studies on the fractionation of cigarette-smoke. A. I. KOSAR and his colleagues (New York) described a smoking-machine which "smoked" 240 cigarettes simultaneously and simulated human smoking habits by taking a 2-second puff of 35-40 ml. at 58-second intervals. The smoke was collected in liquid air-cooled traps, and the tar condensate removed with acetone and subsequently fractionated. W. E. SMITH, N. S. COOPER, and E. L. WYNDER (New York) studied the effect on mouse skin of fractions derived from cigarette-smoke condensates that had been collected in this way. Certain early skin changes, particularly a count of the number of sebaceous glands per sq. cm. of skin, correlated well with the carcinogenicity of materials applied to the skin, and it was possible to predict the relative carcinogenic potencies of test substances within a few days, instead of the many months normally required. One of seven fractions of cigarette-smoke condensates tested gave positive results and long-term tests for actual tumour induction by this fraction are now under way.

Electron Microscopy

L. DMOCROWSKI, C. D. HAAGENSEN, and D. H. MOORE (New York) had studied thin sections of 43 mouse mammary tumours—20 high-cancer-strain tumours and 23 low-cancer-strain tumours. Spherical cytoplasmic particles were found in sections of several high-cancer-strain tumours, but in only 1 single low-cancer-strain. These findings, however, were complicated by the fact that some of the particles closely resembled casein or lipoprotein particles present in mouse

milk and lactating mammary glands. Means of differentiating these two types of particles were discussed and the importance of correlating electron microscopy with biological tests of these tumours was stressed.

Hydatid Mole and Chorioneopithelioma

R. DE RUYCK (Paris) reported that he had isolated a filtrable virus from 15 cases of hydatid mole and chorioneopithelioma. An identical filtrable agent, of which two different strains were distinguished, was found in each of these tumours. The agent grew easily in chick embryos incubated at 38°C and could be transferred from egg to egg by serial passages. de Ruyck believes that hydatid mole is a placental lesion determined by a filtrable virus and that chorioneopithelioma is a malignant virus-induced transformation, not only of the placental trophoblast, but also of the reticulo-endothelial system.

Serum Acid-phosphatase

M. LONDON, R. McHUGH, and P. B. HUDSON (New York) had studied the effect of heating and cooling on elevated serum acid-phosphatase in patients, and they reported a considerable inverse relationship between body-temperature and acid-phosphatase levels. This technique may improve the diagnostic value of serum-acid-phosphatase tests.

Cancer of the Cervix

S. C. KASDON, G. W. MITCHELL, jun., and W. H. FISHMAN (Boston) found a close correlation between the level of β -glucuronidase activity and the presence of benign or malignant states of the uterine cervix; cervical tissue was obtained by biopsy and the exfoliative cytological and histological appearances were studied. Malignant cervical tissue was uniformly associated with increased enzyme activity as compared to benign states.

A Test for Cancer

A. H. DOWDY and his colleagues (Los Angeles) presented the results of diagnostic tests; they used ethyl cholangidionate, a stable crystalline derivative of ox-bile deoxycholic acid, and they found that 97.7% of 922 patients with known cancer gave a positive result when their sera were tested with this substance. But there were false-positive results in 3% of normal patients and in a much larger proportion of patients suffering from other non-malignant diseases. Adjustment of the test to give a negative reaction in all normal patients decreased the percentage of positive results in cancer patients to 85%. The test was negative in cancers that had not broken through the basement membrane of the epithelium.

Chemotherapy

J. W. FROST and R. JONES, jun. (Philadelphia), reported that pyrimethamine ('Daraprim'), the recently developed antimalarial agent, was of value in the treatment of polycythaemia vera. 16 patients had been given 15–25 mg. daily; there was a progressive fall in the haemoglobin level, haematocrit, and red-cell count, and remission of symptoms. These preliminary results suggest that the drug may be as effective as P^{as} . Two advantages over P^{as} are: (1) the toxic manifestations of overdosage are reversible with folic acid (pyrimethamine is a folic-acid antagonist); and (2) it is more readily available than P^{as} .

The new antileukaemic drug, 6-mercaptopurine, aroused much interest at last year's meeting,¹ and a further report was given by L. HAMILTON, G. B. ELION, and R. BASES (New York). These workers found that small doses of S^{35} -labelled 6-mercaptopurine injected into a child with acute leukaemia and an adult with chronic leukaemia became incorporated into the blood-cells and remained there for about two weeks. This suggested that 6-mercaptopurine might work by entering the leukaemic blood-cells and interfering with their function. Radioactive 6-mercaptopurine was rapidly metabolised and only a small amount was excreted unchanged in the urine; about 10% was excreted as an unknown and unidentified compound. Radioactive 6-mercaptopurine also appeared to pass the blood-brain barrier, for there was significant activity in the cerebrospinal fluid five minutes after injection.

Preliminary experiments with thioguanine (2-amino-6-mercaptopurine) were reported by another team, headed by D. A. CLARKE and F. S. PHILIPS, from the Sloan-Kettering Institute, New York. This substance, closely related to 6-mercaptopurine, was reported to be highly selective in its action against bone-marrow, and to have a strong inhibitory

1. See *Lancet*, 1953, i, 981.

effect on sarcoma 180 (a standard transplantable mouse tumour). Although thioguanine was a more potent inhibitor of sarcoma 180 than 6-mercaptopurine, it was more toxic, and adequate therapy of the mouse tumours was limited by a delayed toxicity that was possibly the result of sepsis secondary to agranulocytosis. Clinical trials are now in progress.

Experimental Pathology

H. W. TOOLAN (New York), who reported last year that human tumours could grow in cortisone-treated laboratory animals, has now kept a human soft-part sarcoma growing continuously for over a year in cortisone-treated rats and hamsters. The tumour grows rapidly and kills the host in 13–16 days. About a pound of tumour tissue is harvested weekly from scores of animals, and transplants are sent to investigators throughout the country.

A. H. HANDLER and G. YERGANIAN (Boston) reported that malignant and benign teratomas excised from children could survive and differentiate in cortisone-treated golden and Chinese hamsters and rats.

I. ZELDMAN, B. E. COPELAND, and S. WARREN (Boston) found that there were no lymphatics in an experimental rabbit tumour (V₃ carcinoma). Tumour cells were injected into the afferent lymphatics of a rabbit's pelvic lymph-nodes, and 2–9 weeks later, when a tumour had developed in the node, a tracer substance was injected by the same route. Radioactive gold gave a negative autoradiograph of the tumour; and soluble Berlin-blue as tracer could not be detected histologically in the tumour. Injection of these substances under pressure also gave negative results. These experiments suggest that absence of a lymphatic supply may be a characteristic of malignant tumours.

Some unexpected results were recorded. C. BREEDIS (Philadelphia) found regeneration of hair-follicles and sebaceous glands from scar epithelium in rabbits. E. A. MIRAND (Buffalo) and his colleagues found that sarcomas developed in mice after injection of deoxycortone in sesame oil; when injected alone, the oil was not carcinogenic. K. DUMBELL and P. ROUS (New York) found that a benign pulmonary adenoma of the mouse remained benign despite treatment with the potent carcinogen 20-methylcholanthrene; and yet several control tumours, untreated with methylcholanthrene, became malignant.

Reviews of Books

Modern Trends in Forensic Medicine

KEITH SIMPSON, M.D. Lond., university reader in forensic medicine, Guy's Hospital Medical School. London: Butterworth. 1953. Pp. 327. 60s.

In this book Dr. Keith Simpson has arranged contributions from ten different authorities (including himself), dealing with such widely different interests as biochemistry and the differentiation of blood-grouping, anthropology and reconstruction from skeletal material, a review of physical aids in criminal science (including microscopy, electron microscopy, spectroscopy, flame photometry, and radioactive pressure methods), electroencephalography, civil law in relation to medical practice, and toxicological analysis. The diversity of the contents may well lead the thoughtful reader to ask himself whether today there is such an entity as forensic medicine, and whether any one person can claim to be an expert in such a far-flung science, if science it be. But with the help of his collaborators Dr. Keith Simpson has produced an interesting and stimulating book which is well written and produced, and carefully illustrated. As it includes reports of work in progress, which has not yet been fully established, it is not suitable for the undergraduate student, but the specialist will find in it much that will be helpful even though some of the new sections are inevitably suggestive rather than comprehensive.

Toxic Solvents

ETHEL BROWNING, M.D., H.M. Medical Inspector of Factories. London: Edward Arnold. 1953. Pp. 168. 18s.

Dr. Ethel Browning's book *The Toxicity of Industrial Solvents*, the second edition of which we reviewed last year,¹ is a compendium of information about the toxic

1. *Lancet*, 1953, ii, 170.

solvents: it is a valuable work of reference, but it is non-critical and does not deal with treatment or preventive measures. She has now written a shorter companion volume which describes in four chapters the physical and chemical characteristics of organic solvents; their physiological effects; the individual solvents in some detail; and finally the precautions to be taken against the risk of poisoning.

The book is not specifically addressed to doctors (which is a pity) but rather "to works' managers, chemists, engineers, and similar officials in a factory." It is difficult to present a medical subject to non-medical readers, and, whereas the doctor will benefit from reading this book, its language appears to be too technical for the layman. If it is to be used by non-medical people, little purpose is served by going into great detail about symptoms or treatment other than first-aid. For the layman something much simpler is needed. The risk in "health education" is that we may turn laymen into half-baked doctors, whose last state is more dangerous, to themselves and others, than primeval innocence.

Pointing out that in poisoning by the organic solvents, alterations in the blood picture may be detected long before there are frank signs of ill health, Dr. Browning includes a discussion of normal and abnormal blood pictures; but, as she says, "this may appear superfluous to the medical, and comprehensible with difficulty to the non-medical reader."

In short, the book can be recommended to doctors as a straightforward account of the toxic solvents and of the management of cases of poisoning.

Physical Medicine and Rehabilitation

Editor: BASIL KIERNANDER, M.B., M.R.C.P., D.M.R.E., director, physical medicine department, The Hospital for Sick Children, London. Oxford: Blackwell Scientific Publications. 1953. Pp. 610. 63s.

In his introduction to this work, Lord Horder emphasises that rehabilitation is the concern of all branches of medicine and surgery and not of physical medicine alone, but he points out that "it is in this new and expanding field that physical medicine so amply justifies itself." The text, contributed by 26 authors in different branches of clinical practice, makes it clear how much of physical medicine is concerned with rehabilitation, and how difficult it is to draw a dividing line between the two subjects. But it would be impracticable to include all aspects of rehabilitation in a textbook of physical medicine, and on the whole Dr. Kiernander has struck a happy editorial balance. Both subjects lack satisfactory textbooks, and he has gone a long way towards meeting a double need. His belief that all clinicians of the future will be expected to know the basic principles of physical medicine as it affects their clinical specialty has led him to include a few chapters which fall below the general level. But many of the articles are examples of what is required in an expert contribution to a combined textbook. Especially good are those on the functional anatomy of the locomotor system by Dr. Howard Darcus and on physical methods in neuromuscular disorders by Prof. Ruth Bowden.

Psychological Disorder and Crime

W. LINDESAY NEUSTATTER, M.D., M.R.C.P., physician in psychological medicine, Royal Northern Hospital, London. London: Christopher Johnson. 1953. Pp. 248. 21s.

In attempting to interpret modern knowledge of psychological medicine to non-medical people—jurists and others—working in courts and prisons, Dr. Neustatter has avoided discussion of controversial issues, such as criminal responsibility, the objective reliability of testimony after a lapse of time and under cross-examination, the partisan use of the expert witness, and the separation of the process of determination of guilt from that of sentence. In stating the case for a better understanding of the psychiatrist and psychiatry, he is concerned only with current practice, and from this book no-one would conclude that anything in current juridical conventions needed overhaul. But the descriptions of the main epiphénoména of psychological disorder in relation to crime cannot fail to be of great help to jurists, for Dr. Neustatter is deft in picking his way through such

ill-mapped regions as that of the psychopathic personality. Copious illustrations from case-histories are consistently admirable.

In a book of this size it might well be unwise to discuss general reform of the law and lawyers, but a good opportunity has been missed to use this clear and concise style, which carries the reader along so effortlessly, to introduce the layman to the idea that it is high time that the Law used modern science for more than mere crime detection. The crucial question is how best to use medical psychology and sociology in the courts so that they may do something for mankind, rather than, as too often at present, only exasperate the lawyers.

History of the Laboratory of the Royal College of Physicians of Edinburgh

JOHN RITCHIE, F.R.C.P.E. Edinburgh: Royal College of Physicians. 1954. Pp. 159. 15s.

WHEN the proposal to found this laboratory was being discussed in 1885, the opinion was expressed that the college would be wrong to spend money in such a way that only Edinburgh men could enjoy the advantages it would provide. This argument reads strangely today in view of the history of a laboratory that eventually drew workers from places as far apart as Lithuania and Hong-Kong, that received specimens not only from Scotland and many parts of England but from sources as different as Kansas and Cairo, Lagos and Teheran, and that collaborated in epidemiological research with workers in India. Many famous names are recorded in its roll of fame.

It is sad to think that in the brave new world brought about by the National Health Service Acts, no place could be found for an institution so widely known and with so high a reputation. This may seem odd to us and inexplicable to future generations. But Edinburgh University is the richer for its buildings and staff.

The Eczemas

A Symposium by Ten Authors. Editor: L. J. A. LOEWENTHAL, M.D., M.R.C.P., D.T.M. & H., lecturer in dermatology, University of Witwatersrand, Edinburgh: E. & S. Livingstone. 1954. Pp. 267. 35s.

THIS book is by an international team of ten dermatologists. The most interesting chapters are by Haxthausen, Storck, and Burckhardt, writing on general theory, microbial sensitisation, and the effects of alkalis respectively. The chapter on histology emphasises that the approach to eczema must be clinical and biological. Regional peculiarities are evident in the list of substances recommended for routine intracutaneous tests; bluefish and redtop sound like exotic allergens. The formulary loses value through being a curious mixture of British preparations and unfamiliar American ones. The approach is almost relentlessly organic: a chapter by a psychiatrist would have brought the team up to strength.

Nerve Impulse: Transactions of the Fourth Conference (New York: Josiah Macy, Jr., Foundation. 1954. Pp. 224. \$4.00).—This conference, which was held over three days in 1953, dealt with the mechanisms of vision (opened by George Wald) and hearing (opened by Hallowell Davis), and with sensory receptors (opened by Yngve Zotterman). The discussions are reported in full, and there are good illustrations and diagrams. The editor is Dr. David Nachmansohn, of Columbia University.

Bouquet for the Doctor (London: Heinemann. 1954. Pp. 241. 18s.).—This popular history of medicine is well conceived, well illustrated, and well written. The story starts in the earliest times and ends with the antibiotics, and Miss Dorothy Fisk is to be congratulated on her choice of subjects and emphasis. Of the historic characters only John Hunter fails to receive proper appraisal. He appears mainly as Jenner's adviser and friend, and only creeps into the list of distinguished surgeons as the brother of William; but Koch, Pasteur, Harvey, Leeuwenhoek and his microscopes, and in particular Jenner, come vividly to life. In a book of this kind there must be omissions, and there is no chapter on midwifery or on aids to diagnosis. In fact the last century is almost entirely devoted to bacteriology and antibiotics, with special reference to Sir Alexander Fleming, who contributes a foreword. The book will give medical students a bird's-eye view of the history of medicine; and doctors, too, will like the author's bouquet.

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THE LANCET

LONDON: SATURDAY, MAY 22, 1954

Industrial Bladder Cancer

EARLY in 1947 the dyestuffs group of the Association of British Chemical Manufacturers appointed a committee to organise a large research project on industrial tumours of the bladder.¹ The first task was an accurate field survey of the industrial data. This survey, which was used as a basis for legislation whereby tumour of the bladder arising in certain occupations has been prescribed for benefit under the National Insurance (Industrial Injuries) Act,² has now been reported.³ At the outset no doubt existed that men employed in the chemical industry ran a greater risk of developing tumours of the bladder than those in the general population. What was needed was a statistical analysis of the facts, so that opinions formed by personal observation could be substantiated or refuted, and steps taken to eradicate the disease from the industry without delay. Dr. CASE's report meets this need. The deductions are based on well-devised and cleverly used statistical methods; and the facts, presented in an easily read form, should stimulate other industries to institute similar investigations into their own hazards.

By Feb. 1, 1952, 455 cases of bladder tumour had been found among a population of 4622 men in the British chemical industry: 341 of the affected men were employees of member firms, and the great majority (87%) were known to have had contact with aniline, benzidine, 2-naphthylamine, or 1-naphthylamine. The men at risk were about thirty more times likely than the general population to die of tumour of the bladder. The risk affects men engaged in manufacture, usage, or purification of the chemicals, in this descending order of severity. There is no clear evidence against aniline itself, but magenta and auramine are suspect. Occupational tumours occur on an average fifteen years earlier than spontaneous ones. The age at onset depends on the age at entry into the industry—the induction-time is nearly constant at fifteen to twenty years—but, though the length of exposure profoundly affects the risk, there is no evidence that severity of exposure influences the induction-time. Individual susceptibility, the cause of which is unknown, is a distinct feature, as it is in laboratory animals. The alterations

in plant and technique which took place in 1935 have reduced the risk just significantly, and it is to be hoped that the more stringent elimination of hazardous processes in 1950 will eventually bear fruit. As it is, Dr. CASE has calculated that 243 more cases may be expected among those who make the chemicals. He pleads for accurate records in the industry, earlier diagnosis, and more experimental work.

Already other steps forward have been made on the experimental side. CLAYSON⁴ has formulated a working hypothesis for the mode of carcinogenesis of aromatic amines, the essence of which is that they act by virtue of their conversion in the body to ortho-hydroxy amines. One example of this is the known conversion of 2-naphthylamine to 2-amino-1-naphthol conjugates in the dog,⁵ and there is some evidence of similar conversions of other related chemicals. The value of such a hypothesis, even if it proves wrong or incomplete, is that it can be used as a basis for further systematic work in this field and as a means of selecting suspected compounds for full biological investigation. WALPOLE et al.⁶ have extended their earlier work in rats to show that 4-aminodiphenyl is carcinogenic in the dog, and that, as far as the one limited experiment goes, all the tumours are located in the bladder, and arise early and after small dosage. It is probably highly significant that another aromatic amine acts so similarly to 2-naphthylamine in the dog.

Judging by the rate of progress since the war, we shall know a great deal more about the mode of action of aromatic amines five years from now.

Pathogenesis of Diphtheria

THE main thread of the diphtheria story runs clearly and logically. The Klebs-Loeffler bacillus was identified as the causal agent seventy years ago, and the clinical manifestations of the disease were traced to the effect of a toxin produced by the infecting bacterium.⁷ Sterile culture-filtrates of the diphtheria bacillus, when injected into animals, produced the toxic and lethal effects elicited by living cultures. In the blood-stream of animals immunised by the toxin in graded doses antitoxin appeared, and blood-serum from these immunised animals protected other animals against both toxin and living diphtheria cultures.⁸ Treatment of diphtheria patients with antitoxic serum relieved the symptoms and reduced the mortality-rate dramatically. In the past sixty years technical improvements have resulted in the production of highly refined and potent antitoxin preparations, but the main advance has been the introduction of detoxified toxin for mass immunisation.

It has been suggested that ordinary diphtheria toxin is not the only active agent in the disease and antitoxin not the only antibody. Some clinicians hold that modern highly refined antitoxin is less effective than old-fashioned crude antitoxic sera. Conclusive evidence for this view has not been forthcoming; for, although diphtheria-toxin filtrates have

4. Clayson, D. B. *Brit. J. Cancer*, 1953, 7, 460.
5. Bonser, G. M., Clayson, D. B., Jull, J. W., Pyrah, L. N. *Ibid.* 1952, 6, 412.
6. Walpole, A. L., Williams, M. H. C., Roberts, D. C. *Brit. J. industr. Med.* 1954, 11, 105.
7. Roux, E., Yersin, A. *Ann. Inst. Pasteur*. 1888, 2, 629.
8. von Behring, E., Kitasato, S. *Dtsch. med. Wehr*. 1890, 16, 1113.

1. Association of British Chemical Manufacturers. Papilloma of the Bladder in the Chemical Industry. London, 1953.
 2. Statutory Instrument no. 174, 1953. See *Lancet*, 1953, ii, 1307.
 3. Case, R. A. M., Hosker, E., McDonald, D. B., Pearson, J. T. *Brit. J. industr. Med.* 1954, 11, 75.

been found to contain several antigens and commercial antitoxin a corresponding number of antibodies,⁹ none of these seems to be implicated in the pathogenesis of the disease. Occasionally patients with no symptoms of toxæmia are found to be harbouring diphtheria bacilli that are typical except that they do not kill laboratory animals and produce no toxin either in the body or in laboratory culture-medium. Addition of certain virus preparations from virulent diphtheria strains converts the non-toxigenic strain to permanent virulence.^{10 11} The converted strain is indistinguishable from a naturally virulent organism and is now lethal to animals and produces diphtheria toxin in broth cultures. Apparently the genetic factor responsible for toxigenicity has been conveyed from the original host of the virus to the originally avirulent strain, and this one factor produces typically virulent organisms. Although the *gravis* and *intermedius* groups of diphtheria bacilli are isolated from clinically severe cases more often than is the *mitis* organism,¹² there is no evidence of any difference in the toxin produced by each of these different groups. In animals the lethal effect of diphtheria cultures appears to be due solely to the toxin produced.¹³ Some clinical observations may seem to be at variance with these findings. In a large series of cases of diphtheria alternate patients were treated with antitoxin and with normal serum.¹⁴ The mortality-rate—over 8%—was approximately the same in each group; antitoxin apparently had no beneficial effect. How is this to be reconciled with the experience that in both laboratory animals and man antitoxin saves life and relieves symptoms, and that active immunisation with diphtheria toxoid has helped to reduce the menace of diphtheria in this and many other countries?

The explanation of the discrepancies does not lie in the existence of a hitherto undescribed and malignant form of diphtheria toxin, and there is no need to seek for its corresponding prophylactic or antitoxin. The variable factor is the speed with which different strains of the diphtheria bacillus produce lethal amounts of toxin in the body. AMIES¹⁵ suggests that the toxin inhibits the local inflammatory response of the infected tissues; and this action determines the extent to which the infecting organisms proliferate and produce further toxin. Some diphtheria cultures, when injected into a susceptible animal, cause death within eighteen hours. In this time the organisms have multiplied locally and produced toxin which has been carried to susceptible tissues. Once toxin is attached to the tissues antitoxin is of no avail; to be effective, antitoxin must trap the toxin between the production depot and the susceptible tissue. In treating patients, it is essential to administer antitoxin early, and the failure of antitoxin to influence mortality-rates in some epidemics is due to the impossibility of diagnosing the disease early enough when the infecting agent multiplies and produces toxin very rapidly. This once again illustrates the value of active immunisation, since some antitoxin is already present in the blood-stream of the immunised person to neutralise the early

toxin production, and the stimulus provided by the infection results in the early production of more antitoxin by the immunologically educated cells of the body.

If given early enough, antibiotics and other chemotherapeutic agents may control infections with the diphtheria bacillus,¹⁶ but antitoxin is more rapid and specific in its therapeutic effect. Nevertheless, antibiotics have a definite part to play in the treatment of diphtheria. Both diphtheria carriers and convalescents may have in their blood-stream sufficient antitoxin to neutralise the effects of toxin; but they may still harbour diphtheria bacilli able to infect others, since antitoxin has no direct effect on the bacilli. Antibiotic therapy may cut down the stay in hospital or in quarantine of such carriers; but the organisms lurk in crypts where it is difficult to maintain an adequate concentration of the drug, and the diphtheria bacillus may rapidly become highly resistant to some antibiotics, such as streptomycin.

Removing Tuberculous Lung

THE case for removing parts of tuberculous lungs is apparently based on a few simple facts. People without tuberculous lesions live longer than those with them; and it has been clearly shown that the smaller the volume of diseased lung tissue the better the prognosis. If the most severely diseased part of the lung is collapsed by artificial pneumothorax or thoracoplasty the lesions elsewhere sometimes regress, and it is inferred that removing the part will have the same effect. It is also known that some patients treated by other means relapse and may die from the disease. From these facts comes the hypothesis that patients will relapse less commonly, and live longer, if all or most of the pulmonary lesions are removed. The indications for resection can be no more than opinions until the hypothesis is verified; and verification is possible only by comparison with other forms of treatment. Clearly this is not a case where (as with the introduction of streptomycin for tuberculous meningitis) the benefit of the new method is so obvious that no quantifiable comparison is necessary or ethically permissible. The advantages of lung resection are unlikely to be great—at least in the first few years—in most of the types of disease to which it is being applied, and what is needed is a planned comparison which will reveal the merits of the method to those who do not use it. Controlled concurrent trials with random allocation and other safeguards against bias, well exemplified by the Medical Research Council chemotherapy trials, are likely to give the most accurate answers to certain specific questions; but a comparison of cases less precisely allocated to different treatment groups by a single clinician might also provide useful facts. The least satisfactory technique is to compare the experience of patients who have had a resection in the last few years with the published results of other forms of treatment in the past. Yet even this is better than continuing to justify the hypothesis by inference. The findings should be presented in such a way that they can be set against previous reports or clinical experience. The radiographic extent of lesions and evidence of cavities should be clearly stated, and the account

- 9. Pope, C. G., Stevens, M. F., Caspary, E. A., Fenton, E. L. *Brit. J. exp. Path.* 1951, 32, 246.
- 10. Freeman, V. J., Morse, I. U. *J. Bact.* 1952, 63, 407.
- 11. Hewitt, L. F. *J. gen. Microbiol.* 1952, 7, 362.
- 12. McLeod, J. W., Orr, J. W., Woodcock, H. E. de C. *J. Path. Bact.* 1939, 48, 99.
- 13. Hewitt, L. F. *Brit. J. exp. Path.* 1948, 39, 181.
- 14. Bingol, A. *Dtsch. med. Wschr.* 1949, 74, 101.
- 15. Amies, C. R. *J. Path. Bact.* 1954, 67, 25.

- 16. Hewitt, L. F. *Brit. J. exp. Path.* 1952, 33, 217.

of the follow-up should indicate the experience of the different categories of patients, with the yearly survival-rates calculated by one of the well-known statistical methods.

It will be unfortunate if resection of the lung, of whose worth many competent workers are convinced,¹ is allowed to evolve haphazardly under the influence only of bedside impressions and reasoning from uncertain premises. The clinician does not lightly decide to advise a more or less fit patient to accept even a slight risk of dying from resection in order to avoid the unknown risk of dying from his disease many years later. The difference of opinion about the merits of resection in certain types of disease warrants a fully controlled clinical trial. A start might be made by comparing, in patients with uncalcified tuberculous nodules, the results of resection and those of long-continued antibacterial treatment.

Annotations

"SECTIONAL MEETING"

THE American College of Surgeons was founded in 1913 on the model of the Royal College of Surgeons of England; the first fellowship address was given by the president of the English college, and the great mace was presented by the consultant surgeons of the British Army after the first world war as a symbol of the brotherhood between the two nations. The first London meeting of the American college, which has been held this week, is therefore a memorable occasion, and it is fitting that it should be the first major event in the newly finished great hall of the Royal college.

The territory of the United States is so vast, and the fellows of the American college are so numerous, that scientific meetings are held in sections. This week's meeting, attended by about 450 American surgeons, has been organised by the Americans themselves on the lines of a typical sectional meeting in their own country, and the tempo—so very different from that of our own surgical meetings—has emphasised the difference in the tasks the two colleges are called on to fulfil. The Royal college, although at one time directly concerned in surgical education, became largely an examining body and only in recent years has turned its attention again to fostering the basic sciences and surgical research. The American college, on the other hand, confronted by a rapidly growing population and by universities without the advantage of tradition, has had to direct its attention to postgraduate education and to ethical problems. In this country, with its static population and long-established training centres, it is hard to understand the difficulties inherent in rapid expansion; but those who have watched the great struggle of the American college to ensure that postgraduate training is carried out only at hospitals with proper scientific standards can appreciate the immense service it has rendered to American surgery, and also to the hospitals themselves, which have been obliged to improve. This point gained, the battle continues with the insistence that only the highest ethical standards shall prevail throughout the length and breadth of the country.

The two colleges, although of necessity their approach has been different, are striving for the same end—to provide the best service for the patient that is humanly possible. Close personal and professional bonds link British and American surgeons, and we hope that our visitors have been well enough pleased to come again.

1. See *Lancet*, 1953, ii, 1118.

MAGNESIUM

In the field of electrolyte physiology and pathology there are definite signs of a shift in emphasis away from the electrostatic and osmotic effects of electrolytes, and towards their interactions with organic metabolism. Interest is being shown not only in the decisive effect of aerobiosis in stabilising the osmolarity and electrolyte composition of cells^{1,2} but also in the effects of electrolyte distortion on the activity of enzymes. For example, experimental potassium deficiency was shown to impair carbohydrate utilisation,³ and it has been suggested that the "insulin-resistant diabetes" induced by cortisone may be related to the hormone-induced potassium depletion.⁴ Potassium depletion is also known to impair protein synthesis, even when the dietary intake of protein itself is adequate.⁵ Since magnesium is, next to potassium, the predominant cation of intracellular fluid, and since it is a necessary constituent of various enzyme systems,⁶ much of the interest now shown in potassium may soon be extended to magnesium. Studies are at present handicapped by the lack of a usable radio-isotope of magnesium, and by there being no method of estimation comparable in ease and accuracy to that of flame photometry for sodium and potassium.

There are a few indications from clinical reports that depletion or excess of magnesium may be important.⁷ The effects of induced magnesium depletion on muscle composition have been investigated in rats⁸; and in cattle,⁹ rats,¹⁰ and ducklings,¹¹ such depletion has been found to cause tremors and convulsions. It seems that in man magnesium depletion may develop in circumstances known to be associated with potassium depletion. For example, it has been detected after operation in patients whose fluid balance was being maintained by parenteral fluids not containing magnesium¹²; magnesium excretion continues in the urine even at low serum levels of magnesium.⁷ Magnesium depletion has also been found in patients with diabetic coma,¹³ and in patients with congestive heart-failure treated with mercurial diuretics and with cation-exchange resins.⁷ All these associations would indicate a renal loss of magnesium; and comparison with potassium suggests that the effects of deficient food intake and of abnormal losses of gastro-intestinal fluid should be explored in relation to magnesium. A recent report suggests that magnesium deficiency may be responsible for the tremulous moiety of delirium tremens; low serum-magnesium levels were observed, and treatment with intramuscular magnesium sulphate improved the tremor, assessed by handwriting tests.¹⁴ In this report emphasis is laid on the importance of alcohol, well recognised in other contexts, in preventing an adequate intake of food, which is either unwanted or cannot be paid for.

Although tetany associated with low levels of serum-magnesium has been recognised in animals¹⁰ and in man,^{15,16} this finding has attracted little clinical atten-

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3. Gardner, L. I., Talbot, N. I., Cook, C. D., Berman, H., Uribe, C. *J. Lab. clin. Med.* 1950, **35**, 592.
4. Kinsell, L. W., Balch, H. E., Michaels, G. D. *Metabolism*, 1953, **2**, 421.
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12. Martin, H. E., Edmondson, H., Homann, R., Berne, C. J. *Amer. J. Med.* 1950, **8**, 529.
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14. Flink, E. B., Sturzman, F. L., Anderson, A. R., Konig, T., Fraser, R. *J. Lab. clin. Med.* 1954, **43**, 169.
15. Hirschfelder, A. D. *J. Amer. med. Ass.* 1934, **102**, 1138.
16. Miller, J. I. *Amer. J. Dis. Child.* 1944, **67**, 117.

tion, largely because many patients with comparably low levels of serum-magnesium are free of symptoms. The analogy with potassium is again tempting, and clearly we shall need to learn much more about the rôle of magnesium within the cell before we can explain the occasional occurrence and frequent absence of tetany in patients with a low serum-magnesium. The greater part of the cell magnesium is probably undissociated, being "bound" to protein and phosphate anions.^{17 18} Low serum levels of ionic calcium are much more constantly associated with tetany; and these two divalent cations probably exert different effects on muscle activity, since one type of muscle adenosinetriphosphatase has been found to be activated by calcium ions and inhibited by magnesium ions.¹⁹ These are deep waters, and for the present clinicians may be content to remember the possibility of magnesium tetany.

High serum-magnesium values have been observed in kidney disease, and may contribute to the drowsiness which is sometimes a merciful feature of terminal renal failure. Warnings have been issued against precipitating terminal coma by magnesium sulphate purgation²⁰; and this should certainly be avoided in the reversible syndrome of acute tubular necrosis. A high level of protein-bound serum-magnesium has been reported in hyperthyroidism,²¹ but careful studies by Cope and Wolff²² did not substantiate this claim.

Thus there is more of promise than of fulfilment in the study of magnesium in relation to disease; but the same could have been said of sodium twenty years ago, or of potassium ten years ago.

MORE SELF-HELP

THE early social workers had little to offer the needy except good advice. We now seem to have reached the opposite pole: there are plenty of services to be had, but no-one seems to be responsible for explaining to the needy what these are or how to get them. In view of the large variety of social workers who now have access to the homes of the nation, this is rather remarkable. Nevertheless, as Prof. Leslie Banks²³ told the annual general meeting of the Institute of Almoners, recent surveys have shown that many people, and especially old people, in villages and towns, are unaware that the district nursing service is free, or that they can have the assistance of a home help when necessary. Moreover, they are often completely defeated when they are asked to fill in a form or write a letter in answer to an official inquiry. We need, he thinks, advisory centres capable of helping such people in a friendly unofficial manner.

The kinds of help we now provide are financial and practical; and he is anxious to see that these are given in the right way, and to the right people. Too much help saps initiative; and besides, we cannot afford to supply it. "A small and self-reliant family," he says, "given a healthy environment and a reasonable standard of education, should need help only in times of crisis." If they have a good family doctor, district nurse, and midwife, and a centre to which they can go—and he emphasised "go"—for information, do they need anything more? And will routine visiting by a troop of social workers do more than weaken their self-confidence and self-respect? On the other hand, there are some 5-12% of families in any area who have precious little self-confidence and self-respect to keep them going, and these he thinks, will continue to need intensive

care. It is questionable, however, whether they in fact need the combined care of the health visitor, housing inspector, sanitary inspector, N.S.P.C.C. inspector, probation officer, school welfare officer, boarding-out officer, children's officer, moral welfare worker, and the officers of the National Assistance Board. Professor Banks thinks our society is now so complex that we could not substitute one all-round officer for this little army; but we might reduce the confusion, he suggests, by ensuring at least that all these workers have a common basic training. It is perhaps worth recalling that though American society is at least as complex as ours, most of the functions which here are distributed among so many are undertaken in the United States by a solitary worker, the public-health nurse. At present our National Health Service is employing some 400,000 women; but during the next ten years the number of women in the country aged 18-30 is going to decline by over 200,000; and every year (until 1960) there will be 100,000 fewer girls reaching the age of 18 than there were in 1930. So the field of recruitment is going to be smaller, and to go on diminishing. This means that unless we manage to be more economical in their use, every social worker will have a larger case-load—i.e., she will have to do less for more people.

This is perhaps less serious than it sounds. Dr. H. M. C. Macaulay²⁴ points out that a welfare saturation point is not beyond the bounds of possibility. He does not think that we have reached it, by any means, but he does suggest that if, in the second half of the century, public-health education is as successful as it has been in the first half, the proportion of feckless families in the community may dwindle below their present 7-12%; and that will mean a considerable lightening of the load. Moreover, as Professor Banks notes, we have shaken ourselves free, now, of many of the social and medical ill effects of the Industrial Revolution, and have added nearly thirty years to the expectation of life at birth. Family size is small, the standard of health is high, and the ways of education and instruction—for those able to profit by them—are many. Social workers should now be able to look on many of those they help not as patients, but as clients seeking advice. A population such as we used to have, with a high proportion of children and adolescents, and many illiterates, needed much supervision and inspection; but our present population—older, more mature—should need little beyond security and a healthy environment (in which he includes good housing). The task of the social worker is still to "advise, assist and befriend"; but for our medicosocial services, whether statutory or voluntary, the task is rather to decide which people stand in need of advice, assistance, and friendship, and in what manner it should be given.

MEDULLARY CYSTS OF THE KIDNEY

AN unusual variety of congenital cystic disease of the kidney has lately been described by Hogness and Burnell.²⁵ The cysts are confined to the medulla; and the cortex undergoes atrophic changes from back pressure or from interference with the vascular tree. Clinically, the patients resemble those with the Rose-Bradford kidney in that they develop an insidious uremia without hypertension; and a further strong point of resemblance is the occurrence of osteitis fibrosa in 3 of these cases, with proved hyperplasia of the parathyroid glands in 2. No excretion pyelograms were carried out, and the retrograde pyelograms gave no diagnostic picture.

This cannot be a common condition, for only 1 case could be added from the literature to the authors' 4. It is probably a developmental defect, since associated congenital abnormalities were found in 2 cases, and there

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 19. Kielley, W. W., Meyerhof, O. *Ibid.* 1948, 174, 387.
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 22. Cope, C. L., Wolff, B. *Biochem. J.* 1942, 36 413.
 23. Almoner. April, 1954, p. 3.

24. *Ibid.*, p. 1.

25. Hogness, J. R., Burnell, J. M. *Arch. intern. Med.* 1954, 93, 355.

was no histological evidence of chronic pyelonephritis or of vascular disease. In the Rose-Bradford kidney, too, there is often an associated congenital deformity of the renal tract; and a congenital hypoplasia of the kidney has also been suggested. The medullary cysts may form a link between the common congenital abnormality of extensive generalised cysts and the lesser defects that are associated with the syndrome of renal failure and osteitis fibrosa. The patients succumbed in early adult life, so Hoggness and Burnell have added another diagnosis to the causes of death from insidious renal failure without hypertension. No treatment is of any value.

OSTEOMALACIA AND STEATORRHEA

OSTEOMALACIA means, literally, softness of the bones, but the term is usually restricted to one form of bony softening—adult rickets. It thus differs from "osteoporosis," where the supply and the metabolism of calcium are normal but the organic matrix of bone is at fault, and from other diseases which produce rarefaction of the bones and spontaneous fractures.¹ In osteomalacia calcification has failed through lack or loss of calcium, but simple lack of calcium or of the vitamin D required for its absorption rarely leads to osteomalacia unless pregnancy or lactation make additional demands on the calcium stores of the body.

Microscopically, seams of uncalcified osteoid tissue appear. The symptoms may for a long time be quite mild and so ill-defined as to be confused with those of arthritis or fibrosis. Although some patients are crippled and can sit up in bed only by pulling on the bedclothes, others walk about with fractured ribs and even with fractured metatarsals. Narrow bands of decalcification or pseudo-fractures where an artery lies in contact with bone are characteristic radiographic findings.² The serum-calcium level is often low; but compensatory hyperplasia of the parathyroids may prevent this, in which case the serum-phosphorus level is low. The bone disorder is accompanied by increased alkaline phosphatase activity in the plasma.

In this country the diet is hardly ever so deficient as to produce osteomalacia. Rarely—for instance in renal acidosis—the stores of calcium are drained through the kidneys, but steatorrhœa, with faecal loss of calcium, is a more usual cause. The bowel symptoms, like the bone symptoms, are not always characteristic; but a very low urinary excretion of calcium even with a normal intake will make the diagnosis clear.

Badenoch and Fourman³ have described 6 cases associated with steatorrhœa. 4 patients were unmarried women, and 2 of these were nuns. Deficiency of vitamin D without pregnancy is not likely to account for osteomalacia, and yet 5 of these patients were nulliparous. Some other factor, it seems, may precipitate the disorder. The losses of calcium from the bowel may be much greater than the intake.⁴ Badenoch and Fourman found that in 3 of their patients the bone disease had become obvious while they were receiving small doses of calcium and vitamin D, as well as folic acid. If a large dose of vitamin D was given by mouth, or if a moderate dose, ineffective by mouth, was given parenterally, calcium was absorbed. But vitamin D was effective only if the intake of calcium was large in relation to the amount of fat in the faeces, indicating that fat interfered with the absorption of calcium, possibly by combining with it to form soaps. The disease could be controlled with parenteral vitamin D and large amounts—25 g. daily—of calcium lactate by mouth. This dose sometimes causes severe constipation (calcium salts are useful in controlling the diarrhoea of sprue). A more moderate

intake of calcium may be effective if the patients receive a low-fat diet, but it is hard to achieve an adequate calorie intake in steatorrhœa if the fat intake is restricted any more than is necessary to avoid diarrhoea.

Thus it seems that, in osteomalacia associated with sprue, malabsorption of vitamin D is important, but other factors must be taken into account in planning treatment. Even with the vigorous treatment given by Badenoch and Fourman the absorption of calcium was not very great; and it is likely that such absorption, like that of other simple substances,⁵ may be directly impaired in steatorrhœa. It is not known whether other calcium salts might be absorbed better than the lactate or whether parenteral administration might be useful. Any treatment must be lengthy; for, once osteomalacia has developed, a goodly proportion of the 2 kg. of calcium in the body⁶ must have been lost.

ADAPTATION AND HEREDITY

Professor Wood Jones is a schismatic, not adhering to the orthodox modern account of evolution. Natural selection acting on random mutations is not enough, he believes, to explain the extraordinary variety of living things; or the beautiful correlation between the different parts and organs in any one animal; or the many ways in which variants of a single species will overcome a similar problem in their environment; or the production, in parallel, of the same solutions to a problem by widely different species. He holds, with Lamarck (whom he believes to have been unjustly denigrated), that "the raw material, from which are derived the changes that have taken place in the forms of life, consists in structural adaptations brought about by the functional demands of the environment"; and this of course implies the inheritance of acquired characteristics. The views of so considerable an anatomist and naturalist deserve serious attention; and he has set them out brilliantly in his latest book.⁷

The orthodox view strains his credulity on mathematical grounds. It is easy, he suggests, to suppose that natural selection operating on random genes might produce a single characteristic favouring the survival of a species; it is harder, though still possible, to imagine it producing two; but he simply cannot credit that this agency alone could produce the manifold and harmonious adaptation of every part which enables that species to live at home in its environment. And when he is further invited to believe that all the myriad forms of life on the planet have attained such a harmony in this way, and this way alone, he finds the explanation hopelessly inadequate: the chances against it are too astronomical. The answer of orthodox evolutionists to this objection, of course, is that there has been so much time on the Earth that anything could have happened: the laws of chance have had ample time to operate. On the other hand, the orthodox theory does not seem to make much allowance for the laws of cussedness. The production, for instance, of such an animal as the giraffe—with long legs for running, long neck to reach between them to the grass on which it feeds, hoofs rather than toes, dappled hide for camouflage, and appropriate teeth, eyes, ears, and internal organs—postulates such a run of luck for the dice-throwing genes as to tempt one to agree with the sceptical child at the Zoo that no such animal exists.

The many remarkable examples of adaptation, correlation, and parallelism with which Professor Wood Jones illustrates his views are chosen, he tells us, from among countless others equally striking. He accepts natural selection as one of the agencies producing these things,

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 6. Widdowson, E. M., McCance, R. A., Spray, C. M. *Ibid.* 1951, 10, 113.
 7. Trends of Life. By F. WOOD JONES, F.R.C.S., F.R.S. London: Edward Arnold. 1953. Pp. 191. 10s. 6d.

but thinks that there is good evidence that the environment makes demands which also can result in changes of structure. He quotes Prof. Julian Huxley, who found that 69 generations of disuse failed to affect the eyes of drosophila, as saying that this was "a good example of the failure of disuse to produce Lamarckian effects." A species of drosophila existed, it seems, some forty to fifty million years ago; and Professor Wood Jones is to be forgiven for pointing out with some tartness that though the orthodox evolutionary theory demands something longer than this period for the production of modern drosophila by natural selection, it is content to accept a mere 69 generations as evidence against the fly's ability to inherit acquired characteristics. Perhaps the best hope of settling this venerable controversy lies in the present intensive study of changes in the habits of bacteria, which multiply with such convenient (or inconvenient) rapidity.

BATHING, SEWAGE, AND COWS

EVERY parent knows that bathing leads to infections of the upper respiratory tract. Whether the infection is derived from the water or whether the natural resistance is vitiated by chilling of the body is uncertain. Indeed it is hard to find any convincing evidence whatever to support this dogma so hateful to the young. There are, however, risks of more specific infection associated with bathing, voluntary or otherwise, which are less widely known and the consequences of which may sometimes be more serious. Quite recently we called attention to the possibility of enteric infections being acquired from sea-water: the risk is small but not to be overlooked.¹ Weil's disease may be caught by bathing in a limpid stream with nothing in it to suggest the sewer or the fish market. In this country we run no risks of schistosomiasis, but country doctors may find it worth while to keep in the back of their minds the "bathers' itch" caused by the abortive attacks of cercariae of some species of worm whose adults fail to develop in the human body. We are told that in some lakes in the U.S.A. these are so prevalent as to rob bathing of its pleasures. From Sweden, Australia, and the U.S.A. have come accounts of granulomata developing on the site of minor abrasions incurred in swimming-baths.²⁻⁴ In general these lesions resemble lupus, and treated as such they heal successfully. While no-one has demonstrated tubercle bacilli in them, there have been several reports that they contain new species of mycobacterium, not pathogenic to guineapigs and growing very profusely in vitro at a temperature below 37°C. It is fair to add that other workers have thought these granulomata are due to the specific irritant action of silica in the cement.

Two stories from Newcastle upon Tyne, by Miller and Anderson,⁵ show that we must add another to the possible perils of immersion.

A boy aged 4 fell into a sewer at the point where it discharged into the sea. He was rescued and after resuscitation returned home. Three weeks later he had a febrile illness which in view of the radiographic appearances and a tuberculin test was diagnosed as primary tuberculosis. He recovered quickly but after eight months developed tuberculous meningitis (which was not fatal). No source of infection was found among his family.

Such a chain of events in one child alone could do no more than suggest the possibility of infection by inhalation or ingestion of sewage containing tubercle bacilli. A second accident, however, had a similar sequel.

A younger child fell into a sewage tank at a holiday camp. He was rescued, revived, and within a few hours developed an acute enteritis. Some weeks later a second feverish illness

was accompanied by evidence of an infection of the lungs which was shown to be tuberculous. Once again no familial origin of the infection could be found.

Incidents remarkably like these have been reported previously from Scandinavia,^{6,7} and we think that the authors have made out their case for the acquisition of tuberculous infection from sewage.

Since there are many people at large who suffer from active phthisis, and since it is probable that most of these excrete tubercle bacilli in the faeces, it is reasonable to assume that all sewage, at any rate from towns of any size, contains tubercle bacilli. For technical reasons they are not easy to detect, but proof of their presence in sewage has come from many sources.⁸⁻¹⁰ A fortiori, they are likely to be especially numerous in the sewage from sanatoria, and in fact Gaustad's⁸ original examples of infection by immersion had fallen into a river immediately below the point where the effluent from a sanatorium discharged. The problem of destroying tubercle bacilli in the waste waters from sanatoria has not, we fancy, received the same attention in Great Britain that it has in Germany,^{11,12} and our impression is that none of the methods of sewage purification in general use is effective in this respect. The risk from hospitals in towns is probably small, since urban sewage is seldom discharged into waters to which the public have access; but many sanatoria are in the country, where it is not unusual to run effluent into streams used for bathing, fishing, and watering the cabbage patch. Those responsible for these institutions must not seek comfort in the notion that tuberculous infection by immersion is a rarity. The idea is a new one, and nobody can say how frequent this accident may be.

The discharge of tubercle bacilli in sewage may have another result which, while it may have no direct effect on human health, may well cause administrative difficulties of great consequence. The total abolition of tuberculosis in cattle, based on systematic tuberculin testing, is now within sight; and, though the human strain of *Mycobacterium tuberculosis* does not cause serious disease in the cow, the mild and transient infection which it produces is sufficient to make the animal react to tuberculin. There have been instances of positive tuberculin reactions appearing quite suddenly in a "clean" herd after it has had access to water known to be polluted with human sewage. The case is not proven, but the weight of evidence from many sources has raised some reasonable alarm. We doctors have grumbled for many years at the dilatoriness of the farmer in freeing his animals of diseases communicable to man: we hope that no-one will have reason to say that the boot is on the other leg.

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1. *Lancet*, April 10, 1954, p. 766.

2. Hellerström, S. *Acta dermat.-venereol.* 1951, 31, 194.

3. *Lancet*, 1948, II, 424.

4. Rees, R. B., Bennett, J. H. *J. Amer. med. Ass.* 1953, 152, 1606.

5. Miller, F. J. W., Anderson, J. P. *Arch. Dis. Childh.* 1954, 29, 152.

Medical Conferences

ATLANTIC CITY MEETINGS

THE annual spring meetings of the American Society for Clinical Investigation and the American Association of Physicians were held in Atlantic City on May 3-5. Over 2000 doctors attended, most of whom are engaged in research work. Only a small proportion of the papers submitted could be read in the time available. This report includes papers from each society.

Hæmatology

Preservation of Blood

FINCH and GABRIO (Seattle) described a discovery bearing on the preservation of blood. Red cells stored in acid-citrate-dextrose (A.C.D.) deteriorated after three to four weeks. This change was partially reversible by something contained in fresh blood. The "something" was identified as adenosine; and if adenosine were added to A.C.D.-preserved blood the red cells survived three times as long. Other nucleotides were effective—particularly adenine-desoxyribose which was especially suitable since it was non-toxic on intravenous injection.

Hereditary Spherocytosis

FRANKERD (Rochester) had investigated organic-phosphate synthesis in red cells from people with normal blood and with hereditary spherocytosis (H.S.). In the H.S. red cells there was a metabolic defect which was associated with a peculiar liability to haemolysis in the test-tube under conditions of stasis and low oxygen tension. By analogy it seemed that such cells might be similarly fragile in the spleen. In some H.S. bloods both the metabolic defect and the fragility were reversible with mannose, glucose, or adenosine.

Sickle-cell Disease

CONLEY and SMITH (Baltimore) described clinical features of genetic variants of sickle-cell disease. Paper electrophoresis of haemoglobin had shown that this substance can be one of at least three different types: associated with normal blood, with sickle-cell anaemia, or with "haemoglobin-C" disease. Heterozygous patients with the trait but not the manifest disease had both normal and the corresponding abnormal haemoglobins, while 20 patients had been discovered who were heterozygous for sickle-cells and haemoglobin-C. These "sickle-C" patients showed clinical features different from those of ordinary sickle-cell disease. Bone and joint pain were especially common amongst them, and 7 of the 20 had aseptic necroses of femoral or humeral heads. These patients were peculiarly liable to splenic infarcts, especially on air travel, and tended to have profound haemolytic anaemia during pregnancy. 2 had had subarachnoid haemorrhage.

Destruction of Red Cells

YOUNG (Rochester) described some experiments on the mechanisms of destruction of red cells by their appropriate antibodies. Dog red cells were of at least four types, analogous to human blood-groups. *In vivo*, canine C/anti-C reactions resulted only in agglutination; A/anti-A reactions resulted in strong opsonisation. For other types the reaction proceeded to cell lysis either *in vitro* or *in vivo*.

Treatment of Leukæmia

BURCHENAL (New York) described a new anti-leukæmia agent—6-mercaptopurine—which interfered with nucleoprotein synthesis by being a metabolic antagonist for adenine, thus differing in its method of action both from cortisone and from the folic-acid antagonists. The new drug sometimes worked where the other two agents had failed or had lost their effectiveness. Combined therapy

had produced some of the longest survivals so far in children with acute leukæmia.

Cutaneous Hypersensitivity

SHERWOOD LAWRENCE (New York) had experimented with the transfer of cutaneous hypersensitivity of the delayed type in man by means of constituents of disrupted leucocytes. In 6 consecutive instances the constituents of leucocytes lysed in distilled water, and in 4 consecutive instances the constituents of repeatedly frozen and thawed leucocytes (obtained from the blood of donors sensitive to streptococcal M substance), when injected into M-negative recipients resulted in the development of delayed cutaneous M-substance hypersensitivity. The experiment was repeated on a larger scale for tuberculin sensitivity, with similar results. The mechanism did not seem to depend on any change in the nucleoproteins of the cells. At least a tenth of a millilitre of disrupted cells was required to make the transfer, and the artificial sensitivity so induced might last in the recipient as long as a year.

Purpura

STEFANINI and MEDNICOFF (Boston) had observed two patients who showed both idiopathic thrombocytopenic purpura and the Henoch-Schönlein type of anaphylactoid purpura. A platelet iso-agglutinin could be detected in one of them—suggesting that antibody mechanisms might be responsible for both diseases. They therefore looked for, and found, evidence of a circulating anti-vessel antibody. They prepared a simple, soluble, cell-free extract of human aorta, which was used as a standard antigen. This was allowed to react with sera from normal and purpuric subjects. A positive result was indicated by a precipitin reaction with decalcified serum, complement being consumed at the same time. In 95 sera a positive result occurred in 6 out of 9 cases of anaphylactoid purpura, and in 3 out of 9 cases of periarteritis nodosa. There were 2 false positives.

Endocrinology

Corticotrophin for Eye Diseases

WOLFSON and QUINN (Ann Arbor) reported some remarkable long-term experiments with corticotrophin (A.C.T.H.) therapy of chronic inflammatory and degenerative eye diseases. Initially they observed that a patient who was receiving corticotrophin for suppression of inflammatory disease in his better eye showed a return of vision in the other eye which had previously been thought to have been damaged beyond repair. They extended their study to the 35 miscellaneous cases of chronic eye disease, including chronic retrobulbar neuritis, retinitis pigmentosa, and some retinal atrophies producing either tunnel-vision or wide scotomata. In 27 of these cases useful vision was restored (*in several to normal levels*), and in all but 2 it was maintained. An average of 66 units per day of long-acting corticotrophin had been given for the first 100 days, followed by 22 units per day thereafter in the successful cases. 8 patients showed no response despite higher dosage. The most important feature of this work was the time it took to produce improvement. From 50 to 500 days had been needed before worth-while improvement commenced, but from then onwards vision increased steadily. In one extreme case an eye, practically blind for over thirty years, had been restored to near normal vision. Wolfson postulated a previously unknown action of the adrenal cortex to explain these effects.

Hydrocortisone

Another important paper in this field was that of McEWEN and his associates at Bellevue. They had injected cortisone or hydrocortisone into one knee of patients with rheumatoid arthritis, and had analysed the synovial fluid for steroids, using fluid from the

opposite knee, or from the same knee before injection, as controls. From their work it was clearly shown that (a) cortisone could be changed to hydrocortisone locally, and (b) both hydrocortisone and cortisone could be locally metabolised to other known steroids, and also to an unidentified steroid, present in quite large amounts, which, it seemed, might be clinically active.

HELLMAN and his co-workers (New York) had injected hydrocortisone-4-C¹⁴ intravenously and had observed that half of it was excreted in the urine within about 4 hours, almost all in a conjugated form. In fact, 87% of the administered hormone was conjugated within 15 minutes of injection. None was broken down into smaller, non-steroid molecules. This elimination of hydrocortisone was independent of disease or of the presence or absence of the secretions of the adrenal or ovaries.

Pituitary Dwarfism

CRISPELL (Charlottesville) compared the urea space, the amino-acid pool, and the rate of protein anabolism in 5 normal men and in 1 pituitary dwarf, using heavy-nitrogen-tagged glycine and urea. The dwarf showed a distinctly low rate of protein synthesis which was considerably increased when growth hormone was given. It was on this point that the tracer method and classical nitrogen balances showed an unexplained discrepancy, the balance studies showing little change.

Breast Cancer

PEARSON (New York) reported striking improvement in 2 patients with advanced metastatic breast cancer after their pituitary glands had been removed. Growth hormone made 1 of them worse again, suggesting that the tumours were hormone-dependent. Both patients had undergone prior adrenalectomy and ovariectomy without improvement.

Effects of Progesterone

LANDAU (Chicago) reported that progesterone in physiological amounts produced a pronounced general protein catabolism and salt diuresis, antagonised by adrenal hormones. These reactions were distinct from the restricted protein-anabolic effect on breast tissue or on the uterus, and were most distinct in partial adrenal deficiency.

Infectious Diseases

Spread of Poliomyelitis

HORSTMANN (New Haven) had studied 32 cases of poliomyelitis and their household and daily contacts by means of antibody and tissue-culture methods. Practically all the children under 15 years of age who had come in close contact with an index case had become infected with the virus. But clinical illness rate was commonest among contacts aged 15 or more, even though these contacts were less often infected.

Acute Nephritis

RAMMELKAMP (Cleveland) reported a well-studied epidemic of acute nephritis following in the wake of group-A β-haemolytic streptococcal infection. In the population at risk several types of streptococci were recovered. Only those who had carried type-12 streptococci showed a nephritis as defined by gross or moderate haematuria occurring after an interval following the initial throat infection.

Acute Respiratory Disease

DINGLE and his colleagues (Cleveland) had made extensive studies on the aetiology of "acute respiratory disease" (A.R.D.).¹ This disease was distinct from the common cold and also from atypical pneumonia. They had found a specific antibody and had characterised the infecting agent as a virus. Innoculation of the virus produced the specific illness in 94% of those without antibodies, but in none of those with antibodies.

1. See *Lancet*, April 24, 1954, p. 867.

Pyrazinamide

MACDERMOTT (New York) had studied the pharmacology of pyrazinamide. This was a metabolic antagonist of nicotinamide, and in conjunction with isoniazid had a powerful antibiotic action on tuberculous infection in man and animals, eradicating both active disease and reservoirs of infection in a high proportion of cases. So far the combination is too toxic for routine use.

Cardiology

Cardiac Output

STARR (Philadelphia) described an extension of earlier work in which he had studied cardiac output and arterial pressure in cadavers intermittently perfused through the aorta by an apparatus which could simulate various pulse-rates and stroke-volumes. The formula :

$$\text{Stroke volume} = 93 + 0.54 \times (\text{brachial blood-pressure}) - 0.47 \times (\text{diastolic pressure}) - 0.61 \times (\text{age in years})$$

could predict cardiac output with surprising accuracy. He had tested the formula by applying it to the data reported by independent workers who had made direct measurements of the cardiac output. The two methods correlated extremely well, especially in recent work.

Vectorcardiography

DOCK (New York) reported on the value of lateral ballistocardiograms, and showed that the lateral heart vector might at times show striking changes as the result of drugs or other factors affecting heart action at a time when simultaneous longitudinal vector-tracings showed little change. This was particularly true of older people where tortuosity of the aorta might play a part.

Phonocardiography

MCKUSICK (Baltimore) had succeeded in obtaining phonocardiographic records of the heart sounds and murmurs by a method that could distinguish quality as well as intensity. The heart sounds were analysed by six electrical bandpass filters and were written on a moving paper so that height of the record indicated sound frequency, blackness of the spot indicated intensity at that frequency, and a simultaneous electrocardiogram or ordinary phonocardiogram indicated the timing. The various qualities of murmurs and chest bruits produced characteristic tracings, and sounds beyond the range of the human ear could be recognised. Whether the machine can be made more sensitive than the human ear in picking up and distinguishing faint aortic diastolic murmurs—the severest test—remains to be seen.

Congestive Failure

At last year's meeting cardiologists started a controversy as to whether there was evidence for increased blood volume in congestive cardiac failure, and this year the question was reopened by FUNKHOUSER and PRITCHARD (Cleveland), who presented evidence which, they claimed, showed that the volume was increased. But their data were not very complete.

BURCH (New Orleans) had measured peripheral venous tone in heart-failure and found it increased, while EICHNA and his colleagues (New York) pointed out that many cases, where congestion of the great veins and other manifestation of increased venous pressure were found, were often called congestive heart-failure, when in fact the heart itself was not failing; rather the condition was due to plethora, or to increased peripheral vascular tone, or to obstructions to the circulation, including valvular stenosis. In this last case the distinction might seem academic, but it was important in that digitalis would not be expected to effect any improvement in circulatory status.

Recurrent Arterial Spasm

BAY (Chicago) reported three interesting cases of what appeared to be localised but recurrent arterial spasm. The patients had shown episodes in which a limb would

become pale and pulseless, simulating embolism, the condition recovering again completely in a day or two but recurring irregularly and without apparent cause in the same or another limb. In one patient this had continued for over thirty years. Although the limbs were usually affected, episodes of amnesia, transient unilateral blindness with retinal pallor, vertigo, abdominal pain, and haematuria suggested that visceral arteries could also be involved.

Myocardial Fibrosis

BURWELL and ROBIN (Boston) had carefully studied 6 patients, initially diagnosed as having constrictive pericarditis, who had been found at operation to have diffuse myocardial fibrosis. They pointed out that the two conditions might be indistinguishable without thoracotomy; clinical, electrocardiographic, and catheterisation findings were the same. Furthermore, the two conditions might coexist.

Intractable Angina and Congestive Failure

BLUMGART (Boston) reported on the experience of his own and forty-five other clinics in treating a total of 829 patients crippled by intractable angina pectoris or congestive failure, by administering radioactive iodine to suppress thyroid secretion and to reduce oxygen requirements. In about 80% of cases of angina the result was described as good or excellent, and in 50-60% of patients with failure the result was good or worth while. Over 40% of the patients had been followed for more than a year. The recommended dose was 10-20 millicuries weekly, up to three times if required. Higher single doses might cause dangerous radiation thyroiditis. Clinical hypothyroidism occurred within two months; from then onwards the patients were maintained on the smallest dose of thyroid hormone consistent with comfort.

Pulmonary Diseases

Chronic Pulmonary Insufficiency

BERCU and MANDELL (St. Louis) had similarly had some success with radioactive iodine administered to decrease thyroid function and oxygen requirements in patients with chronic lung insufficiency.

COURNAND and his group (New York) had found that the work of the respiratory muscles themselves might consume up to 1 litre per minute of oxygen in patients with chronic pulmonary insufficiency or obstruction.

Pulmonary Resistance

DUBOIS (Philadelphia) had measured pulmonary resistance to air-flow by an ingenious "whole-body plethysmograph." This is an airtight box in which the subject sits, breathing the outside air through a tube. Another tube allows displacement of air from the cavity of the box. In a normal person, as air is breathed in the chest expands, and an equal amount of air is displaced out of the plethysmograph. Where there is obstruction to air-flow inspiratory efforts displace air from the box, but air intake lags behind (alveolar air-pressure falls). Electrical flowmeters measured: (1) the rate of flow of air to and from the lungs, and (2) the volume of air displaced from the box. The signals from the flowmeters displaced a cathode-ray beam so as to make it describe a loop with inspiration and expiration. The loop was narrow in normal people, but wide where there was increased resistance to air-flow. The airway resistance could be expressed mathematically, and the method had already proved of value in the objective assessment of bronchodilators, in the differential diagnosis of bronchial obstruction, and in the detection of spurious respiratory cripples.

Metabolism

Hepatolenticular Degeneration

Several papers dealt with work on copper metabolism. The most comprehensive came from WINTROBE's group

at Salt Lake City. In normal people the plasma contains about 120 µg. of copper per 100 ml., of which only 7% will give a direct chemical reaction; 93%, which is protein-bound, will not. In hepatolenticular degeneration there is much reduction in the indirect-reacting copper and a small rise in the direct-reacting copper. Balance studies showed that patients with this disease accumulated copper, despite an abnormally high urinary copper excretion. Faecal excretion, however, was very low. All the vital organs, but especially the liver, showed increased copper deposition. Amino-aciduria was often present but was not an essential feature. A copper-free diet was not practicable, so treatment was aimed at decreasing copper absorption from the gut by feeding potassium sulphide, and at promoting renal excretion, taking advantage of the fact that renally excreted chelating agents bind the metal and so remove it. These workers recommended giving 1 litre a day of a 5% solution of casein hydrolysate, plus a high-protein diet, to promote amino-aciduria, and dimercaprol (BAL) 25 mg. per kg. body-weight twice daily. 'Versene' was not effective.

HODGES and his colleagues (Iowa City) had sought to define more closely the renal lesion in this disease. They found a reduction in renal plasma-flow associated with normal glomerular filtration-rates, and believed that the sequence of events might be: (1) a primary renal defect (possibly arteriolar spasm in the region of the proximal tubules); (2) competition of amino-acids and oligopeptides for diminished reabsorption in the renal tubules; (3) increased urinary oligopeptides (which bind copper); and thus (4) increased urinary copper. This mechanism would account for the copper-removing effect of giving increased dietary amino-acids.

Copper Control of Maternal and Fetal Blood

SCHEINBERG (New York) had found that maternal blood contained eight times as much copper as did foetal blood. The difference was due to the fact that protein-bound copper cannot pass the placental barrier.

Treatment of Gout

GUTMAN (New York) reviewed the treatment of chronic tophaceous gout. Although tracer studies had shown that dietary purines were not the only source of exogenous uric acid, dietary control was still of value. There was an average fall of 2 mg. per 100 ml. in the serum-uric-acid in 71 patients with chronic gout when they changed from normal to a low-protein, low-purine, low-fat diet. 70 cases of chronic tophaceous gout had been followed for from 6 to 48 months on probenecid ('Benemid') therapy. In almost all patients there was a pronounced fall in serum-uric-acid levels, and in urinary uric-acid output, accompanied by shrinkage of pre-existing tophi and diminished frequency of acute attacks. During this time no new tophi developed. In 12 especially severe cases sinuses healed and crippling joint involvement was considerably improved. In patients who failed to improve the dosage was increased, but even on a dose as high as 3 g. per day there were still a few who did not respond.

Calcium

HENNEMAN, from Albright's group in Boston, demonstrated the interesting resemblance of the derangement in calcium metabolism in patients with sarcoidosis and hypercalcaemia to that found in vitamin-D poisoning, and wondered whether vitamin-D-like substances might be produced endogenously in this disease.

Renal Diseases

Renal Functions in Chronic Nephritis

CRAWFORD (Boston) had studied the homoeostatic limits of several renal functions in patients with advanced chronic nephritis. The failing kidney did not fail uni-

formly; for example, in some cases the power to adjust renal excretion of sodium in response to a varying sodium load might be normal when the range of adjustability of the total water output was much limited. The different functional end-results of renal failure might correlate with the differing clinical pictures (which include such diverse conditions as renal rickets, hypertension, and water intoxication). By mapping out residual renal functions they had accurately matched the patient with an appropriate régime.

Nephrosis

ROSENMAN (San Francisco) reported experiments in rats in which the kidneys were damaged by injections of anti-rat-kidney serum, so as to produce a picture resembling nephrosis in man. The clinical picture followed the injections in a high proportion of instances, but could be greatly modified or completely prevented if heparin were given with or before the anti-kidney serum. This action was only suppressive, as shown by the emergence of the complete syndrome 48 hours after heparin was withdrawn. Administration of heparin to animals or to patients in whom nephrosis was already established only reduced the lipæmia and hypercholesterolemia, but did not otherwise improve the condition.

Personal Papers

AN ULCER COMES OF AGE

MY ulcer dates from when I was 19 and an undergraduate. At that time I had a number of chronic anxieties, and for months on end I could not get to sleep till 3 or 4 A.M. I became careless of my food and used to eat a lot of snacks in cafés. After a year of this, I began to experience the well-known dull pain in the epigastrium, coming on just before meals. The condition became established and I would have bouts of pain of this kind lasting a few weeks at a time. As the years passed, it became more severe and came on earlier, till it normally occurred about two hours after a meal. I cannot now remember when I started to have pains at night, but in the end they became my main symptom and more troublesome than the day pains. Usually an attack began with causeless waking without pain, and this happened earlier night by night until I found myself waking at about 3 A.M. with a severe epigastric pain. On subsequent nights I would waken still earlier, till at the height of an attack I woke at about 1 A.M. As the attack abated the waking would become later, till painless, causeless waking supervened. Then after a few more nights, I would be back to normal.

After about ten years of the disease, I had an exceptional attack, lasting a month, during which I was unable to get out of bed without experiencing severe pains which did not respond to the usual dieting and alkalis. Apart from this attack, which fell during my annual holiday, I have never spent more than one or two days in bed at a time and I have never had to take time off work. After the month in bed, I consulted a well-known surgeon, who with great forbearance advised against operation. Radiography at that time showed an active duodenal ulcer.

As time went on, I became more experienced in handling the attacks and in avoiding new ones—or may it be the natural history of the disease? Anyhow for over five years I had no pain at all. Lately I have again had some dyspepsia and night pains. Now that my ulcer has come of age, I yield to the temptation to write about it—giving as it were a progress report, setting down my dogmatic assumptions and tentative speculations.

Perforation, haemorrhage, and vomiting, I am thankful to have so far escaped. My main problem has been to avoid or mitigate pain. It is important to stop pain quickly, and for this purpose I use a tepid, dilute solution of sodium bicarbonate. I sip it slowly and take only just enough to relieve the pain—after which I take milk. In this way I have kept my total intake of bicarbonate of soda small, and I have used it mostly at night. I do not like the *National Formulary* mixtures, because they contain peppermint, which I suspect of being a gastric irritant. (Its inclusion is a gesture towards the Victorian theory of “wind”—pain is due to wind, and gastric irritation helps to get the wind up.) Of the alumina tablets I have tried, I have found most useful ‘Tabnet’ (Calmic)—a tablet of aluminium amino-acetate. It has solved for me the problem of day pain, which often I had to put up with for want of an effective tablet.

Butobarbitone (“Soneryl”) has been my choice of sleeping-tablet, and I use it after one or two nights disturbed by pain. As I may have to drive my car during the night, and swallowing a whole tablet leaves me very drowsy if I am called out in the small hours, I find it better never to swallow a tablet at all, but to place it in the labiodental groove and suck it, swallowing small amounts in solution till I drop off to sleep. If I wake up in the night I swallow a little more. Most of the tablet will be under my lip in the morning and can then be discarded. In practice, half or even a quarter of a tablet will often suffice. I have not experimented with other sedatives—but a tablet of barbitone sodium used in the same way once caused some degree of injury to the gums by next morning. Butobarbitone will not do this.

I suspect that I become slightly anaemic during attacks: so at irregular intervals I take occasional doses of iron. Tab. ferri. sulph. is useless for this purpose because it causes pain, but I find a solution of ferric ammonium citrate taken very weak in water or milk after meals is satisfactory. The tonic effect of iron is felt after a few hours—long before it can have had any effect on the blood-count. It may perhaps be due to the oxidation of reduced sulphur compounds in the bowel by the ferric iron. I use no other drugs.

* * *

From the onset of my ulcer, I have set my face against bed rest. It is painfully obvious that six weeks' bed rest per attack is not practical politics and turns people into invalids. But one or two days in bed is useful in reducing the pain to bearable levels, and perhaps once or twice a year I use this convenient method of checking an attack which is threatening to get out of control.

A strict and rigid diet is neither desirable nor practicable, and I eat what I can “get away with.” There have been days—fortunately few and far between—when I have had nothing but milk, but immediately the pain diminished I begin to eat other foods, beginning with boiled fish and eggs and rapidly extending my menu. A little dyspepsia is a small price to pay for a varied diet. I generally find that it is safe to eat “unsuitable” foods for breakfast but that I must be increasingly careful with foods taken later in the day.

Despite what has been said and written, I do not believe that anxiety causes attacks. The most anxious time can be surmounted without trouble, provided that insomnia is never allowed to continue for more than one night, and provided that, at an anxious time, dieting and regularity of meals are carefully watched. The danger of anxiety lies in its ability to disturb sleep and interfere with meals.

I do not rest after meals. To eat one's meals rapidly, and to work as soon as possible after them, is as good a way as any of delaying digestion, and I hope to prevent the stomach from becoming empty long before the next

* * . *

meal is due. Reckless departures from diet are often without ill effect, and a large and uninhibited meal has sometimes ended an attack which has not yielded to gentler methods. On the other hand some attacks have so closely followed a memorable meal as to make me proceed with caution. The sedative and irritant effects of smoking tend to cancel one another out, though the balance of my experience is slightly against it. The hot-water bottle on the epigastrum is well known and useful. So is eructation. Less well known is the reduction in epigastric pain after micturition—useful in the middle of the night. When I expect a night pain I always keep by the bedside a glass of boiled milk. Sometimes I use one of the patent baby milk products. This is a useful standby when I am reduced to a strict milk diet, for it can be made as thick as required and enables one to get adequate nourishment. At the peak of an attack I avoid coffee and tea. Curiously enough, shop jams are irritant, whereas home-made ones are not. Vigorous exercise, such as cross-country running or rowing, are innocuous, while certain special movements, such as sawing a branch off a tree with one's hands above one's head or using a plane, are apt to bring on the pain.

* * *

So far, I have dealt with the practical politics of living with an ulcer—but that is only the bread-and-butter issue. Two problems remain my constant companions. What causes ulcers? What is a gastric diet? The first concerns the man without an ulcer and the second the man with one, and I believe they are closely allied.

Gastric and duodenal ulcers occur in those parts of the stomach and duodenum which come into contact with the scum on the stomach contents, when the stomach is almost empty and the abdomen is in the vertical position. Such a scum is likely to contain fats and fat-soluble substances and essential oils and substances soluble in them. Such a scum can exist in the ulcer sites, but beyond them it is emulsified and dispersed by the bile. In a stomach emptying through a gastrojejunostomy it would tend to gravitate towards the stoma, while after a gastrectomy the rapid emptying of the gastric relic should safeguard these patients against recurrence. Fats in themselves are harmless, for the man with a peptic ulcer can drink olive oil or eat lumps of butter with impunity.

If I compare the kind of diet I eat with what is regarded as normal food, the most conspicuous difference is that I eat raw or boiled foods, while my neighbours eat also roasted, toasted, baked, and fried foods; and this I believe to be the gist of the problem. Civilised man has become accustomed to eating (and also likes) foods which have undergone partial destructive distillation, often at relatively high temperatures—that of boiling and decomposing fat in the frying-pan. We have recently become only too well aware of the hazards inherent in the destructive distillation of biological matter as represented by the tobacco leaf—on the one hand carcinoma of the lung, on the other a benign irritation giving rise to smoker's cough. An ancient biological material is coal, and its destructive distillation yields carcinogens and irritant non-carcinogens. Have I wandered too far along the beguiling paths of speculation if I suggest that there may be an ulcer-provoking non-carcinogen in the fat-soluble (or essential-oil-soluble) products of the destructive distillation of our food, and that there may also be a carcinogen from the same source, among the more generally dispersed part of the stomach contents, which is responsible for the prevalence of gastric carcinoma? The fact that carcinoma is common in the large bowel but rare in the small one might be explained by such a hypothetical carcinogen being hurried, diluted, along the small bowel, whereas it is concentrated, and moves slowly, in the large.

Coming down to brass tacks I would say that my diet includes nearly all foods which have not been subjected to destructive distillation. In its simplest form a gastric diet is a diet without browned foods. I generally stick to this and I am reasonably satisfied with it.

Medicine and the Law

Failure of Allegations of Negligent Nursing

Mrs. Pickering's claim, brought at the recent Leeds assizes against the governors of the United Leeds Hospitals, involved no allegation of negligence on the part of a surgeon or physician. Her complaint was that, through lack of care on the part of the nursing staff, she had developed severe bedsores; she was now unable, 18 months later, to attend the court; she had suffered great pain and could not walk or stand. After a hearing of several days,¹ Mr. Justice Slade gave judgment for the defendants, with costs.

The plaintiff, aged 82, was taken to the infirmary with a fractured femur, caused by a fall. She was described as mentally alert and in no way senile, but weighing about 15 st. and suffering from a mild form of Parkinson's disease. After the operation for the fracture, she suffered from pressure sores. The defendants contended that, at her age and in her condition, these gangrenous sores were unavoidable. Her own witnesses suggested that the bedsores could have been avoided by better nursing, or at any rate that they should not have been allowed to develop so severely. Mrs. Pickering was subsequently moved to a nursing-home where two operations were performed for removal of gangrenous tissue.

The learned judge observed that there were three allegations against the nursing staff—failure to keep the bed dry, failure to change the patient's position, and failure to inform the hospital doctors of her condition. The orthopaedic officer at the infirmary testified that he examined the bed at least once every day and always found it dry. The judge held that the question of changing the patient's position was one for the surgeon, not for the nurses. The surgeon forbade the turning of the patient on to her side in the early stages; later he directed that she should be moved on to her right side. The judge said he accepted the evidence of the surgeon that he saw the patient every day. He was satisfied that punctilious attention was given to her. The only direct evidence of the bed being wet was that of the patient's daughter who visited her in hospital. "With complete frankness," added the judge, "she said she did nothing about it."

In concluding his judgment he said "I not only find that Mrs. Pickering has not made out any of these allegations against the nursing staff; I also find as a fact that there was no negligence in relation to these matters on the part of the nursing staff; this action fails."

The medical evidence disclosed a difference of opinion. Dr. J. T. Ingram, physician in charge of the skin department at the General Infirmary, said there were two types of bedsores—superficial sores (which could usually be avoided by nursing care) and deep sores due to pressure on vessels. For the latter type almost perpetual movement was the only treatment. He would have expected in Mrs. Pickering's case that an operation lasting 1½ hours, and a blood-transfusion lasting 10 hours afterwards, would be far more than enough to make a deep-type sore inevitable. Another medical witness agreed that bedsores were of two types. On the other hand, Prof. R. A. Willis, professor of pathology at Leeds University, who said he had undertaken special research into bedsores at Melbourne University, rejected the theory that there were two types. The difference between sores was, he said, one of degree or severity. He did not regard the patient's sores as inevitable; he thought they could be avoided by careful nursing. To whichever side in this controversy medical authority may lean, it is important that the court did not regard bedsores as creating an unanswerable presumption of negligent nursing.

¹ 1. Yorkshire Post, April 22, 23, and 30, and May 1 and 4, 1954.

Special Articles

REGIONAL HOSPITAL BOARDS

THE following doctors have been appointed to the boards. They will hold office until 1957. New appointments are indicated with an asterisk.

Newcastle.—R. E. Jowett, F. J. Nettrass, R. S. Venters.
Leeds.—W. A. Hyslop, *G. Whyte Watson.

Sheffield.—Sir Ernest Finch, G. H. Gibson, J. L. A. Grout, C. S. O'Flynn.

East Anglia.—A. Leslie Banks.

North East Metropolitan.—George Graham, Arthur Moody, R. W. Reid, *T. Rowland Hill.

North West Metropolitan.—Sir Zachary Cope, Katharine Lloyd-Williams, *E. C. Warner.

South East Metropolitan.—C. W. Brook, Sir William Kelsey Fry, V. F. Hall, W. G. Masefield.

South West Metropolitan.—H. E. Harding, Sir Geoffrey Todd, *A. Lawrence Abel.

Oxford.—W. C. Gledhill.

South Western.—R. J. Brocklehurst, L. C. Hill, *A. V. Neale.

Wales.—E. Wyn Jones, R. M. F. Picken, J. H. O. Roberts, E. K. Roy Thomas, *J. P. J. Jenkins.

Birmingham.—J. H. Sheldon, A. P. Thomson.

Manchester.—V. F. Lambert, Miles Parkes, Sir Harry Platt, *D. W. Luxton.

Liverpool.—W. M. Frazer, H. L. Sheehan.

Parliament

School Meals

MR. KENNETH PICKTHORN, parliamentary secretary to the Ministry of Education, in an adjournment debate, said the latest returns showed that 51.3% of children were taking school meals in October, 1952, and 45.1% in October, 1953—a fall of 6.2%. No-one knew how closely or directly the extra 2d. charged was really connected with the fall in the percentage of children taking meals. The fall in the percentage when the price was raised to 6d. in 1950 was considerable—from 53 to 50.2%. One would have thought that the raising of the price to 7d. in 1951 would have had the same, or a greater, effect, yet it had hardly any effect at all. Moreover, the general effect of these two 1d. increases dwindled soon afterwards. Thus they might hope that the effect of the latest increase would pass off fairly quickly. So far as hardship was concerned, there had been an easing of the scale for free meals.

QUESTION TIME

Tuberculosis on Tyneside

Replying to Mr. E. W. SHORT, Mr. IAIN MACLEOD, Minister of Health, said he was advised that any relationship between the incidence of tuberculosis on Tyneside and the pollution of the tidal part of the river was highly improbable.

Mr. SHORT said that the incidence of tuberculosis on Tyneside was still almost twice the national figure. The Tyne was one of the most heavily polluted rivers in the country. Would the Minister not at least look into the problem?—
Mr. MACLEOD : It was as a result of doing so that I gave the answer. It is certainly true that the incidence of tuberculosis in this area is much higher than in the rest of the country, but I am advised that of the one or two cases mentioned in medical literature there is only one on the North East coast, in 1949, which might be linked up with polluted water.

Nurses in Hospitals for Mental Defectives

Replying to questions by Mr. R. W. SORENSEN, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the estimated shortage of nurses in mental-deficiency hospitals amounted to about 2300 in December, 1952. At Sept. 30, 1953, nursing staff numbered 6600 full-time and 2200 part-time—an increase of 480 full-time and 740 part-time over the figures at Dec. 31, 1948. At Dec. 31, 1952, there were 1587 unstaffed beds. The waiting-list at Dec. 31, 1953, was 8521. Between 60% and 70% of student nurses in this field fail to complete training. The Minister was now concentrating on the recruitment of nurses for this work.

Cost of Advertising Hospital Appointments

Replying to Dr. A. D. D. BROUGHTON, Mr. MACLEOD said that complete information was not available regarding the cost to the National Health Service during 12 months for advertising to invite applications from medically qualified men and women for hospital appointments. The expenditure of all regional hospital boards and hospital management committees in England and Wales, and half the boards of governors, during the year ending March 31, 1953, was £191,000.

Waiting-lists for Thoracic Surgery

Dr. BARNETT STROSS asked the Minister of Health whether he had noted the variation in the average waiting-time for patients who required major surgery for tuberculosis, cancer of lung and bronchus, or bronchiectasis.—Mr. MACLEOD replied : The length of waiting-time is due primarily to the rapid increase in demand for thoracic surgery and the comparative shortage of thoracic surgeons and trained theatre staff. The number of surgeons has increased by 50% over the last three years and is likely to increase further, and the annual number of patients dealt with by thoracic surgery departments rose by over 18% in 1953 and has nearly doubled since 1949.

Dr. STROSS : Is the Minister aware that in Wales, for example, the waiting period for tuberculosis before treatment is offered is up to two years and for bronchiectasis up to five years, which is rather a long time? Will he increase the number of appointments of consultants for this specialty so that geographical considerations do not determine whether people live or die?—Mr. MACLEOD : We are doing all we can to iron out the serious discrepancies between the regions. One of the methods is by consultation between the senior assistant medical officers to see whether a region, where the situation is comparatively good, can help another where it may be nothing like so good. This problem has become much more urgent, because the enormous advances in surgery in the last few years have meant that so many cases are amenable to operation.

Immigrants and Tuberculosis Infection

Replying to a question, Mr. MACLEOD said that the Central Health Services Council had recommended that appropriate action be taken to ensure that those seeking work in this country from abroad should be free from infectious tuberculosis. The Standing Tuberculosis Advisory Committee, on the other hand, had expressed the view that the position did not indicate a serious menace to the health of the country. Inquiries suggested that the number of those entering with active tuberculosis was small. Only about 3 out of each 1000 occupied tuberculosis beds in England and Wales were occupied by temporary residents during the preceding twelve months who were thought to have active tuberculosis on arrival. Of this small number the majority were Commonwealth citizens or citizens of the Republic of Ireland, over whose entry into the United Kingdom there was no statutory control. As regards the minority who were foreigners coming from abroad, as workers or otherwise, he had decided, after consultation with the Home Secretary and the Minister of Labour, that the establishment of a health check sufficiently thorough to ensure that tuberculous foreigners were denied entry to the United Kingdom would involve the imposition of fresh restrictions quite out of proportion to the danger to public health.

Supply of Cortisone and A.C.T.H.

Replying to a question in the House of Lords, Lord MANCROFT said that the Board of Trade were now, in general, prepared to issue import licences in response to applications made by, or on behalf of, those who needed cortisone or A.C.T.H. for their personal use, if the application was accompanied by a medical certificate stating the condition from which the patient was suffering and the quantity and form of the drug required.

Thiourea Contamination of Oranges

Replying to a question, Major GWYNNE LLOYD GEORGE, Minister of Food, said that 23 food and drugs authorities had reported samples of oranges found on analysis to contain thiourea. So far the Derbyshire County Council and the Nottinghamshire County Council had instituted proceedings against importers. The importation of oranges containing thiourea was already prohibited. The Spanish authorities had warned all their fruit-inspection offices that this prohibition must be strictly enforced.

In England Now

A Running Commentary by Peripatetic Correspondents

THERE are so many sleek and shiny monsters on the road now, all speeding along at rates fabulous to me in my 1932 (late 1932 mind you) baby Morris. They overtake me and look supercilious; they're off first when the lights become green, and sneer; they're next to me in a park when I'm cranking the engine round, they pull their starters and are away with a haughty snort. When this has gone on for a time I get what they call a complex. Original describers of diseases have the honour of naming them, and I'm going to call mine, "Automobile Hypochondriasis." In my admittedly small series of one case (my own) there are two main manifestations.

Shame. It embarrasses me when my car shows its shortcomings. I flush and sweat, or pretend that it's not my car, and join in the laughter with the others. I decide that I will overtake that arrogant bounder and I flog the last guts out of the old engine till every rivet shudders. When my brakes screech and squeal and send children scurrying to their mothers, I stare accusingly at the glistening sedan alongside.

Anxiety.—What's the rattling at the back? My back axle's going. Another £10. I get out and look. The back of the car looks crestfallen and sunken. I drive the next ten miles at 20 m.p.h., and then realise my stethoscope is vibrating on my 'Thermos' flask. Then, my Good Heavens, there's a knock in the engine. This is it this time. A Big End—whatever that means—but I know they knock in the engine. I accelerate and it gets worse. I stop at the next garage and ask the man—always superior and omniscient—"Piston slap," says he and charges 9d. I stop an A.A. man. "Ah," says he, "it's your tappets, they need a few thou. more." Depressed, I arrive home to discover it was the B.M.A. badge on my radiator.

Every new noise, every new smell, every new sensation now spells doom to me. I am a complete hypochondriac, and have taken to patent medicines and quackery. I cannot resist a new petrol, a new additive, a new tablet to put in the petrol or the oil. "Fill your tank with Zoomph," say the adverts., and I do. "Put Zwick in your oil," and I do. Everyone knows more about cars than I do, and I take everyone's advice. They all diagnose something different, but always sinister and always likely to involve stripping the car to pieces. They all look so wise, and I know now what patients must feel like.

Of course, I know the real cure—but I can't afford a new car. I spend all my money on "Zwick," "Zoomph," and advice.

We take most of the national dailies in our hospital common-room. But newspapers are long, lunch-time (like life) is often short, and most of us are selective in our reading, hurrying feverishly from paper to paper in search of our favourites. It occurred to me the other day that the Ministry, or perhaps the B.M.A. in its wisdom, might issue a composite daily newspaper for medical common-rooms, made up of the items most often read—a sort of *Excerpta Journalistica*. With what cries of gratitude would hard-pressed hospital staffs fall on a layout such as this:

Page 1. The strip cartoons of the *Daily Mirror*.

Page 2. The *Daily Express* editorial, the *Times* fourth leader, and Cassandra.

Page 3. The marriage and engagement columns of the *Daily Telegraph* (medical protagonists in heavy type).

Page 4. The crossword puzzles from the *Times*, the *Daily Telegraph*, and the *Manchester Guardian*.

Pages 5 and 6. Sport.

Page 7. Advertisements for women's clothes and second-hand cars.

Page 8. Top half: Such topics as Parliament, international affairs, and so on. Bottom half: left blank for crossword clues and anagrams.

Now that I am thoroughly accustomed to the free and easy life of retirement, it was quite a shock to receive the agenda of a medical meeting and see the weighty subjects down for discussion. Was this the world I used to live in—with its abstruse problems and policies, its questions and answers, its day-to-day activities, its dark searchings into the future? It seems a strange reality compared with the reality of my present life of fine freedom—my just-you-wait-for-it attitude to a ringing telephone, the calm of an afternoon nap, the solace of no night calls. I shall go to the meeting, not just to keep in touch with my friends, but to strengthen my firm belief that I am lucky to have reached this quiet backwater after a fairly long and sometimes stormy voyage.

* * *

African gates have the same fascination as English gates, and we were leaning over one surveying a field with a miscellaneous collection of livestock. Compared with the African breeds of goats and cattle, the Yorkshire pigs looked like animals in a toy farmyard which had been bought a size too large. "What you doctors want to do," said my companion, "is to keep the milk which should be going to the rising generation of animals, to feed human infants. But feeding during weaning is a problem which concerns all the young animals of this country." My own sympathies lay with the human animals, but I could see his point when he talked about the next generation. "When an animal is stunted during weaning," he said, "it never recovers. It takes longer to mature, and though it may ultimately reach almost the same weight as a normal animal, it hasn't got the same stamina and resistance." This, I felt sure, was what was happening to most human animals in Uganda, but one cannot be so dogmatic about humans as one can about cows.

My attention returned to the Yorkshire pigs, and I asked whether, with English rations, the local cows and goats would grow as big as the English animals. "You can't alter the size of an animal's frame," he answered, "but a well-fed animal is better covered and reaches maturity more quickly." Here again was something which applied to humans; for I have read that English children nowadays are bigger because they grow faster and reach maturity more quickly. "Of course," he went on, "being small has an advantage when the food-supply is uncertain." This was a new idea to me. And with a world shortage of food threatening perhaps we should be cultivating a smaller size of human.

* * *

At the age of nearly four, one should be allowed complete freedom in one's choice of subjects for study. At least so Andrew thinks. If my wife decides to teach him arithmetic, he says firmly, "I think I do read." The lesson then develops into a polytechnic session until one or the other, usually not Andrew, gives way. The results of this method became apparent some days ago when he met me on the doorstep and proudly flourished a sheet of paper on which he had written OE.

"Do you know what that spells, Daddy?"

"Er . . .," I murmured cautiously.

"No, not er."

"Oh."

"No."

This sort of conversation was going to lead us straight to the stage of Moss Empires, so I tried a quick guess before the theatrical agency boys could sign us up. "I mean we," I said.

He shook his head patronisingly. "It spells naughty."

It took me the remainder of the evening to work out the solution.

MUTUAL AID

With litigation what it is,
A doctor's life is harassed;
But I've ensured that my two sons
Will never be embarrassed.

An Orthopaedic Surgeon one;
A Barrister his brother;
No matter then if either slips,
It benefits the other.

Letters to the Editor

REMUNERATION OF HOSPITAL MEDICAL STAFF

SIR.—So many misconceptions have been expressed about the recent negotiations on the salaries of hospital medical staffs that I must ask to be allowed to state a few facts.

It seems necessary to recall that the negotiations were conducted, and the settlement reached, by the Staff Side of Whitley B Committee, which contains six members of the Consultants and Specialists Committee established by the British Medical Association.

When the Staff Side is being criticised, it is only fair that it should be recognised that it was the Staff Side alone who took the initiative in putting forward a claim. Indeed, as lately as in June, 1952, the Central Consultants and Specialists Committee resolved that "a formal claim" should be lodged, "but that such claim be not pressed at the present time." If we had followed that advice, we should have got nothing now. Because the Staff Side were convinced that unless action was taken at once there was great danger that the claim of the hospital medical staffs would go by default we decided to press it in Whitley immediately.

What had happened to make it so urgent? The general practitioners, having asked to be allowed to take action independently of the consultants, had obtained the Danckwerts award, and thereby, as it turned out, made it impossible for the consultants to achieve anything comparable. For the Government's immediate reaction to the award was the statement of the Chancellor of the Exchequer in July, 1952, that it was not to be regarded as applicable to other branches of the profession. Whitley procedure made arbitration unobtainable except with the consent of the other side, which was refused. We were thus left with a moral claim which the Management Side refused to meet, and which was completely unenforceable.

By negotiations we saved from the wreck £3 $\frac{1}{4}$ million, which was distributed where it was most needed to redress the balance upset by the Danckwerts award and to restore the financial attractiveness of the consultant branch.

There is much confusion of thought about Spens. An agreement is not invalidated because one side repudiates it: if so, the County Courts could close their doors. If it is true that "Spens has gone," it went when the Chancellor made his statement before the negotiations began. But the Staff Side has never taken that defeatist view. The settlement in no way ties our hands, and our claim to cost-of-living betterment is as valid as it was before—and as unenforceable.

Finally, I hope that there will be an end to attempts to exploit the dissatisfaction, which we all feel, in order to cause dissension in the profession. Can we not continue to put unity before sectional interest?

W. RUSSELL BRAIN

Chairman, Joint Consultants Committee and
Staff Side, Whitley Committee B.

DIET AND CORONARY DISEASE

SIR.—I was greatly interested in Professor Duguid's authoritative and critical review (May 1) in which he added new material to his ingenious theory of the pathogenesis of human atherosclerosis. I have neither the experience nor the knowledge to comment on his conclusions from the morphological standpoint, but I want to ask for further clarification of some of his statements on a general medical problem which became very urgent during the past few decades.

Professor Duguid, referring to the hypothesis that an excess of fatty foods has often been accepted as a cause of coronary disease, says in his introduction:

"Nevertheless the incidence of coronary disease did not seem to decline in this country during the war when our intake of fats was restricted." How far in reality has it been restricted? Before the war the countries with the highest fat consumption were the United Kingdom, Holland, Germany, the United States, and Scandinavian countries.¹ Assuming the pre-war percentage as 100, the mean fat supply in the years 1940–45 in the United Kingdom was 86, a reduction of about 14%.² This restricted fat consumption, however, was still considerably higher than that of the much envied France in 1949–50.¹ On the other hand, in countries with really severe restriction of fat supplies (leaving the experiences during and after the siege of Leningrad aside)—e.g., in Norway with about 40% reduction in comparison to pre-war levels—the mortality rate from "arteriosclerosis and chronic myocarditis" in the years 1943–45 fell by about 25% compared with pre-war figures.⁴ This remarkable change in the mortality was attributed in a subsequent detailed analysis to the reduction in the total dietary fats.⁵

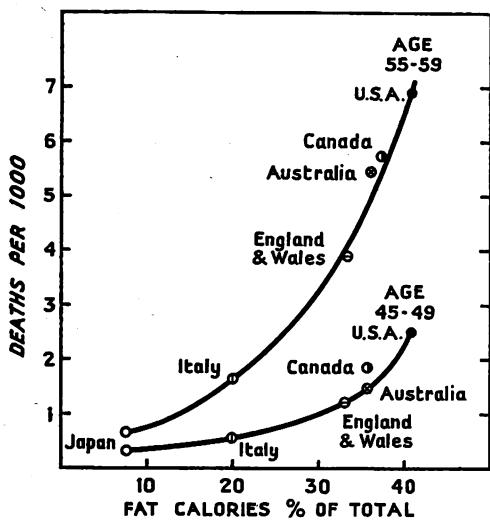
Originally, the basis of the diet hypothesis for coronary disease was the fact, as Professor Duguid confirms, that arterial lesions could be produced in animal experiments by feeding an excess of cholesterol. But modern nutritional science opened some other approaches in support of this hypothesis. The inconsistency in translating animal feeding experiments to man has been repeatedly emphasised. It is true that all animals, including man, synthesise cholesterol, mainly in the liver, and excrete it with the bile; but when exogenous cholesterol is given in quantities the synthesis in the liver may be inhibited.⁶ Whilst man, dog, and rat have great capacity and experience in handling and in disposing of cholesterol the same cannot be asserted for the rabbit and chicken, two animals used extensively in experiments with cholesterol feeding. This fact may have given rise to much confusion. In the rabbit experiment a diet is often given containing 5 mg. of cholesterol per calorie in the diet; in order to reproduce the experiment in a man with 3000-calorie intake, 15 g. of cholesterol ought to be given daily, and this is about 15–20 times higher than the amount contained in a usual high-cholesterol diet.⁷ But from experiments with H³-labelled cholesterol in man it appears that only about 20% or little more of the cholesterol ingested will be absorbed. Even after massive doses the cholesterol concentration in the blood rises only by about 3–4%.^{8,9} No reliable similar experiments with rabbits are at hand.¹⁰

Most clinical investigations at present try to implicate the cholesterol content of the blood, which was always found increased in groups of patients suffering from coronary heart-disease. But although these measurements always seem to indicate statistically significant correlations in the groups examined, their reliability for the individual patient is sometimes less convincing.¹¹ This objection holds good for total cholesterol levels, and for the cholesterol-phospholipid ratio, as well as for the so-called "giant molecules."¹¹ Gofman's group, in a series of brilliant but not universally accepted studies, tried to demonstrate that certain classes of lipoproteins, which are fractions of total cholesterol,

1. Second World Food Survey, Food and Agriculture Organisation, Rome, 1952.
2. Food Consumption Levels in the United Kingdom. H.M. Stationery Office, 1949; p. 5.
3. Brozek, J., Chapman, C. B., Keys, A. *J. Amer. med. Ass.* 1948, 137, 1569.
4. Strom, A., Jensen, R. A. *Lancet*, 1951, i, 128.
5. Phil, A. *Scand. J. clin. Lab. Invest.* 1952, 4, 122.
6. Gould, R. G. *Amer. J. Med.* 1951, 11, 115.
7. Keys, A. *Circulation*, 1952, 5, 115.
8. Biggs, M. W., Kritchevsky, D., Colman, D., Gofman, J. W., Jones, H. B., Lindgren, F. T., Hyde, G., Lyon, T. P. *Ibid.* 1952, 6, 359.
9. Keys, A. *J. Mt Sinai Hosp.* 1953, 20, 118.
10. Biggs, M. W., Kritchevsky, D. *Circulation*, 1951, 4, 34.
11. Gofman, J. W., Lindgren, F., Elliott, H., Mantz, W., Hewitt, J., Strisower, B., Herring V. *Science*, 1950, 111, 166.

appear in increased quantities in patients with coronary disease.¹² They postulate that the increase of these lipoprotein fractions is a more reliable indicator of the degree of atherosclerosis than the level of total cholesterol, which at times is not increased proportionally. The same group of workers also demonstrated that increased fat content of the diet raises the proportion of these specific lipoproteins within the cholesterol spectrum, and that subsequent weight reduction decreases it, thus connecting the fluctuation of the proportion of "giant molecules" with the development of obesity and atherosclerosis.¹³

Perhaps even more impressive is the comparison of the incidence of coronary heart-disease with prevailing food habits in different countries. Coronary heart-disease is infrequent not only in primitive countries like China,¹⁴ but also in Japan, which has a more comparable life to Western countries. In Western civilisation the



Mortality from degenerative heart-disease (1948-49, men). National vital statistics from official sources. Fat calories as percentage of total calories calculated from national food-balance data for 1949 supplied by the Nutrition Division, Food and Agriculture Organisation of the United Nations. (After A. Keys, *J. Mt. Sinai Hosp.* 1953, 20, 134.)

level of fat consumption is highest in the U.S.A., with about 40% of the total ingested calories, followed by Canada and Australia with 38-39%, and England and Wales with about 34% of the total calories, whilst in Italy it is only about 20%.¹⁵ The accompanying figure shows the incidence of mortality from degenerative heart-disease in the U.S.A., Canada, Australia, England and Wales, Italy, and Japan. There appears to be a strong if not convincing correlation between the amount of fat in the diet and the death-rate from degenerative heart-disease. Whilst it would be injudicious to claim that fatty food is the only causative factor of atherosclerosis, it would be very surprising if the proportionate increase of the mortality-rate in degenerative heart-disease and of the fat content of the diet were merely fortuitous.

London, W.1.

Z. A. LEITNER.

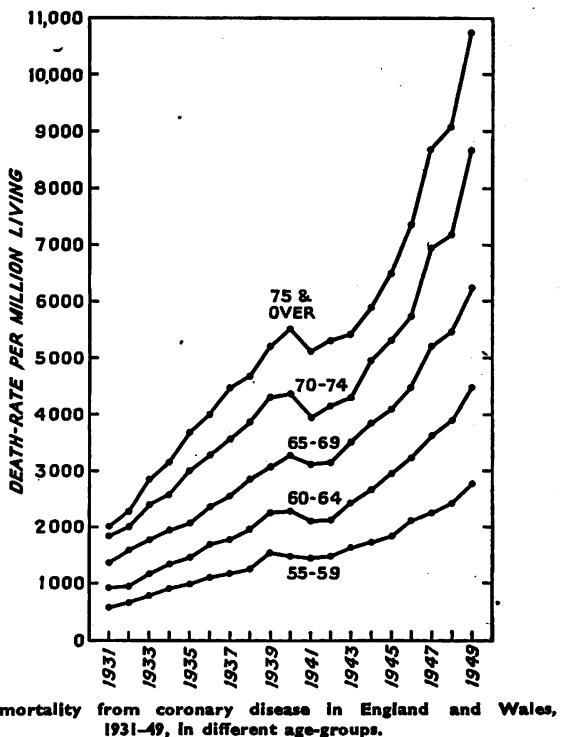
SIR,—I feel that Professor Duguid's statement that "the incidence of coronary disease did not seem to decline in this country during the war when our intake of fats was restricted" requires some amplification. If "incidence" is taken to mean "deaths"—perhaps a more limited interpretation than Professor Duguid intended—a study of the Registrar-General's figures shows that during the war years there was a definite discontinuity

12. Gofman, J. W. *Bull. N.Y. Acad. Med.* 1952, 28, 279.

13. Gofman, J. W., Jones, H. B. *Circulation*, 1952, 5, 514.

14. Snapper, I. *Chinese Lessons to Western Medicine*. New York, 1941; p. 160.

15. Keys, A. *Amer. J. publ. Hth*, 1953, 43, 1399.



Male mortality from coronary disease in England and Wales, 1931-49, in different age-groups.

in the recorded death-rates for "diseases of the coronary arteries and angina pectoris." This is clearly seen in the accompanying figure which shows the male death-rates in England and Wales for the years 1931 to 1949. The rates for females, although lower, show similar features.

It will be seen that the coronary-disease death-rates fell in 1941 and that thereafter the upward trend was resumed but it was not until about 1947 that the rates reached the level which would have been attained had the upward trend of 1931 to 1940 continued. The general upward trend is probably due largely to changing fashions of certification and classification as well as to better diagnosis of coronary disease, but it seems difficult to explain the war-time trough in this way. There were of course many changes in living conditions during the war, of which reduced consumption of fats is only one. Nevertheless there is some biological evidence which can be interpreted as pointing to fat intake having something to do with coronary disease. It therefore seems to me that Professor Duguid tends to dismiss the national statistics too lightly in his discussion of the possible influence of fat consumption on coronary disease.

Harrow, Middlesex.

R. H. DAW.

PORPHYRIA TREATED WITH NEOSTIGMINE

SIR,—The report by Dr. Gillhespy and Mr. Smith in your issue of May 1 describes the successful treatment of haematoxylinuric polyneuritis with neostigmine and prompts me to report the unsuccessful use of the same drug in a similar but more severe case.

The patient was a 23-year-old woman who presented with a mild polyneuritis in August, 1953, which remitted, but relapsed in September; she again deteriorated in October, 1953, when porphyrins were noted in her urine (acid porphyrin, porphyrinobilinogen, and coproporphyrin). During the first 2 weeks in October she developed a rapidly progressive paralysis, which by Oct. 13 affected all four limbs, diaphragm, and lower intercostals. On Oct. 14 her breathing became so shallow that it had to be assisted intermittently with an Oxford insufflator and, later, a box respirator. During this day (Oct. 14) she was given a test dose of 1.25 mg. of neostigmine subcutaneously, followed by 2.5 mg. subcutaneously 6-hourly. This dosage was continued for 48 hours, during which no beneficial effect on the weakness was observed,

but rather a deterioration, in that during this period her weakness became more severe, affecting her upper intercostals, face, and larynx, and by the evening of Oct. 16 she needed to be continuously in a box respirator, when the use of neostigmine was abandoned. During the next 4 days she developed a bulbar palsy from which she recovered, but she died in a relapse in March, 1954.

The dose of neostigmine in our case (2.5 mg. 6-hourly subcutaneously) was more than double that of Gillhespy and Smith, and was given by us at a stage when the weakness was increasing, without any beneficial effect. Gillhespy and Smith also mention that the electrical reactions of the muscles in their case were *not* of the myasthenic type, and it appears that their patient was, at least, not getting worse at the stage in which they treated her. It is therefore possible that myasthenic weakness is not the main factor in the paralysis of acute hematoporphyrinuric polyneuritis, although it is obviously worth while to try any treatment in such a severe disease of unknown aetiology.

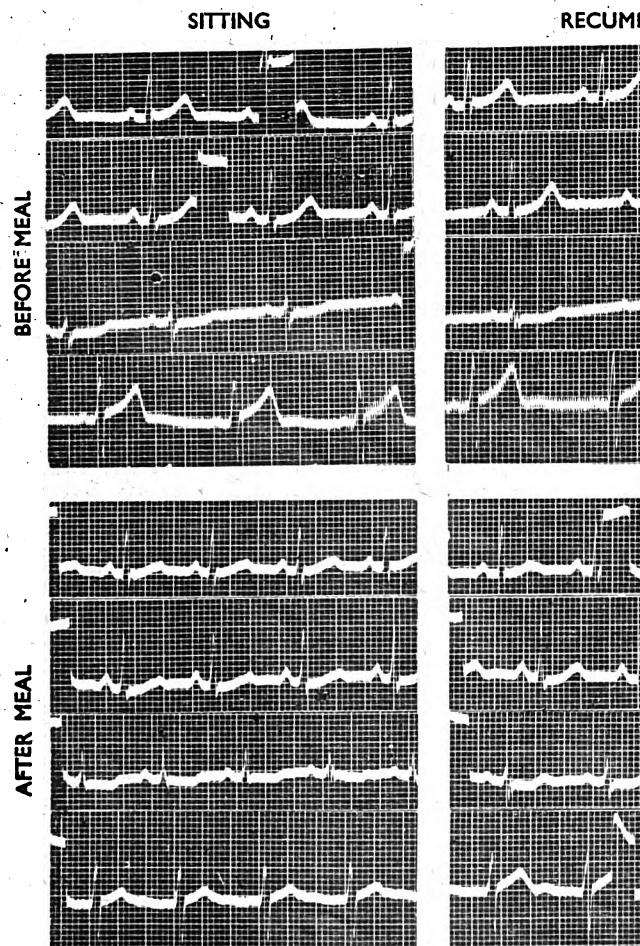
London Hospital, E.1.

J. W. FAWCETT.

ELECTROCARDIOGRAPHIC CHANGES IN THE DUMPING SYNDROME

SIR.—In relation to the article by Dr. Pulvertaft in your issue of Feb. 13 it is necessary to point out that similar electrocardiographic changes occur after meals in normal persons. The accompanying figure shows a set of tracings, all taken from the same healthy person, published¹ in the *American Heart Journal* in 1939. All the subjects in this investigation were healthy young

1. *Amer. Heart J.* 1939, 17, 725.



Electrocardiograms in a healthy young person before and after meals.

individuals and in no instance were the electrocardiographic changes accompanied by symptoms. These changes were found to occur in over 50% of the subjects.

The electrocardiographic change after food is diminution of the T wave in all leads. In some persons T₂ and T₃, previously upright, become inverted. The electrocardiograms published by Dr. Pulvertaft and associated by him with the dumping syndrome do not differ qualitatively from those observed after food.

In view of these observations, Dr. Pulvertaft's conclusion that the dumping syndrome is accompanied by electrocardiographic changes requires qualification.

New Orleans, U.S.A.

MANUEL GARDBERG.

WHAT ABOUT THE JONESES?

SIR.—The account of the Smith family which you extracted from the Widdicombe File and published on May 1 prompts me to say a few words about their London cousins, the Joneses, who happen to be under my care. The absence of discipline in their household is recognisable in all their activities.

Whereas Mr. Smith provides £7 a week Mr. Jones's contribution to the family budget seems to be about £4 to £4 10s., and his wife has to supplement it by doing a part-time job cleaning offices. Jones always has his cups of tea and cigarettes, and his dinners, in a small café fairly near his work; and when his day's work is over, he frequents the dog track and the "local." On his return thence, round about midnight it is not uncommon for him to summon his doctor to see a child for whom he suddenly shows deep concern. Or when his wife does not welcome him home with open arms, need may arise for a suture in Jones's scalp, or radiography of Mrs. Jones's elbow.

Once Jones decided to be a really good fellow, and to stay at home on Wednesday and Thursday evenings. No more entertaining Rosie of the Rose and Crown. Instead, he increased from 5s. to 10s. his weekly contribution to the pools. Perhaps one day he will be able to take his missus to the South Seas . . . and there possibly meet Dorothy Lamour. Naturally, he has his regular "flutters" on horses, and he sees nothing wrong with leaving his children to their devices on Saturday afternoons when he follows his favourite football team, the Rotherhithe Academicals—both at home and away. After all, football is a healthy exercise; and one million people develop muscles vicariously watching football on Saturdays. Sometimes—and if it can be managed—some also watch a game on a weekday; and Jones usually "manages." But Mrs. Jones, whether or not she goes out to do extra work during the week, still has to carry the youngest children and the shopping unaided on Saturdays. Little wonder then that her backache and her sciatica make life a misery.

During his last leave from his unit, Mrs. Jones's youngest brother came to me suffering from pharyngitis. He had a slight pyrexia. I considered he would be fit to return to his unit two days later. Sixteen days later his unit phoned me from Bristolshire to find out whether he was still under treatment. He had not returned.

Usually Alf and Ernie will have left school and will be glad to have taken on blind-alley occupations before entering the Forces. The last I heard about one of my Alfs was that he was in a remand home until his case was due to be heard. He was accused of breaking into and entering a local sweet-and-tobacco shop kept by a widow (also my patient), suffering from rheumatoid arthritis. Jones père simply could not understand it.

The eldest girl is in her last term at school. There are 42 others in her class—an impossible task for any school-teacher. Judging by the late hours the girl keeps and her complete lack of discipline, her future vocation will surprise no-one.

But what is at fault with "Our Bills" and "Our Ritas"? A diagnosis of "high-grade mental deficiency" helps administrators more than the patient. It takes little or no account of his emotional state, his thought processes, or his physical condition. Nor does it describe the interaction between the patient and society. Moreover, there are innumerable high-grade defectives capable of profiting by instruction and wise discipline. Hence the need for more schools, and, of course, many more teachers—not forgetting playing-fields. Otherwise more borstal institutions and prisons. In the long run the Ministry of Education will pay greater dividends than the Home Office.

I. H. M.

SURGICAL TREATMENT OF ACUTE OSTEITIS IN CHILDHOOD

SIR.—May we congratulate Mr. Bremner, Dr. Neligan, and Dr. Warrick on a paper (May 8) which continues worthily the valuable contributions made to paediatric surgery by the Newcastle school. We are pleased to see that it confirms the claims which we (with Mr. Twistington Higgins) put forward in 1947 as to the excellent results which can be obtained by aspiration alone in the osteomyelitis of childhood.¹ This is the more gratifying as our report was attacked with almost theological vehemence by Trueta and Agerholm; and, although our criticism of their criticism put an end to the argument, this must have prevented the method being taken up as widely as it might otherwise have been. The criticisms made by Bremner, Neligan, and Warrick that our cases must have been slight because the doses of penicillin were low seems to carry the corollary that if the doses had been higher the cases would have been more severe. Actually the smallness of the doses and their surprising success were both due to temporary conditions—namely, the scarcity of penicillin and the absence of resistant strains of infection. We have not ourselves tried a similar series of contrasted cases, because of our conviction that it was hardly fair to the patients to use on them a method we were convinced was not the best available. The criteria on which we came to this conclusion were different from those of Bremner et al. They were:

1. *The avoidance of chronicity.*—This we regard as far the most important of all considerations. All our experience and the published papers we have studied appear to show that chronicity is less common with aspiration than with open operation.
2. *Scarring* we rate higher as a disadvantage than do many surgeons, though probably not as highly as do the general public in these days of bodily exposure.
3. *Duration of treatment.*—The sole criterion mentioned by Bremner et al. we consider of hardly any importance in a child, unless the difference were extremely large. It is interesting to note that it hardly exists.

Your annotation suggests that, although first-class surgeons may use aspiration, others should employ open operation. It seems to us that it is just when experience and perfect asepsis is lacking that chronic osteomyelitis is likely to be produced, and a good many cases entering our hospital bear this out. However, it is certain that very few surgeons throughout the country have any notion of the excellence of the results to be obtained by aspiration: let us hope that the suggestion that open operation is for the less expert may stimulate the alternative method.

As to technique, one of us (D. B.) has for some years been using what may be called lavage rather than

aspiration. It needs an anaesthetic and two surgeons, sitting on either side of the abscess. They each insert needles, and when the first gush of pus has subsided one slowly injects normal saline, while the other keeps the lumen of the exit needle on his side clear with a stylet. When the effluent is completely clear a final washout with penicillin is given, and firm pressure with a thick pad of cotton-wool is used to obliterate the abscess cavity as much as possible. The improvement in results when the abscess cavity involves a joint is particularly marked; and such cases are far from uncommon in children.

The Hospital for Sick Children,
Great Ormond Street,
London, W.C.1.

DENIS BROWNE
MARTIN BODIAN.

THE PLIGHT OF SENIOR REGISTRARS

SIR.—The unfortunate position of many senior registrars and their families, so well outlined by a senior registrar's wife in your issue of May 8, must make us all think hard about this problem, especially those of us who are hoping for a post in this grade.

Now that the National Health Service has been in existence for over five years we should be in a position to see what kind of medical staffing hospitals require, and to boldly reorganise the various grades. One of the major difficulties has been due to the employment of "trainees" to do the basic work of hospitals in almost all grades short of consultant. It is doubtful whether they are being "trained" any more than anyone else in medicine who is constantly learning in his job. Yet we see an experienced senior registrar doing essential work being sacked simply because his period of "training" is up and no consultant has died or retired to make a vacancy for him. Another man is then put in his place for "training."

Surely we should now be able to offer a man of the status of senior registrar a relatively permanent appointment to do a job of work, until he finds a more senior post. The reorganisation of junior hospital staffing must not be allowed to wait much longer before the present senior registrars are lost to the hospital service.

Royal Southern Hospital,
Liverpool, 8.

J. E. FORSTER.

GRADUATE WIVES

SIR.—Dr. Mary Lennox in her letter of May 8 draws attention to the difficulties that women doctors are experiencing who seek part-time sessional work during the years when they are rearing their children. This is a problem of growing urgency to an increasing number of women medical graduates.

There are many statements in Dr. Lennox's letter which are matters of personal opinion and on which I could well comment at length. I would like, however, to deal with the last paragraph in which she suggests that part-time public-health work is ceasing to exist because "the large fee" per session encourages local health authorities to economise by using full-time staff for their clinics. Here she seems to be misinformed, for there is little difference between the scale for full-time assistant medical officers (£950–1300 per annum) and eleven weekly sessions at £2 5s. per session (£1287 per annum). Moreover, under a recent Whitley agreement (M.D.C. circular no. 19) part-time medical officers, previously paid a "flat rate" annual salary, are now remunerated at the appropriate salary scale—i.e., they become entitled to annual increments in the same way as their whole-time colleagues.

Dr. Lennox's proposal that many married women doctors might feel prepared to undertake part-time work at a reduced rate of remuneration is dangerous in the extreme. The British Medical Association has for many years worked most vigorously, in collaboration with the Medical Women's Federation, to eradicate undercutting

1. *Brit. med. J.* 1947, i, 757.

by members of the profession, men or women. Much of the good feeling within the profession is founded upon long-standing co-operation on this very point.

It cannot be stated too clearly that, when the rate for the job has been agreed by proper negotiation, that agreement must be honoured whatever the personal circumstances of any individual doctor. Too often this aspect of the matter escapes the attention of the young woman doctor who concentrates only on the short view when she marries. It is, of course, true that the present high cost of domestic help, and the system of taxation of income of husband and wife as one (which falls particularly hard in cases where the joint income exceeds £2000) may make the net value of part-time work comparatively small, but this must not be allowed to confuse the main issue.

The Medical Women's Federation is giving particular attention to the problems of the married woman doctor. The predicament of the many medical graduate wives whose experience with their own families enriches their professional training, but who can find no opportunity to make use of it, is a serious one; but the fact remains that it is essential that the married woman doctor, like her unmarried sister, must equip herself fully by undertaking adequate postgraduate work, and, where at all possible, obtain the recognised specialist diploma. She must offer her services based on more than the personal family experience, valuable though this may be, and in undertaking any medical work, whole-time or part-time, she must clearly recognise her responsibilities to the job and (more important) to her patients.

A suggestion such as the one put forward by Dr. Lennox is only too readily made, but it is short-sighted and dangerous to all concerned. I hope, however, that it will help to draw the attention of the profession to the loss to the community which may result if this group of medical women is unable to obtain the work for which it should be so eminently suited.

Medical Women's Federation,
Tavistock House North,
Tavistock Square,
London, W.C.1.

ANNIS GILLIE
President.

SIR.—Dr. Lennox's letter contains an error of reasoning and proposes a course of action which I think would be to the detriment of this profession.

The idea that a woman doctor who has brought up a family is, *ipso facto*, well suited for infant welfare is as sensible as saying that a doctor who has looked after one brother a schizophrenic and the other a manic-depressive is well suited to treat psychotic patients: the latter in fact has a certain advantage over the former.

In her last paragraph, what Dr. Lennox is in fact suggesting is that married women should undercut their colleagues: this is acceptable in Petticoat Lane but hardly in a supposedly learned profession.

London, N.10.

A. W. BEARD.

PSYCHIATRIC EVIDENCE AT MURDER TRIALS

SIR.—I read your leading article of May 8 with great interest and I would strongly support your four recommendations—especially the period of observation by at least two psychiatrists before a report is made.

I feel, however, that some of your statements may be misleading. I believe it is the practice for a prisoner accused of murder and remanded to an ordinary prison to be transferred to a prison where there is a full time medical officer with psychiatric experience, usually indeed to Brixton Prison, and in my own experience I have had the fullest possible co-operation from the principal medical officer of Brixton Prison, as well as the local prison medical officer. I must also say that I, myself, have not experienced any hostile cross-examination in court, and I feel that when it does occur it may

largely be the fault of the ill-considered and dogmatic evidence offered by the medical witness.

You refer to a recent murder trial in which the accused was convicted, although the only medical witness declared him to be suffering from a serious mental disease; but a much more disturbing case occurred a few years ago when the accused was convicted and the sentence of death later carried out, although at the trial all three medical witnesses, two for the prosecution and one for the defence, agreed that the prisoner, at the time of committing the crime, was insane. I do not think that sufficient attention has been paid to this case, which, in my opinion, marks the lowest point to which psychiatric evidence has sunk in the estimation of a judge and jury.

It is, to say the least, a disturbing state of affairs when a jury can return a verdict which completely ignores the opinion of three medical men on the state of mind of a man accused of murder.

St. Andrew's Hospital,
Thorpe, Norwich.

W. J. McCULLY.

ISOLATION OF CASTLE'S INTRINSIC FACTOR

SIR.—The preliminary communication (March 6) by Dr. Latner and his colleagues does not, I think, satisfy the customary requirements for a report on the first isolation of a substance. I should say that these requirements are:

- (1) A short reference to the present position of the problem.
- (2) A description of the isolation procedure.
- (3) Analytical data about the newly isolated substance.
- (4) Proof of its chemical purity.
- (5) Evidence of its differentiation from similar materials isolated previously.
- (6) Data on its physiological activity (if it is known to be physiologically active).

My reasons for this criticism are:

(1) No reference to the question of the mucoprotein nature of intrinsic factor, prior to Latner's work, is made in this or in any of the other papers to which he has contributed.^{1,2}

(2) All that is said about the isolation procedure is: "The major part of the intrinsic factor activity can in the first place be extracted by a suitable buffer solution at pH 6.35. The active fraction finally obtained has proved easily soluble at pH 2 . . ." This leaves us with the expectation that "full details of this isolation procedure will shortly be published."

(3) The analytical data merely confirm the mucoprotein nature of the intrinsic factor, about which evidence was presented three years ago by our group,^{3,4} but they do not include the elementary analysis of the newly isolated intrinsic factor. Even the data on the carbohydrate composition are rather fragmentary and conflicting. Thus, in September, 1953, the nitrogen content of Dr. Latner's intrinsic factor preparation obtained by electrophoresis was given as 10% and the hexosamine content as 6%,^{1,2} but in this latest paper the electrophoretic fraction contains 9.0–9.7% nitrogen and as much as 11–12% hexosamine.

(4) The proof of chemical purity is based on data from paper-strip electrophoresis and the ultracentrifuge, and it appears convincing, although the electrophoretic findings would have more value if data were included indicating the homogeneity of this fraction at various pHs and ionic strengths.

(5) In order to satisfy the fifth requirement, Dr. Latner has sought to show that his mucoprotein is different from the "glandular mucoprotein" the intrinsic factor activity of which we demonstrated a few years ago and on which we have since accumulated further data. For this purpose he tries to dissociate himself from any work done previously, and he mentions three points as evidence

1. Latner, A. L., Ungley, C. C., Cox, E. V., McEvoy-Bowe, E., Rains, L. *Brit. med. J.* 1953, i, 467.
2. Latner, A. L., McEvoy-Bowe, E. *Biochem. J.* 1953, 55, xxiii.
3. Glass, G. B. J., Boyd, L. J., Rubinstein, M. A., Svirgals, C. S., Chevalley, J. E. *Fed. Proc.* 1951, 10, 50.
4. Glass, G. B. J., Boyd, L. J., Rubinstein, M. A., Svirgals, C. S. *Science*, 1952, 115, 101.

that his intrinsic factor mucoprotein is different. Let us analyse these three points:

(a) Dr. Latner implied earlier¹ that the material present in his first cathodic electrophoretic peak, which contains much mucoprotein but little intrinsic factor activity, "may well represent the fraction isolated by Glass et al."; by inference he contrasts this with his active material, which exhibits high intrinsic factor activity and travels to the anode. This statement is disturbing in view of his knowledge of our earlier publication,⁴ which he quotes, where we have insisted that our mucoprotein fraction showing intrinsic factor activity travels to the anode on electrophoresis and forms one of the leading anodic peaks.⁴⁻⁶ This high negative mobility of glandular mucoprotein (-7 to -8×10^{-4}) has been confirmed by others.⁷ This obviously precludes that a substance having such a high negative charge could travel on paper electrophoresis to the cathode at pH 6.35 even by electro-osmosis, and makes Dr. Latner's statement groundless. To prove his point, Latner would have to compare the electrophoretic mobility of his fraction and ours, using the same technique. Otherwise there is no evidence that his intrinsic factor mucoprotein differs from ours in electrophoretic mobility.

(b) The second argument for specificity of the fraction is: "Its chemical analysis indicated that it could not possibly be identical with so-called 'soluble glandular mucoprotein.' This has already been pointed out elsewhere." To us, the only two differences which appear valid are: Dr. Latner's preparation contains about 1% less nitrogen than ours (11.2% according to Werner⁸); and there is no hexuronic acid, as determined by Dische's carbazol method, and as contrasted to the presence of this acid in our material, using Tracey's technique. All the other data appear to be similar. As I pointed out in a discussion of Dr. Latner's paper,⁹ the hexosamine content is similar in both cases (8.8% in ours⁶ and 6%⁸ and 8% in Dr. Latner's). Also the carbohydrate spectrum is similar and includes fucose and galactose, but no glucose. Finally, the Folin-Ciocalteu reaction for tyrosine and tryptophan is positive in both instances; since we did not determine whether it is tyrosine or tryptophan in our substance which gives the positive Folin-Ciocalteu reaction, the absence of tyrosine in Dr. Latner's preparation cannot be accepted as a differentiating point. Also the difference in hexuronic acid content cannot be accepted without a comparative study with the same technique.

(c) The third argument is that this substance "has proved easily soluble at pH 2.0 which is an additional indication that it is not identical with soluble 'glandular mucoprotein.'" This is wrong. Our mucoprotein fraction is perfectly soluble at pH 2.0 after electrophoretic separation. It flocculates at pH 2.0 only after it has been previously denatured by acetone precipitation, which we use for its fractionation; this denaturation decreases its solubility in the neighbourhood of the isoelectric zone.

Since all these arguments can be faulted, I think that there is as yet no adequate evidence for differentiating Latner's intrinsic factor mucoprotein from our mucoprotein fraction carrying intrinsic-factor activity.

(6) The only characteristic feature of Castle's intrinsic factor is its ability to promote the intestinal absorption of vitamin B₁₂ in patients with pernicious anaemia. This can be assessed by any of the available isotope techniques.¹⁰⁻¹² Because of the delicacy of all these methods, the evaluation of the results requires clear-cut data. Dr. Latner performed only two tests using Heinle's method¹⁰; he observed a fall of about 30% in the faecal excretion of radioactive B₁₂ after addition of his preparation. In Heinle's original work, the fall was of the order of at least 60%. Meyer¹⁴ has recently shown that a fall of 30% can occur without any obvious reason even in normal subjects, and we have observed retention of

radioactive materials within the lumen of the bowels for as long as 10-12 days.¹⁵ Dr. Latner and his colleagues must produce much more clinical evidence if they wish to prove that the newly isolated fraction has definite intrinsic factor activity.

Department of Medicine,
New York Medical College,
New York.

GEORGE B. JERZY GLASS.

ADDISON'S DISEASE WITH DIABETES MELLITUS

SIR.—The case reported by Dr. Baird and Dr. Munro (May 8) is most interesting. In view of the suggested influence of adrenal overactivity in the pathogenesis of diabetic retinopathy, it would be interesting to know if this patient had diabetic retinopathy, and, if so, whether the condition of the fundi improved with the onset of Addison's disease. Poulsen¹⁶ recorded a case in which diabetic retinopathy regressed with the development of Simmonds' disease.

National Maternity Hospital,
Dublin.

M. L. DRURY.

STRIPPING OPERATION FOR VARICOSE VEINS

SIR.—I would like to support Mr. Bolton Carter's advocacy (April 10) of the stripping operation for varicose saphenous veins. It is indeed a good operation, especially when it supplements a complete diagnosis and a flush sapheno-femoral or sapheno-popliteal ligation. Stripping will not clear up inefficient communicating veins, such as those above and below the knee or above the ankle, nor in many cases will it relieve ulceration above the ankle. In my experience only about 40% of ulcerated legs are due to varicose veins: many of the rest follow phlebitis of the deep veins. With these qualifications, I agree that stripping does clear varicose veins and reduces much of the need for postoperative sclerosing injections. In this respect I have found it superior to the former method of internal abrasion and fractional injection of sclerosing fluid, which, though effective, did need a fair number of injections to remove varicose veins from the legs.

Although stripping is a somewhat crude operation, it can be performed under a local anaesthetic and it is followed by comparatively little pain and few complications. None of my patients are given antibiotics unless there is active ulceration present; the wounds of fat persons are usually "frosted" with sulphanilamide powder.

I note Mr. Bolton Carter's use of ethamoline injections: I bracket this with sodium morrhuate as an undesirable and dangerous sclerosant, because it causes such intense pain afterwards that patients are often incapacitated for from 1 to 7 days, which gives ideal conditions for a clot to propagate deeply, not to mention the occasional syncope immediately after its introduction.

Since October, 1946, when Mr. Riddoch introduced me to his phenol-glycerin solution, I have used it with consistent success and safety; the present formula is phenol 3% and glycerin 30% in pyrogen water, and the dose is $1\frac{1}{2}$ ml. It is supplied by most chemists.

In dealing with bilateral varicosities, I agree that it is permissible to do both legs simultaneously with two surgeons, but otherwise it is safer to do one leg per session with an interval of 2 or 3 days. The incidence of deep calf thrombosis in my patients was quite appreciable when both legs were done at one operation with only one surgeon.

I began using the stripping operation occasionally in 1951, and from Jan. 1, 1952, I have used it exclusively over 400 times. It is clearly an effective and safe method needing the minimum of aftercare, although patients are followed up for 5 years or more afterwards.

London, W.1.

HAROLD DODD.

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7. Mack, M. H., Wolf, S., Stern, K. G. *J. clin. Invest.* 1953, 32, 862.
8. Werner, I. *Acta Soc. med. Uppsal.* 1953, 58, 1.
9. Latner, A. L. Gordon Symposium on Metabolism and Vitamins. New London, New Hampshire, 1953.
10. Heinle, R. W., Welch, A. D., Schart, V., Meacham, G. C., Prusoff, W. H. *Trans. Ass. Amer. Phys.* 1952, 66, 214.
11. Schilling, R. F. *J. Lab. clin. Med.* 1953, 42, 860.
12. Glass, G. B. J., Boyd, L. J., Gellin, G. A., Stephanson, L. *Fed. Proc.* 1954, 13, 54; *Arch. Biochem.* (in the press).
13. Glass, G. B. J. *Clin. Res. Proc.* 1954, 2, 32.
14. Meyer, L. M. *Proc. Soc. exp. Biol., N.Y.* 1953, 82, 490.

15. Glass, G. B. J. *Bull. N.Y. Med. Coll.* 1953, 16, 1.
16. Poulsen, J. E. *Diabetes*, 1953, 2, 7.

JUVENILE SPRING ERUPTION

SIR.—I have just seen the article by Dr. Anderson and her colleagues (April 10). It was extremely interesting to read of the approach of dermatologists and the L.C.C. school medical service to this condition.

It must be very well known to anyone who looks after children of the preparatory school age-group and younger. As medical officer to several schools, I have found it exceedingly common in boys, and less so in girls who cover their ears with their hair. It can give rise to intense itching and unhappiness, and this is rapidly relieved by an anti-histamine drug, such as chlorcyclizine ('Histantin') or mepyramine ('Antisan'), and by zinc and castor-oil cream applied to the eruption. The worst sufferers must wear sun-hats on sunny days in April and May. By mid-May or June (in an average summer) the ears become adapted to sunlight and can be exposed with impunity, but not other parts of the body. As clothes are shed, sleeves rolled up, or short socks worn, the papules can appear on new areas. The ears, knees, and hands of these children are then free, but the forearms and legs are affected. And later, when bathing begins, the upper trunk and thighs are involved. This seems to me to exclude completely the influence of cold in causing the eruption. I have had exceptional opportunity to observe and treat this condition, not only in numerous children in boarding-schools, but also in my own son, who is particularly badly affected from early April every year, until each part of his body which is exposed is acclimatised to sunlight. By August he can sunbathe with impunity. It is interesting to note that as an infant he was violently allergic to cow's milk until he was desensitised.¹

St. Leonards-on-Sea,
Sussex.

H. S. BRODRIBB.

SIR.—In my practice this April, I have seen about 15 cases of an eruption on the ears of children beginning a week or so previously, when the light was becoming noticeably brighter but the air was still cold; and this resembled the juvenile spring eruption recorded by Dr. Anderson and her colleagues during similar weather conditions. There was no evident contact between these children: in fact one noticed his rash at a school camp in another district.

This same boy developed an itching rash on hands, forearms, legs, and feet a few days after his ears were affected. I did not note the type of eruption on his extremities. The mother of another boy with an apparently similar condition said that her son had had the rash on his ears all the winter, and she had brought the child to see me as the "chilblains" had not subsided with the warmer weather.

I have no information as to the duration of the complaint, for the parents were satisfied with reassurance and have not made a second attendance.

Ilford, Essex.

R. N. C. SMITH.

THE BOMBS

SIR.—Dr. Stafford-Clark's letter seems to have little to do with the moral challenge of the hydrogen bomb but merely repeats the familiar argument that "Communism" aims at world domination "by violence or treachery" and that therefore everyone must be either for it or against it, and (by inference) against it to a degree which makes employment of the bomb justifiable. This ignores the problem (emphasised in your leader and in Professor Haddow's appeal to scientists everywhere) of what is morally permissible in war. The atomic bomb brought us very near, and the hydrogen bomb brings us nearer still, to the state of mind which Dr. Comfort describes as psychotic, in which, as a recent letter to the *Times* declared, total destruction of humanity is said to be a lesser evil than "world communism."

1. *Arch. Dis. Childh.* 1944, 19, 140.

Even if one believed Communist Russia and China to be governed by the most corrupt and sadistic of tyrannies, no people who hoped to preserve civilisation could consent to the employment, in the effort to prevent the extension of such tyranny, of a weapon intended to kill millions of people, a whole population. This seems to me the greater evil, incomparably the greater. Fydicible submission to a political régime which was considered repugnant and unjust would be no new event in world history. Housman epitomised this situation with his "Let us endure an hour and see injustice done." It is what we do to others, not what they do to us, which is our responsibility and which must weigh on our conscience. The murder of thousands of innocents is not compatible with a clear conscience, but only with heavy feelings of guilt.

Bickley, Kent.

DUNCAN LEYS.

SIR.—Dr. Stafford-Clark and myself continue, I am afraid, to pass one another without meeting. The points which he answers are not quite the points I made, and while adrenergic words like tyranny and liberalism are rather blunt instruments for the description of human cultures (which, I wonder, should we apply to the Cromwellians, or to Augustan Rome?), we are in much greater agreement on the demerits of coercive societies than he realises. Of all contemporary cultures, I am quite sure that the Marxist countries would be the least ready to accept, or even tolerate, the kind of objectivism which I have been advocating.

But that was not the point at issue. This correspondence was headed "The Bombs." Of the two main possessors of these weapons, I still think that the American government and culture are subject to forces, some of them the product of liberalism itself, which might lead them to regard the existence of universally-destructive weapons as a source of emotional satisfaction. I still think that the Communists are not subject to comparable forces. And I am still certain that where we are dealing with a weapon which is virtually devoid of purposive significance (even for the commission of political crimes), emotional factors, and the pressure of guilt feelings within a liberal and self-critical culture, are more dangerous than political ambition. Nobody but a madman would use this weapon. Its possession by a liberal culture may of itself generate such a madness, where a less liberal and less self-questioning culture might keep its head. That is all I said. As for neutrality, we can either abuse the Russians and the Americans in terms of fear and anger, or we can attempt to understand their actions, however unlikeable, and reconcile their antagonisms. I would have thought that it was the second course which is inherent in the medical obligation.

Loughton, Essex.

ALEX COMFORT.

SIR.—Curiously, Dr. Stafford-Clark himself takes the British Communists' depressing view that "we are inevitably faced with the necessity of deciding on which side we stand." But it is possible to be appalled by Communism and still to appraise the horrifying dangers of the American attitude. This "neutralism" is no more a precursor of Communism than it is, say, of Fascism or, from another point of view, of Pacifism. Dr. Stafford-Clark must resign himself to the existence of very many people in Britain who will not agree with him, and whose principles will allow them to choose neither the Russian nor the American culture.

London, S.W.7.

BENJAMIN LEE.

SIR.—Dr. Stafford-Clark, in spite of his efforts at "clarification," is a great confuser of issues. The issue presented to us by the hydrogen bomb is not whether we should or should not prefer this or that pattern of culture: the issue is whether any pattern of culture is likely to survive the use of such weapons and whether therefore

they should not be banned. Those of us—the majority, I think—who believe that the bombs should be banned, would be helped by the avoidance of the confusion between international ownership and international inspection of atomic-energy plants. The Soviet Union has always opposed the former and has repeatedly proposed the latter.

London, N.21.

E. MONTUSCHI.

Obituary

FRANK DUTCH HOWITT

C.V.O., M.A., M.D. Camb., F.R.C.P.

THE death of Frank Howitt will be widely regretted, for few men have been better liked by their colleagues. In taking up the cause of rehabilitation and resettlement at a time when its importance was still generally underrated, and in promoting the better practice of physical medicine, he performed a valuable service. This leadership he was able to exert because he was gay, generous, and loyal.

Born in 1894, he was the son of Arthur Gibson Howitt of Nottingham, and was educated at Uppingham and Trinity College, Cambridge. In

the first world war he served at Gallipoli and in France, in the R.A.S.C., and as a pilot in the R.A.F. From Cambridge he went to Guy's Hospital, and after qualifying in 1923 he held resident appointments there before joining the actinotherapy department as chief clinical assistant. His M.D. thesis in 1928 was on light therapy, and it so impressed Sir Humphry Rolleston that during the illness of King George V in the following year he suggested that Howitt should be called in to give this form of treatment.

For his help at this anxious time Howitt was appointed c.v.o.

He had intended to become a general physician, but he now decided to specialise in physiotherapy. He spent some time as assistant to Dr. C. B. Heald at the Royal Free Hospital, and in due course joined the staffs of the Prince of Wales's General Hospital, Tottenham, and the British Red Cross Clinic for Rheumatism (now attached to the Middlesex Hospital as the Arthur Stanley Institute for Rheumatic Diseases). In 1933 he took a big part in the fusion of the Royal Society of Medicine's sections of balneology and medical electrology to form the section of physical medicine; and it was not least through his efforts, both then and later, that the subject of physiotherapy was raised to a level above that of electrotherapy. In 1937 he was elected F.R.C.P. and about the same time he became physician to the Middlesex, with charge of the physiotherapy department. Under his direction this department was enlarged and its scope was greatly increased.

In 1940 Howitt was invited by the Army to become its consultant in physical medicine—a term to which he gave a far wider meaning than was usual. To him physical medicine did not imply only (as he put it) the turning of taps and switches, but included most of what others might now include under such headings as preventive and social medicine. To him all medicine could be divided into two categories—pharmacological medicine and physical medicine—and the latter included healthy living as a potent prophylactic measure. In the Army, in which he was given the rank of brigadier, he found great scope for his ideas and applied them to the physical upgrading of recruits, and in the rehabilitation centres which he sponsored. He was largely responsible for the establishment of the physical development centres¹ and convalescent depots in the Army, and, with the help of a small group of colleagues, for the recruitment and training of the command specialists in physical medicine. Also during the war, he was one of

the select group of men invited by Ernest Bevin, then Minister of Labour, to help to create the first industrial rehabilitation unit at Egham, and he became the Ministry's adviser in rehabilitation.

After the war his professional interests were in rheumatology, physical education, and reablement, and his contribution to these subjects was acknowledged by his appointment to membership of the Nuffield Foundation committees on rheumatism and industrial medicine, to the chairmanship of the Research Board for the Correlation of Medical Science and Physical Education (which he had founded), and to a directorship of the Disabled Persons Employment Corporation (Reemploy Ltd.). He saw that physical medicine had much to contribute to these problems and he stimulated the men who were following him to take a wide view of their opportunities and responsibilities. He continued to be hon. consultant in physical medicine to the Army; he showed keen interest in the national provision of playing-fields for the young; and he was at one time vice-chairman of the Empire Rheumatism Council.

Howitt mixed easily and well in many walks of life, and his mastership of the Society of Apothecaries was, partly for this reason, one of the most successful of recent years. Full of youthful energy, he was a great sportsman: fond of shooting, fishing, and golf, he excelled at lawn-tennis, in which he was of county class. His love of country life was illustrated by his keeping bees on the roof of his Harley Street house and he had the unusual distinction of winning a national award for honey from this source. As would be expected, he was a fine and discerning host.

He remained a bachelor until 1945 when he married Violet, daughter of Alfred Leverton. His wife ("Ann") and he had many interests in common, from physiotherapy to their hobbies. Together they rebuilt a charming old farm in the depths of Gloucestershire, where pigs and gardening happily occupied their spare time. When, a year ago, at the height of his career, his excellent health suddenly deteriorated, he faced the implications "with a fortitude which is beyond praise."

He died on May 14.

MABEL LIDA RAMSAY

M.D. Edin., F.R.C.S.E., M.R.C.O.G., D.P.H.

Dr. Mabel Ramsay, who died on May 9 at the age of 75, was the daughter of Paymaster-in-Chief Andrew J. Ramsay, R.N., and before starting to study medicine she trained for two years as a gymnast. Geographically, her education was distributed widely, between schools in Plymouth and London, Owens College, Manchester, the London School of Medicine for Women, and the University of Edinburgh where she graduated in medicine in 1906. She became a house-surgeon at the Glasgow Maternity Hospital, assistant medical officer of health for Huddersfield, and then senior house-surgeon at the Women's and Children's Hospital at Leeds. Having taken the D.P.H. in 1908, she settled at Plymouth, where she was the second woman doctor to work in the city and where she soon built up a large general practice.

In 1914 she joined a medical unit in Antwerp, where she narrowly escaped capture, and she then worked as surgeon in the Anglo-French Hospital, staffed only by women, which the Women's Imperial Service League established at Cherbourg in November, 1914. With Dr. Florence Stoney, she described the surgical experience of this hospital in the *British Medical Journal*¹ in 1915. On returning from the war she took the Edinburgh F.R.C.S. in 1921, being the third woman to do so, and she became gynaecologist to the Plymouth Infirmary. Soon she gained further appointments in her chosen specialty, obstetrics and gynaecology, at other institutions and hospitals in Plymouth and in Devon and Cornwall.

From early days a vigorous and formidable champion of women's rights, Dr. Ramsay took an active part in the women's suffrage movement and also in the Medical Women's Federation of which she was a founder member and at one time president. She regularly attended meetings of the Plymouth Medical Society, of which she was president in 1931, and made many contributions. She held downright views but always expressed them cheerfully.



Lafayette

1. Howitt, F., Wesson, A., *Lancet*, 1942, i, 373.

1. *Brit. med. J.* 1915, i, 966.

Although for many years towards the end of her life her health was precarious and her eyesight was poor, her energy and cheerfulness never failed. In 1950 she flew to America to attend a women's medical congress and she undertook an extensive tour which included the West Indies. It was with considerable relief to her hosts abroad and her friends in England that she made the return journey safely.

Such a record shows that Dr. Ramsay was endowed with vitality and enterprise far beyond the average. No-one who knew her could fail to admire the enthusiasm and sincerity which she brought to everything to which she turned her hand. She was generous and unstinting in helping all who sought her aid in any capacity, and she leaves a remarkable legacy of gratitude and affection. Her death, when it came, was sudden, and she died among her many friends of the Medical Women's Federation at their recent meeting at Sheffield.

ARTHUR AUGUSTUS MUSSEN B.A., M.D. Dubl., D.P.H.

Dr. A. A. Mussen, a former medical officer of health for the city and port of Liverpool, died on May 3 at the age of 84.

He was born in Antrim and he studied at Trinity College, Dublin, graduating in arts and medicine in 1892. Three years later he proceeded to the degree of M.D. He held resident posts at hospitals in Ireland and England before he began his public-health career as an assistant medical officer of health in Huddersfield. His experience there of the social conditions under which the very poor lived prepared him for the still tougher conditions which obtained in the Liverpool of 1900, the year in which he was appointed assistant M.O.H. in that city.

Mussen took up his post at a critical moment. Hitherto, public health had been largely concerned with sanitation; but by 1900 this task had been largely completed, and the medical officer of health, in an infinitely smaller way, was in a similar position to Alexander the Great—*aestuat infelix angusto limite mundi*. But new worlds were coming into sight. The first Midwives Act was passed in 1902, and Liverpool was one of the pioneers in maternity and child welfare in this country. Mussen played a large part in the development of these new services, and of the other personal health services—the medical inspection of school-children, the notification and treatment of tuberculosis, and the treatment of venereal diseases—which were established in rapid succession throughout the country during the first quarter of this century.

His work in the public-health department was interrupted by the war in 1914. He joined the R.A.M.C. and at first was attached to the Liverpool Merchants' Mobile Hospital, later serving as a specialist sanitary officer on the lines of communication. He retired at the end of the war with the rank of major.

When Prof. E. W. Hope retired in 1924, Mussen, who had been deputy medical officer of health since 1912, was chosen to succeed him. He had fully earned the senior appointment by first-class work which he had done in the department since 1900. He did not, however, seek the professorship of public health, and Hope continued in that appointment until 1931.

W. M. F. writes: "I met Dr. Mussen in 1921 when, for a short time, I was a junior medical officer in the Liverpool public-health department. At that period, accommodation in the municipal offices was excessively crowded, and Mussen, Hanna, and Stallybrass shared one small room. It was something of an ordeal to go to see Mussen in such circumstances, but the kind and friendly attitude which he always adopted to his juniors quickly dispelled any apprehension."

In his younger days Dr. Mussen was keenly interested in sport, especially in skating and climbing. He was a member of the Liverpool Racquets Club, the Liverpool Athenaeum, and the Liverpool Chess Club. For a time he was chairman of the Philharmonic Society and he became a vice-president of the Liverpool Medical Institution. The later years of his life were saddened by the loss of his only child. On his retirement in 1931, he and his wife went to live in Surrey, but during the last few years he had lived in Harrogate.

Dr. J. L. LOVIBOND

J. H. writes: "As one who knew Jock Lovibond from the time we were fellow dressers, may I add a few words to last week's obituary?"

"The first thing that impressed you on meeting him was his lean fitness of body and his gaiety of spirit. These two qualities endowed him with a prodigious capacity for work, and no queue of querulous old outpatients could damp his enthusiasm or dull his blithe good-humour. Even Saturday afternoon in the medical outpatients on a hot summer's day left him cheerful and undismayed, and, to a line of dreary candidates for a jab of N.A.B., he brought a smile of tolerance and understanding.

"In many ways Jock was a product of the old school, into whom duty and discipline had been rigorously inculcated over a long line of soldier forebears. The Army was in his blood, and in it he was destined to spend a large part of his all too precious leisure hours in peace-time and to serve with some distinction in war. To him it was perfectly natural that a man should serve his country in one of the Armed Forces; it was part of his heritage as an Englishman, and his career as a Territorial amply vindicated his ideal.

"He was really a countryman at heart and to the drab London scene he lent a certain air suggestive of Surtees. I think his great love was horses—not the race-meeting kind but the fell ponies that he rode over his beloved Northumbrian uplands or his hunter on whom he regularly rode to hounds and with whom he shared the supreme exhilaration of competing in many point-to-point races. For pure technique of riding, he certainly had few equals in our profession, and it was a pleasure to see the ease and certainty with which he would put a complete stranger through his paces.

"His trim and agile military figure, his impeccable clothes, his quizzical humour, and his invariable good spirits endeared him to porter and patient, student and chief. He was a great character and a lovable personality; and he died as he did everything else, without fuss, neatly and efficiently."

Births, Marriages, and Deaths

BIRTHS

BAKER.—On May 13, to Mr. T. A. C. Baker and Dr. Hazel Baker (née Hill) of Wednesbury, Staffs—a third son (Francis William).

HARRISON.—On May 11, to Mary (née Marryat), wife of Kent Harrison, F.R.C.S.—a son.

MARRIAGES

FLETCHER—ASTILL.—On April 22, at St. Andrew's Church, Aylestone, Leicester, Ronald Frank Fletcher, M.B., B.Sc., of Bromsgrove, to June Margaret Astill, M.B., of Leicester.

DEATHS

HARDCastle.—On May 17, Douglas Noël Hardcastle, M.R.C.S., D.P.M. Camb., F.B.F.S., of Bishop's Stortford, aged 62.

Appointments

BIRCH, E. W. G., M.B. Lond.: asst. M.O., Bradford.

BURGHELL, G. B., M.R.C.S., D.A.: whole-time asst. anaesthetist (S.H.M.O.), Leeds A and B groups.

HEDDEN, F. J., M.B. Wales, F.R.C.S.E.: part-time senior registrar to orthopaedic department, The Hospital for Sick Children, Great Ormond Street, W.C.1.

KNAPPE, W. T., M.D. Warsaw: asst. psychiatrist (S.H.M.O.), Hensol Castle Institution, Pontyclun, Glam.

MCLAUGHLIN, J. P., M.B. N.U.I., D.M.R.D.: radiologist, Limerick.

SEAMAN, JOAN, M.B. Lond.: asst. to the V.D. department (women), Royal Free Hospital, London.

SHAW, D. L., M.B. Leeds, F.R.C.S.: part-time consultant in general surgery, Pontefract and Goole.

SZAYNOK, WANDA, M.D. Lwow: asst. psychiatrist (S.H.M.O.), Morganwg Hospital, Bridgend, Glam.

TAGGART, J. MCA., M.B. Belfast, D.P.H., D.P.A.: deputy M.O.H., and deputy port M.O., Belfast.

Liverpool Regional Hospital Board:

DRIVER, A. A., M.D. Leeds, D.P.H.: deputy senior administrative M.O., Liverpool Regional Hospital Board.

JONES, H. P., M.B. Lond., F.R.C.S.: whole-time senior casualty officer, Birkenhead group of hospitals.

LANCELEY, FREDERICK, M.D. Lpool: whole-time asst. venereologist, Liverpool Royal Infirmary and Newsham General Hospital.

LAW, W. B., M.B. Queensland, M.C.H. (ORTH.): Lpool, F.R.C.S.: whole-time asst. orthopaedic surgeon, North Liverpool area.

MCCAREY, A. G., M.D. Glasg., D.M.R.D.: consultant radiologist, North Wirral and Birkenhead areas.

SHATWELL, G. L., M.B., M.C.H. (ORTH.): Lpool, F.R.C.S.: part-time consultant orthopaedic surgeon, Bootle Hospital.

SLOWIK, O. J., M.B. Polish School of Medicine, Edin., D.P.M.: whole-time asst. psychiatrist, Deva Hospital.

SMITH, C. J. C., M.B. Edin., F.R.C.S.E.: whole-time senior casualty officer, Warrington group of hospitals.

Notes and News

WORLD HEALTH ORGANISATION

Dr. Joseph N. Togba, director of public health and sanitation in Liberia, was unanimously elected president of the seventh World Health Assembly at Geneva on May 5. In his inaugural address Dr. Togba remarked that W.H.O. was the first worldwide organisation to elect a true African as its president; in W.H.O. the concept of democracy was being acted on without distinction of country, race, colour, or creed. Dr. Togba mentioned the financial obstacles preventing the Organisation from meeting many requests for help from member States. He also referred to the fact that no meeting of the committee for the Eastern Mediterranean region had been possible since 1950, and hoped that the assembly would solve this problem without creating political difficulties.

Mr. Milton P. Siegel, assistant director-general for administration and finance, told the committee on administration, finance, and legal matters that, after five full years of operation, the Organisation was in a sound administrative and financial position. In 1953 the shortage of technical-assistance funds had had a serious effect on planning and execution of health programmes; many projects agreed on with governments could not be carried out. Every effort should be made to avoid such situations in the future. Contributions from member governments to the regular budget had consistently improved since 1949 and, while not perfect, the present position was very good; 95% of the contributions due in 1953 had been collected.

The committee on programme and budget, after a long debate, recommended that the 1955 regular budget of W.H.O. be set at \$10,300,000—an increase of \$1,800,000 over the current budget of \$8½ million. This decision was taken by 28 votes to 25, with 11 abstentions. Mr. W. H. Boucher (United Kingdom) opposed it, saying that a sharp distinction should be drawn between projects undertaken from technical-assistance funds and those financed from the regular budget. He deplored any tendency to offset a shortfall in technical-assistance funds by an increase in the regular budget. This recommendation later came before the assembly, which fixed the regular budget at \$9½ million (*Times*, May 18). This is an increase of \$1 million; but the total includes \$950,000 of non-recurrent income and savings.

The Léon Bernard foundation prize for outstanding achievements in social medicine was awarded to Prof. Jacques Parisot, dean of the medical faculty of Nancy and chief delegate of France to the World Health Assembly. Dr. G. Robert Coatney, of the laboratory of tropical medicine, National Institutes of Health, Bethesda, and Prof. George Macdonald, director of the Ross Institute of Tropical Hygiene, were awarded medals and prizes from the Darling foundation for work in malaria.

The subject of the technical discussions at this year's assembly is Public-health Problems in Rural Areas; and these began on May 8, under the chairmanship of Prof. A. Stampar, of the Yugoslav Academy of Sciences and Arts, Zagreb. Professor Stampar said that 1300 million of the world's 2400 million inhabitants lived in rural areas and were engaged in agriculture. In rural communities there was relative lack of food, clothing, houses, and educational facilities. In some rural regions disease was so widespread as to be an important hindrance to economic development. There was shortage of medical aid in rural areas; Bombay had 1 doctor for 2218 people, whereas in the United Provinces there was 1 doctor for as many as 13,586; 70-75% of India's doctors seemed to be practising in the towns. The situation of the rural population was getting worse throughout the world. Prof. Fraser Brockington (Manchester) spoke on the development of health units in rural areas. He said that in the countries where economic and social conditions were most advanced much less care was given to the health of rural dwellers. In the U.S.A. 30 million people in rural areas were still not covered by local health services. Government action alone could help rural populations, and health services designed for the particular needs of each country should be decided on. Prof. K. F. Meyer (San Francisco) spoke on zoonoses in rural areas. In preventing and controlling these diseases the veterinarian was as necessary as the public-health engineer. Farmers tended to have a fatalistic or superstitious outlook on animal diseases; if they could be taught that their own prosperity and health depended largely on the action they took, the veterinarian would receive the attention due to his expert knowledge.

OUR CHANGING MENTAL HOSPITALS

METHODS of managing and treating chronic disturbed patients at Bexley Hospital were described at the meeting of the Royal Medico-Psychological Association on May 6 by Dr. L. C. Cook, the physician-superintendent. In 1938 the average daily total of inpatients was 2258. Some 1066 (47%) were recorded as unemployable. Quiet chronic patients were mainly employed in the utility departments, occupational therapy being available only to the select few. Of 40 wards, 13 male and 14 female were closed, 2 male and 5 female were open to the ward garden, and only 4 male and 2 female were open to the grounds. Only 155 male and 105 female patients were on grounds parole; there was no system of town parole, except for occasional day-passes; overnight passes were granted to 150 male patients but to no female patient. 186 patients were secluded for a total of 10,580 hours during the year. Casualties numbered 1749, of which 875 (50%) were due to patients fighting and 186 (11%) to self-inflicted injuries. In 1953-54, by contrast, the average daily inpatient total was 2244, and 1681 (75%) were employed. Of 38 wards, 3 male and 9 female were closed, 2 male and 3 female were open to the ward garden, and 10½ male and 10½ female were fully open. Average parole totals during 1953 were 278 males and 249 females on grounds parole, and 125 males and 179 females on town parole; overnight leave was granted to 260 male and 481 female patients, and during the year 5651 leave passes for one or more nights were issued. During the year 84 patients were secluded for a total of 352 hours. There were 1091 casualties, of which 474 (43%) were due to disturbed conduct. In the past few years, the policy had been pressed of giving more freedom and privileges, reducing sedation, and replacing it, where necessary, by electric convulsion therapy (E.C.T.). Continuous sedation produced far more serious deterioration than well-spaced maintenance E.C.T. or leucotomy, or both combined. Occupational and social facilities had been greatly increased, and the patients were now encouraged to run their own clubs, a magazine, discussion-groups, and other recreational activities.

Dr. J. S. McGregor, medical superintendent of Saxondale Hospital, Radcliffe-on-Trent, said that in 1946 a reconstruction subcommittee was formed at this hospital. The bed accommodation was increased from 732 to 1500. Improvement had been achieved without costly reconstruction. The wards had gradually been redecorated and re-equipped and new toilet annexes built. All padded rooms had been converted into siderooms. Other rooms had been converted into an operating-theatre and X-ray unit. In 1952 a prefabricated building was opened as a combined shop, canteen, and recreation-room; it was used by patients during the day and by staff in the evening as a licensed recreation room. Under-staffing still existed, but was less on the male side. The use of E.C.T. for disturbed patients was being reduced in the male wards, as nursing attention lessened the need for it. Of 10 male wards 7 were now open, and most of the hedges and railings around the buildings had been removed.

SPREADING THE MEDICAL LOAD

ON the initiative of the Oxford Regional Hospital Board a conference between general practitioners and hospital clinicians was held in Oxford last month, with members of the board and management committees attending. At a previous conference called by the regional board in 1952, representatives of all three branches of the service met for discussions.

Sir George Schuster, chairman of the board, referred to the present impossibility of large-scale building and asked whether the best use was being made of existing resources. The load in a region of comparatively low morbidity was increasing, until 1 in 7½ of the population was a new outpatient and 1 in 12 a new inpatient in 1953. Despite a relatively small increase in the number of staffed beds, the number of patients treated had increased enormously, as had the number of outpatients. The board would welcome constructive criticism as to how the load could be more evenly spread.

The general-practitioner viewpoint was put by Dr. F. A. Bevan, chairman of the Oxford Local Medical Committee, when he drew attention to the need for more general-practitioner beds, for clinical assistantships, and for access to X-ray and pathology departments. Complaint was made of long waiting periods for outpatient appointments, too long periods of aftercare by hospitals, and occasional difficulty in obtaining the admission to hospital of emergencies. Dr. Bevan suggested that general practitioners must be prepared to accept

the burden of more work and consultants must trust general practitioners more to look after cases.

Mr. Willoughby Cashell, chairman of the Reading Medical Advisory Committee, described the heavy load the hospital service was carrying and the difficulty in assessing the relative urgency of cases. The great increase in turnover had placed a great strain on hospital staffs. He thought maternity cases should be an integral part of the general-practitioner service, only abnormal cases being sent to hospital. He advocated more home-nursing facilities. This view was supported by other speakers, one of whom thought that more acute work would be welcomed by district nurses.

Better training of general practitioners, both in the use of the modern weapons now available to them and in psychosomatic medicine, were among points made in the discussion. A number of practitioners asked for open access to physiotherapy departments and the opportunity of prescribing domiciliary physiotherapy. Others feared that physiotherapy departments might become a dumping-ground. The suggestion was made that one physiotherapist might serve 12 to 15 general practitioners.

Dr. Stephen Taylor, summing up, praised the Oxford board for having provided access to X-ray and pathological departments and emphasised the need for the G.P. to be able to drop into the clinical laboratory to discuss his problems with the pathologist. He suggested that the Oxford region might treat itself as an experimental region, trying out new ideas and seeing how far the general practitioners, who were less heavily burdened than their colleagues in Lancashire and South Wales, might relieve the hospital service of some of its load. He commended the idea, which had received support in the discussion, that the district nurse should be closely allied with the G.P., and another suggestion that more opportunity should be given to the G.P. to do his own minor surgery. At present only half the total number of G.P.s undertook any minor surgery at all, but with a regular theatre session—perhaps fortnightly—skilled anaesthesia, and a consultant at the head of the department, much more work in the field could be undertaken by G.P.s.

On clinical assistantships Dr. Taylor thought that they should be paid, of short duration (say six months), and consequently available to a large number of practitioners. The benefit to the hospital service of close association between consultants and practitioners in this way would, in his view, make for easier admission of patients, encourage earlier discharge, and improve the standard of work in general practice. The practicability of clinical assistantships, however, depended a great deal on group practice.

The three particular ways of saving hospital accommodation were in connection with chronic sick, mental defectives, and mental-hospital patients. Much could be done, he thought, using day hospitals. This might mean a reorientation of certain aspects of the general practitioner's work.

REPORTS FROM RUSSIA

FOUR Russian doctors attended a meeting of the medical section of S.C.R. (the Society for Cultural Relations with the U.S.S.R.) held in London on May 14. Dr. Mary Barber presided and Dr. L. Crome interpreted.

Dr. S. V. Kurashov, who is clinical psychiatrist at the Moscow Postgraduate Medical Institute and also deputy minister of health, spoke on the prevention of mental illness. In the Soviet Union, he said, psychiatry has a less prominent part in medicine than it is given here—and he did not regret this. Such problems as delinquency, crime, and suicide lay within the province of the criminologist, and he would therefore confine his remarks to clinical psychiatry. In the past the interaction of man and his environment had been insufficiently considered. For normal development it was decisively important that a person should be able to realise his potentialities, especially through his work, and great improvement had come of abolishing unemployment and giving equality of status to women. In the U.S.S.R. the influence of art and the cinema was directed towards freeing the population from the noxious influence of war hysteria. Since all mental patients were registered with the district psychiatrists—who provided early treatment either in the home or at the neuro-psychiatric dispensary—it could be shown with confidence that mental disorders were diminishing, and he referred especially to decreases in manic-depressive psychosis, in addiction to alcohol and drugs, in schizophrenia, and in functional disorders. The psychiatric after-effects of the

second world war had been far more easily dealt with than those of the first. Answering questions, Dr. Kurashov said that in the U.S.S.R., as in this country, it is very difficult to secure enough nurses: every large mental hospital had its training-school, but there was nevertheless a shortage. Asked about certification, he replied that, in his approach to the patient, the Russian doctor is both physician and representative of the State, and the psychiatrist and practitioner acting together were in a position to use "light compulsion" with safeguards of appeal by the relatives. He went on to explain that, despite the influence of German psychiatrists, the views of Freud are not highly esteemed in the U.S.S.R.: without being dogmatic, he felt that the most promising line of advance in psychiatry is physiological, through the study of the higher nervous activity: the exaggeration of sexual factors and the unconscious mind was unworthy of the dignity of man.

Prof. L. K. Khotsyanov, discussing legal aspects of industrial medicine, pointed out that in England industrial medicine comes under the Ministry of Labour and the Home Office. A similar situation had prevailed in Russia till 1934, when industrial medicine was taken over by the ministry of health; and since then there had been rapid progress. For nearly 400 factors in industry—e.g., concentration of dust in the air, sulphur fumes, and temperature of the workshop—precise norms had been established; systematic inspection was undertaken, tests were made at some 300 laboratories, and action could be taken when the standards were not met. As probably in other countries, there were still not enough industrial medical officers in the Soviet Union, but this temporary lack was overcome to some extent by intensive instruction of the workers by the ministry of health and its local agencies the "houses of medical education." Answering a question on the prevalence of industrial diseases, Professor Khotsyanov spoke of decreases in brass-workers' fever and poisoning by tetra-ethyl lead: there were still a considerable number of cases of lead-poisoning, and this risk needed continuous watching. In the pottery industry, after long exposure to silica, tuberculosis sometimes developed, but he could not say which came first—silicosis or tuberculosis. Pyogenic infections were a problem in the mines, but a diminishing one. He regarded industrial smoke as harmful to the respiratory tract, especially in children: no correlation had yet been established between atmospheric pollution and cancer of the lung, but careful attention was being paid particularly to possibly dangerous products of the distillation of oils. Dr. Kurashov remarked that undoubtedly cancer of the lung is increasing, but he was doubtful about other forms of cancer. Statistics would become more accurate because under a new law every death must be followed by a post-mortem examination. Exceptions were made where the relatives objected, but these exceptions were mostly for old people.

Dr. I. K. Berkas, as tuberculosis specialist for a population of some 150,000, said that in the past few years she had not seen a case of tuberculous meningitis. B.C.G. vaccine was given at birth, and usually again at 2 and 7 years of age, after 4 years at school, and on leaving school. It was also given to adults who might be exposed to infection either as contacts or through working in medical institutions.

BELFAST INSTITUTE OF CLINICAL SCIENCE

THE Institute of Clinical Science in the Queen's University of Belfast was opened by Lord Wakehurst, Governor of Northern Ireland, on May 7. This institute, which comprises two new buildings, is the largest development in the university since its foundation in 1845. The west block houses two lecture-rooms, seating 282 and 221; the departments of therapeutics, obstetrics and gynaecology, child health, and social and preventive medicine; and laboratories and medical artist's and photographic studios. This block also contains the library, which in its main reading-room commemorates members of the staff and students who gave their lives in the second world war. Two rooms for special study and a staff common-room have been provided as memorials to medical graduates of the university. The east block contains the departments of medicine and surgery, and its third floor has been specially designed for research and experimental work, on the model of the Mayo Clinic. A covered-in bridge at first-floor level links the two blocks across the main hospital road. The architects have produced a pleasing exterior of russet brick and Portland stone. Interior wall surfaces are mainly finished in lemon and pale grey. In the library teak

and olive veneers have been used for panelling, and a frieze round the room displays six paintings of typical Northern Ireland scenes by Mr. Norman Wilkinson, P.R.I.

INJECTION OF ANTIBIOTICS

To illustrate their recommendations¹ for an improved technique for the injection of antibiotics, the Ministry of Health have just completed an excellent film, which is designed primarily for nurses. The film opens with a demonstration of the usual procedure for charging the syringe, giving the injection, and washing the syringe, but for the purpose of the film a fluorescent liquid is used in place of the antibiotic. In ultraviolet light this liquid glows brightly, and droplets contaminating the nurse's hands, arms, and face after the injection are readily seen. A sister and a doctor suffering from sensitivity dermatitis are shown, and the recommended technique, which avoids contamination, is demonstrated with the fluorescent fluid. Directed by Margaret Thomson, the film maintains the high standard of her earlier productions.² It is concise and explicit, and will be very helpful, not only to nurses, but to doctors and medical students. The film which runs for ten minutes, is available (on 35 mm. and 16 mm.) from the Central Film Library, Government Buildings, Bromyard Avenue, Acton, London, W.3.

AN INDIAN JUBILEE

The April issue of the *Antiseptic*³ is a special number celebrating the journal's fiftieth year of publication. It contains a foreword from Sir A. L. Mudaliar, vice-chancellor of Madras University, messages of congratulation from the medical press in many countries, and 58 original articles, in which experts in various branches of medicine review the progress made in their specialty during the half-century of the journal's life.

The *Antiseptic* was founded in May, 1904, by the late Dr. U. Rama Rau and the late Dr. T. M. Nair, and has been active in promoting reforms in public health, preventive medicine, and medical education and legislation. When Dr. Nair died in 1919, Dr. U. Rama Rau took over the editorship; in 1924 he was joined by his son Dr. U. Krishna Rau, now the proprietor; the present editor is his grandson Dr. U. Vasudeva Rau. The jubilee issue strengthens the hope that our semi-centenarian contemporary may play an increasingly important part in the sound development of medicine in India—a development on which so much and so many depend.

University of London

The title of professor of oral pathology in the university has been conferred on Dr. R. B. Lucas, in respect of his post at the Royal Dental Hospital of London School of Dental Surgery.

The title of professor of chemical pathology in the university has been conferred on Dr. F. T. G. Prunty in respect of his post at St. Thomas's Hospital Medical School.

The title of reader in chemical biophysics in the university has been conferred on Mr. R. A. Kekwick, D.Sc., in respect of his post at the Lister Institute of Preventive Medicine.

University of Leeds

At a congregation on May 14 the Princess Royal, chancellor of the university, conferred the degree of doctor of laws honoris causa on Prof. Evarts A. Graham and Sir Cecil Wakeley.

University of Edinburgh

At 5 p.m. on Monday, May 31, at 60, George Square, Edinburgh, Prof. Bruce Mayes (Sydney) will deliver a Macarthur postgraduate lecture on Experience in the Management of Pregnancy Toxæmia in Sydney. Dr. J. W. Clegg will also deliver a lecture in this series at 5 p.m., on Tuesday, June 1, at the University New Buildings, Teviot Place. He has chosen as his subject the Surgical Pathology of Pulmonary Tuberculosis.

Royal College of Physicians of London

Prof. E. B. Verney, F.R.S., will deliver the Bertram Louis Abrahams lecture at the college, Pall Mall East, S.W.1, on Thursday, July 8, at 5 p.m. He has chosen as his subject Renal Excretion of Water and Salt.

1. See *Lancet*, 1953, ii, 33.

2. *Ibid.* p. 624.

3. The *Antiseptic*, April, 1954. 323, Thambu Chatty Street, Madras, 1. 12s.

Royal College of Surgeons of Edinburgh

On May 11 the college, under the presidency of Prof. Walter Mercer, held a reception in honour of fellows of the American College of Surgeons attending meetings in Edinburgh. The following were admitted to honorary fellowship of the Royal college: Dr. Alfred Blalock, Dr. Evarts A. Graham, Dr. Henry W. Cave, and Dr. Frederick A. Collier. Dr. Frank Glenn, vice-president of the American college, admitted Professor Mercer to honorary fellowship of that college.

British Association of Urological Surgeons

The annual meeting of this association will be held this year at the Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin, from June 24 to 26. The proceedings are to include a discussion on Irradiation Therapy in Urology.

Institute of Neurology

At the National Hospital, Queen Square, London, W.C.1, a course of lectures on Cerebral Vascular Disorders is being given weekly at 5.30 p.m. on Tuesdays until July 20; and a course of lectures on Trauma is being given weekly at 5.30 p.m. on Thursdays until July 15.

Beit Fellowships for Medical Research

The following elections have been made to junior fellowships (£630 a year):

R. G. TUCKER, B.A., B.Sc., B.M. Oxf. To investigate the action of divalent metals on the multiplication of bacteriophage, at the Sir William Dunn School of Pathology, University of Oxford.

D. S. H. W. NICOL, M.A., M.B. Camb. To study the chemistry and pharmacology of peptide fractions of insulin, at the Dunn Institute of Biochemistry, University of Cambridge.

B. T. DONOVAN, B.Sc. Lond. To study the hypothalamic control of the secretions of anterior pituitary hormones, at the University of London Institute of Psychiatry, Maudsley Hospital.

Chesterfield Clinical Society

Proposing The Society at the annual dinner on May 11, Sir Terence Nugent spoke of entertaining aspects of his work as comptroller of the Lord Chamberlain's office. Judge J. B. Blagden and Sir Heneage Ogilvie responded to Mr. S. H. Wass's toast of The Guests. Judge Blagden contrasted the differing ways of man and of animals: whereas the lion roared at its prey, man gave voice postprandially in after-dinner speeches. Finally Mr. Victor Riddell was installed as president in succession to Dr. Nigel Loring.

A Travelling Bookshop

Messrs. John Wright & Sons, the Bristol publishers, have put on the road a mobile medical bookshop, which will visit hospitals in the West Country and in Wales. In this "bus," doctors and other members of the hospital staff will be able to see a selection of the latest books. The service is designed to be of particular help to those who cannot get to bookshops regularly and who have hitherto seldom been able to examine a book before they buy it. Last week the shop's tour included hospitals in Gloucester, Monmouth, Abergavenny, and Hereford.

Exhibitions in Turkey and Afghanistan

An exhibition on British medicine and nursing, arranged by the Turco-British Association and the British Council, was held in Ankara during March and in Istanbul during the second half of April. A large section of the exhibition commemorated the centenary of Florence Nightingale's work in the Crimea. More than 13,000 people saw the exhibition during its two weeks at Ankara University. The Florence Nightingale centenary was also commemorated in Afghanistan by a World Health Organisation exhibition in Kabul on April 7.

National Blood Transfusion Service

At a reception held at the Ministry of Health on May 10, Mr. Iain Macleod, the Minister of Health, remarked that when the National Blood Transfusion Service was established in 1946 the panel of donors had shrunk from the war-time peak of about a million to just over a quarter of a million. But at the end of 1953 the national panel had passed the half-million mark, with a strength of 515,000 donors; and last year blood donations totalled 660,000, which was only 9000 less than the total given in 1944 at the peak period of the war. Seventy times more blood was used in 1953 than before the war; and the aim now was to build up the national panel to at least 600,000 regular donors.

The Royal Tour

Surgeon-Commander D. D. Steele-Perkins, medical officer of the Royal Yacht *Britannia*, has been made a commander of the Royal Victorian Order.

The Friends of Vellore

Dr. Hilda Lazarus, who has lately retired from the directorship of the Christian Medical College and Hospital, Vellore, will address a meeting of this society at Caxton Hall, Westminster, on Thursday, May 27, at 7.30 P.M. Sir Samuel Runganadhan and Dr. Howard Somervell will also speak.

Committee of Inquiry on the Rehabilitation of Disabled Persons

The closing date for submitting written evidence to this committee is June 30. Memoranda should be addressed to the joint secretaries of the committee, Ministry of Labour and National Service, 32, St. James's Square, London, S.W.1.

Medical Auxiliaries

The Board of Registration of Medical Auxiliaries has issued a register of operating-theatre technicians, and revised editions of the register of chiropodists and of the register of orthopists. Copies are obtainable, without charge, by doctors who apply to the board, British Medical Association House, Tavistock Square, London, W.C.1.

Indian Medical Service Dinner Club

The annual dinner of the Indian Medical Service Dinner Club will be held at the Connaught Rooms, Great Queen Street, London, W.C.2, on Friday, June 18, at 7.30 P.M. Further particulars may be had from the secretary of the club, Medical Board Room, Commonwealth Relations Office, Matthew Parker Street, S.W.1.

International Society of Medical Hydrology

This society is holding a congress from Sept. 20 to 27 at Vichy, in Paris, and at Enghien. The programme includes discussions on the treatment of cardiac and of hepatovesicular pain, on the effect of hydromineral treatment on cholinesterase activity of the blood, and on the care of the injured in hydromineral spas. Further information can be had from Dr. Françon, 55, rue des Mathurins, Paris, 9.

Harvelian Society of London

This society's Buckston Browne-Gray Hill dinner was held on May 12. The Rt. Rev. Gerald Ellison, Bishop of Willesden, proposed the toast of The Society. Today, he said, was the birthday of Florence Nightingale, whose amazing achievements had been possible because she cared for her fellow beings. And this was a parable immediately relevant to the present day, when State influence was becoming greater and greater and personal responsibility less and less. Without personal responsibility, all our plans did no more than lay the foundations of decay and final collapse. In the past, there had been three people who had done a great deal to preserve this sense of personal concern: the parson, the family solicitor, and the family doctor. Today, it was on the medical profession that the responsibilities of the Welfare State were largely laid, so the doctors could do much to ensure that, in an age when the Welfare State was an established fact, we may preserve this intimate individual concern for one another. In his reply, Dr. R. Cove-Smith, president of the society, reported that improvements had been made to Hempstead Church, where Harvey is buried, and that the condition of the sarcophagus was now much better. Money raised by the society for the purpose of rehanging the church bells (a plan which in the end proved impracticable) had helped to make these changes. The society had established a prize of £25 at the Harvey Grammar School, Folkestone, to be awarded to a scholar who distinguished himself by some original work—a choice of which Harvey would have approved. Dr. D. G. H. Sylvester welcomed The Guests, for whom Mr. John Moncrieff, mayor of Folkestone, and Mr. Charles Hamblen-Thomas replied.

CORRIGENDUM: *Institute of Hospital Administrators.*—In our report of the institute's conference last week (p. 1038) we incorrectly referred to Lord Burden as president of the institute. This year's president is Mr. George Watts, secretary of the Oxford Regional Hospital Board.

Diary of the Week.**MAY 23 TO 29****Monday, 24th**

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, W.C.1

5.15 P.M. Prof. W. M. Frazer: The Industrial Era. (First of three Newsholme lectures on State Medicine in the Nineteenth Century.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. A. C. Dornhorst: Respiratory Function in Failure.

BRITISH ASSOCIATION OF SPORT AND MEDICINE
5 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Symposium on Athletic Injuries and their Treatment.

MANCHESTER MEDICAL SOCIETY
9 P.M. (Medical School, University of Manchester.) Section of General Practice. Dr. A. F. Dunn Carrie: First Impressions.

Tuesday, 25th

UNIVERSITY OF LONDON

5.30 P.M. (Senate House, W.C.1.) Air Marshal Sir Harold Whittingham: Medical Science and Problems of Flying. (First of two lectures.)

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE
5.15 P.M. Professor Frazer: The State and Medical Research. (Second of three Newsholme lectures.)

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2

5 P.M. Prof. G. Payling Wright: Recent Studies on Tetanus. INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2

5.30 P.M. Dr. F. R. Bettley: Eczema-asthma Syndrome.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY, Hammersmith Hospital, Ducane Road, W.12

3 P.M. Prof. J. Louw (Cape Town): Constriction Ring Dystocia

ROYAL SOCIETY OF ARTS, John Adam Street, W.C.2
5.15 P.M. Commonwealth Section. Sir Leonard Rogers, F.R.S.: Progress Towards Eradication of Leprosy from British Commonwealth.

ROYAL STATISTICAL SOCIETY

5.45 P.M. (Westminster Medical School.) Study Circle on Medical Statistics. This House Welcomes the Growing Influence of Statistics in All Branches of Medicine. For: Dr. R. J. Asher. Against: Mr. R. S. Murley.

Wednesday, 26th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2

3.45 P.M. Dr. D. R. Haynes: Relations of Facial Nerve in Temporal Bone. (Arnott demonstration.)

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE
5.15 P.M. Professor Frazer: State Hospital Policy. (Last of three Newsholme lectures.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON

2 P.M. Dr. A. Thackray: Pathological Conditions in Salivary Glands.

INSTITUTE OF DERMATOLOGY

5.30 P.M. Miss B. M. Partridge: Diagnosis of Ringworm Infections.

EUGENICS SOCIETY

5.30 P.M. (Burlington House, Piccadilly, W.1.) Lord Simon: Aspects of World Population and Food Resources.

Thursday, 27th

UNIVERSITY OF LONDON

5.30 P.M. Sir Harold Whittingham: Air Transport of Sick and Wounded. (Second of two lectures.)

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. J. O. Oliver: Inflammation.

ROYAL SOCIETY, Burlington House, Piccadilly, W.1

4.30 P.M. Sir Howard Florey, F.R.S.: Mucins and Protection of the Body. (Croonian lecture.)

HONYMAN GILLESPIE LECTURE

5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. Ralston Paterson: Some Radio-sensitive Tumours.

UNIVERSITY OF ST. ANDREWS

5 P.M. (Medical School, Small's Wynd, Dundee.) Dr. J. E. Caughey (Dunedin): Treatment of Acute Poliomyelitis.

Friday, 28th

UNIVERSITY OF LONDON

5.30 P.M. (University College, Gower Street, W.C.1.) Prof. B. R. Fisher (Wisconsin): Study of the "Projection" of Attitudes Towards Social Groups.

POSTGRADUATE MEDICAL SCHOOL OF LONDON

2 P.M. Prof. G. A. G. Mitchell: Innervation of Blood-vessels.

4 P.M. Dr. I. C. Gilliland: Diabetic Complications and Allied Disorders.

GUY'S HOSPITAL MEDICAL SCHOOL, London Bridge, S.E.1

5 P.M. Prof. G. Stead: Making Sound Visible. (Fison lecture.)

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2

5 P.M. Sir William Gilliat: Minor Disturbances of Pregnancy.

INSTITUTE OF DERMATOLOGY

5.30 P.M. Dr. P. J. Hare: Necrobiosis Lipoidica and Granuloma Annulare.

INSTITUTE OF LARYNGOLOGY AND OTOLGY, 330, Gray's Inn Road, W.C.1

3.30 P.M. Mr. Wallace Black: Ulcers of Mouth and Pharynx.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

11 A.M. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Professor Louw: Eclampsia.

Saturday, 29th

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

11 A.M. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Professor Louw: Eclampsia.

AORTIC STENOSIS DIAGNOSIS AND TREATMENT

ANDREW LOGAN

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RICHARD TURNER

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THE success of valvulotomy for mitral stenosis and for pulmonary stenosis is established. Bailey (1954) has reported a considerable series of patients successfully operated on for aortic stenosis. We are reporting our early results in the surgical treatment of aortic stenosis because initial experience in severe cases has been encouraging. Although aortic stenosis is far less common than mitral stenosis, there must be many who are severely disabled and in urgent need of relief from what is fundamentally a mechanical defect.

The left ventricle has a remarkable capacity for compensatory hypertrophy, and patients with aortic stenosis may remain for many years free from symptoms related to the heart. It is well known that the degree of left ventricular hypertrophy which results from aortic stenosis is greater than that from any other cause (cor bovinum). Marked aortic stenosis is, however, a serious condition, and once symptoms have appeared it usually pursues a steadily progressive course to death from cardiac failure within a year or two.

Medical treatment is of little avail. For a time cardiac failure may respond to customary measures, but, since sinus rhythm is usually maintained, digitalis is less effective than in mitral stenosis with auricular fibrillation. Restriction of physical activity is necessary and is often self-imposed because of the discomfort produced by exertion, but it does little to slow the progression.

The principal symptoms are breathlessness on exertion and later at rest, with episodes of paroxysmal dyspnoea, angina pectoris, and syncope.

The physical signs of aortic stenosis are sometimes overlooked because attention is focused on a loud systolic murmur at the apex, and, as has been increasingly appreciated of late, not all the classical signs of aortic stenosis are necessarily present in any particular case. Nevertheless, attention to detail with regard to each sign and a summation of the evidence should lead to an accurate clinical diagnosis in most cases. A useful review of the signs of aortic stenosis, together with an analysis of personal experience, was published by Lewes in 1951. A brief summary of our own views, based on a comparison of clinical and post-mortem findings over a period of some years, and on the present series is given in this paper.

Symptoms

Dyspnoea.—Breathlessness may be attributed to the pulmonary congestion which results from obstruction at the aortic valve. Other factors which may operate in the later stages of cardiac failure need not be discussed here. Paroxysmal dyspnoea on exertion may result from temporary inability of the left ventricle to increase its cardiac output adequately, with consequent increase in pulmonary congestion. Attacks during sleep or at rest may be precipitated by emotion or by the normal increase in venous return in the horizontal posture, the reabsorption into the circulation of oedema fluid which has accumulated during the day, and the decreased sensitivity of the respiratory centre during sleep which allows a build-up of the normal stimuli.

Angina Pectoris.—Angina of effort is presumably due to coronary insufficiency resulting from the lowered

cardiac output, and possibly in part to the fact that the hypertrophied muscle of the left ventricle needs a blood-supply greater than normal. Angina cannot be explained on the basis of coronary atheroma which may be only slight in this condition. Angina at rest may be induced by tachycardia—e.g., with emotion—but sometimes the immediate cause of the pain is not obvious.

Syncope.—Syncope on effort is common in patients with severe aortic stenosis and may occur also at rest. Various suggested mechanisms include Adams-Stokes attacks from heart-block, ventricular arrest or ventricular tachycardia, cerebral atheroma, and hypersensitivity of the carotid-sinus reflex. A more probable explanation for the syncopal attacks is cerebral anoxia from a reduction in cardiac output such as is responsible for angina pectoris. There have been a number of papers on this subject, and the evidence was reviewed by Hammarsten in 1951. Minor manifestations of cerebral anoxia include mental confusion and giddiness. Attacks may be preceded by angina or followed by convulsions. Sudden death is not unusual in patients with severe aortic stenosis.

Signs

Left Ventricular Hypertrophy.—The apical impulse may be displaced to the left and is characteristically heaving, but considerable hypertrophy may exist with relatively little increase in heart size (fig. 1). In one patient in this series palpation was made difficult by emphysema.

Thrill.—The presence of a thrill is not essential to the diagnosis of aortic stenosis, but an aortic systolic thrill is usually palpable if the examination is made with the patient sitting up, leaning forward and with the breath held in expiration. The thrill may be palpable over the carotid arteries also.

Pulse.—A slow rising "plateau" pulse of small volume is characteristic of aortic stenosis but is by no means always present and is not necessary for diagnosis. In the presence of aortic incompetence the pulse may be of full volume despite severe stenosis.

Murmurs.—A loud, harsh systolic murmur is usually heard best near the right border of the upper part of the sternum and conducted into the carotid arteries. A similar murmur can often be heard at the apex and occasionally it is loudest in this position. The murmur is maximal in mid-systole. Sometimes the murmur is faint and can be detected only if the examination is made with the patient in the same position as that recommended for palpation.

An early diastolic murmur from aortic regurgitation is commonly present. It is usually best heard at the left sternal border and is sometimes audible at the apex. A loud aortic diastolic murmur may accompany severe stenosis.

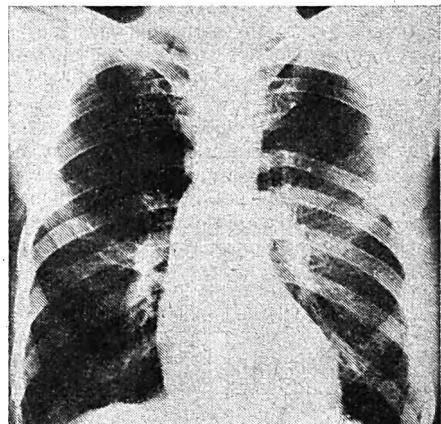


Fig. 1 (case 1)—Postero-anterior radiograph showing heart of almost normal size although the electrocardiogram showed left ventricular hypertrophy.

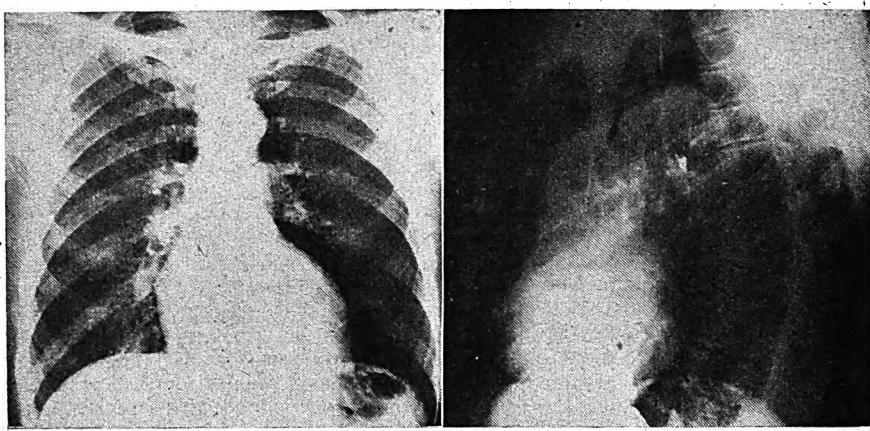


Fig. 2 (case 3)—Radiographs showing moderate enlargement of left ventricle and dilatation of the first part of the ascending aorta : (a) postero-anterior ; (b) left anterior oblique.

Heart Sounds.—The first heart sound at the apex may be obscured by the loud, harsh murmur. The aortic second sound at the base is often diminished in intensity or absent but may be unchanged. A presystolic triple rhythm is uncommon but may occur.

Blood-pressure.—The systolic blood-pressure may be reduced by aortic stenosis, and the diastolic pressure may be reduced by aortic incompetence or increased by concomitant systemic hypertension. Hence the pulse pressure may be low, normal, or somewhat increased.

Direct Arterial Pressures.—Direct arterial pressures from the brachial or femoral artery have been recorded but have not, so far, proved of additional value.

Cardiac Rhythm.—Sinus rhythm is usual but not invariable in isolated aortic valvular disease. In one of our patients paroxysmal auricular fibrillation had occurred before operation.

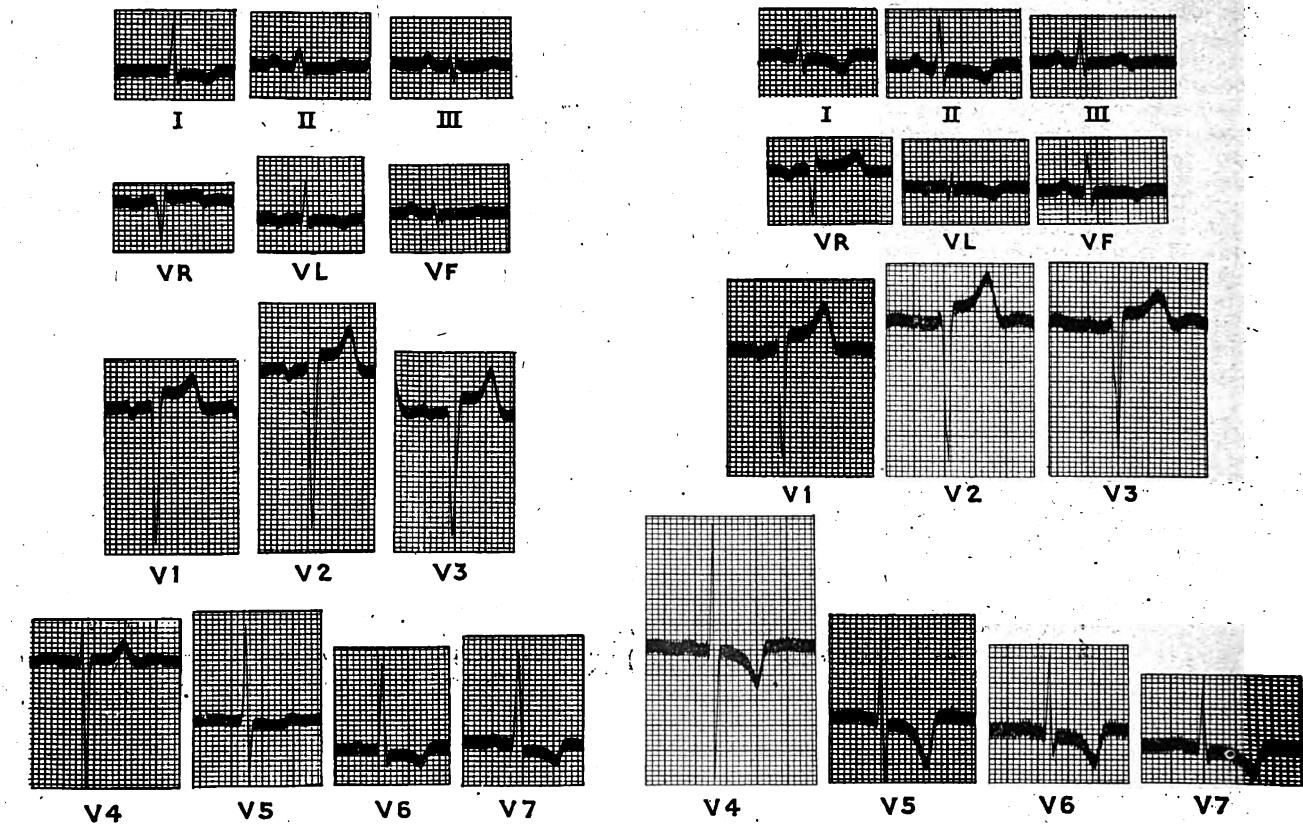


Fig. 3 (case 3)—Electrocardiograms showing increase in signs of left ventricular hypertrophy.

Radiology.—Reference has already been made to the fact that considerable left ventricular hypertrophy may exist with little cardiac enlargement (fig. 1). However, left ventricular enlargement is usually obvious radiologically and may be considerable (fig. 2). Rounding of the left ventricular contour in the postero-anterior and left anterior oblique views is the earliest radiological sign. If deliberately sought, calcification of the aortic valve leaflets can usually be seen on radioscopy in the left anterior oblique position.

Dilatation of the first part of the ascending aorta is common (fig. 1).

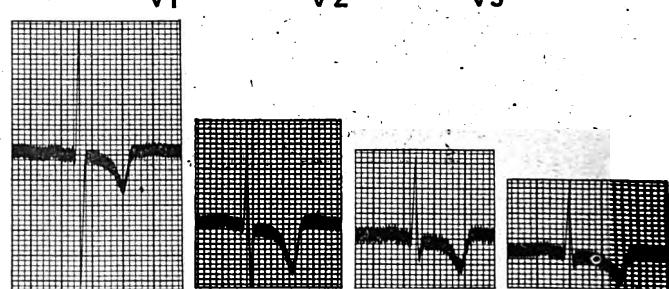
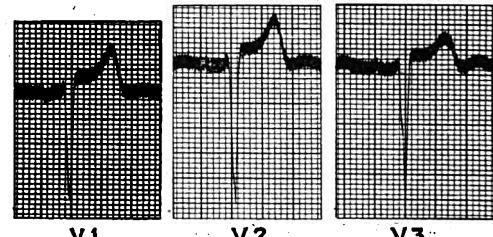
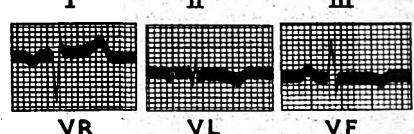
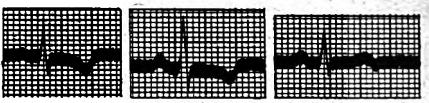
Electrocardiography.—If full

series of precordial leads are recorded, electrocardiographic signs of progressive left ventricular hypertrophy will always be present in cases of the severity under consideration (fig. 3).

Phonocardiography.—That the systolic murmur of aortic stenosis, in contrast with that of mitral incompetence, is maximal in mid-systole was first pointed out by Leathem (1951), and phonocardiography in our cases has confirmed this observation (fig. 4).

Operation

After induction of general anaesthesia with sodium thiopentone and cyclopropane, the patient was placed in the right lateral position and a standard left thoracotomy was made through the bed of the resected 5th rib. The pericardium was opened from apex to base of the heart, 1 cm. anterior and parallel to the phrenic nerve.



The surface of the heart and great vessels was examined for thrills, and the region of the aortic valve was palpated for calcification. An incision 1 cm. long was made in the anterior wall of the left ventricle close to the interventricular septum as indicated by the larger branches of the anterior interventricular artery, and 5 cm. below the atrioventricular sulcus. Bleeding from the incision was controlled with two opposed mattress sutures and by digital pressure. While the origin of the aorta was held between the fingers and thumb of the left hand, a curved sound was introduced into the ventricle and guided upwards and backwards along the interventricular septum into the aorta. With the sound the state of the aortic valve was again examined and the valvular orifice was located. The sound was withdrawn and an expanding dilator was passed (fig. 5) and widely opened in two planes at the level of the aortic valve. Because of the risk of detachment of fragments—especially calcareous fragments—of the aortic cusps, and consequent embolism, during this manipulation the common carotid arteries in the neck were occluded by digital pressure. The opening of the dilator was accompanied by a sensation of tearing or breaking. To avoid entanglement in the chordæ tendineæ the dilator was closed before withdrawal from the aorta. The dilator used in the first



Fig. 4.—The systolic murmur of aortic stenosis is maximal in mid-systole.

instance was a heavy forceps angled at the pivot and with a 10-cm. blade. Because of the divergence of the blades, it proved difficult to hold the forceps so that the widest gap between the blades was at the level of the valve. In the others an expanding dilator with parallel blades similar to that designed by R. C. Brock (1950) for pulmonary valvulotomy, but larger (4 cm. spread), was used. The ventricular wall was repaired with fine silk sutures and the surface of the heart was re-examined for thrills. The edges of the pericardial incision were loosely approximated and the chest wall was closed with pleural drainage.

The Cases

Case 1.—A.B., aged 54, had never had rheumatic fever.

History.—For 20 years he had observed slight dyspnoea on exertion, but this had not seriously inconvenienced him in his work as an engineer. For 18 months he had felt unduly tired. 15 months previously he had first experienced, on exertion, constricting retrosternal pain which forced him to stop, whereupon the pain ceased in about 3 minutes. The pain sometimes extended down the left arm. It never came on during rest or lasted longer than 10 minutes but recently had been induced by less and less effort so that it severely limited his exercise. For the past year he had had severe attacks of dyspnoea which would awaken him at night and oblige him to sit for $\frac{1}{2}$ –2 hours on the edge of the bed. He had no sputum. He had dizzy turns, when he was unable to stand but did not lose consciousness. His ankles were swollen towards the end of the day. He had lost 1 stone in weight in 6 months.

He was admitted to hospital for left ventricular failure with bilateral pleural effusion. He responded well to rest, digitalis, and mercurial diuretics and was assessed with a view to operation.

Clinical Examination.—General condition fair; radial pulse of low volume and tension; no abnormal arterial pulsations; blood-pressure 95/65 mm. Hg; slightly heaving apical impulse; no thrill; loud, long, harsh systolic murmur maximal in the aortic area, well heard in the neck, over the sternum, and at the apex; soft blowing early

diastolic murmur of aortic incompetence best heard at the left sternal border; aortic second sound not audible; no signs of mitral valvular disease; no abnormal signs in lungs; Wassermann reaction negative.

Radioscopy.—Slight enlargement of left ventricle; extensive calcification of the aortic cusps.

Electrocardiography.—Well-developed left ventricular hypertrophy.

Operation and its Effects.—He was considered to have a severe progressive disability and was advised to undergo aortic valvulotomy. At operation the surface of the left ventricle was unusually vascular and the ventricular action seemed laboured. There was a rough systolic thrill in the intrapericardial part of the aorta. The calcified valve was readily palpated with the finger through the aortic wall and with the sound in the ventricle. After rupture of the valve the ventricular action was apparently easier. There was no alteration in the aortic thrill.

Since operation nearly a year ago he has not experienced dyspnoea on exertion, angina, dizzy turns, or swelling of the ankles and has gained weight. He can climb three flights of

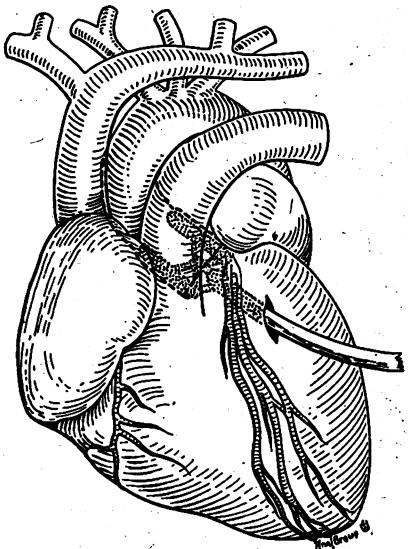


Fig. 5.—Diagram to show the relation of the ventricular incision to the leash of vessels indicating the width of the interventricular septum. Dilator passed through the left ventricular wall and into the aorta.

SUMMARY OF THE CASES

Case no.	Age (yr.)	Sex	Rheumatic fever	Atrial fibrillation	Angina	Syncope	Paroxysmal dyspnoea	Congestive failure	Blood-pressure	Cardiothoracic ratio	Calification aortic valve	Electrocardiogram	Mitral disease
1	54	M	0	0	+	+	+	+	95-100 65-80	45	+	LVH	0
2	50	M	+	0	+	+	0	+	130-150	57	+	LVH	0
3	56	M	0	0	0	0	0	+	80-110 120-125	40	+	LVH	0
4	37	M	0	P	+	0	0	+	110-120 60-80	57	0	LVH	0
5	49	F	+	+	0	0	+	+	140-150	67	0	LVH	+
6	32	F	+	0	0	0	0	0	90-95 100 80	60	0	RVH	+
7	43	M	+	0	0	0	0	0	120-125 55-60	60	+	LVH	+
8	44	F	+	+	+	0	+	+	150-160	70	0	LVH	+
9	52	M	0	0	+	+	0	0	90-100 150-160 100-105	50	+	LVH	0

LVH = Left ventricular hypertrophy.
RVH = Right " "
P = Paroxysmal."

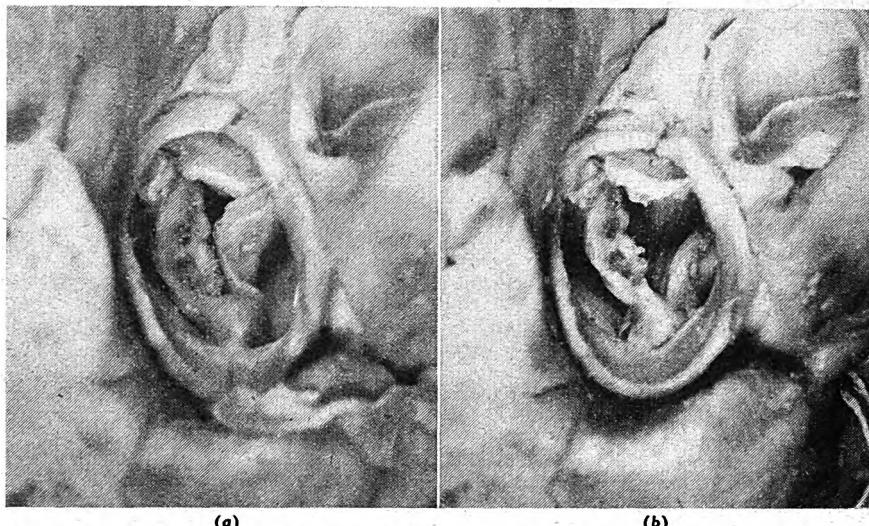


Fig. 6 (case 5)—Post-mortem specimen. Aortic valve after valvulotomy: (a) closed; (b) open.

stairs with ease. The physical signs are unchanged. 2 months after discharge he returned to work as an engineer.

When it appeared that the first patient had done well and improvement had been maintained for 6 months, other patients who had been kept under observation were reviewed and eight were subjected to aortic valvulotomy. One died. Although it is too soon to assess long-term results we believe that the early results warrant the consideration of surgical treatment in all patients with symptoms arising from aortic stenosis.

The main features of all nine cases are shown in the accompanying table. The case of the early postoperative death follows:

Case 5.—C.D. was a woman of 49.

History.—At the age of 16 years she had rheumatic fever. In 1942 she began to have progressive dyspnoea on exertion and during the next 12 years was frequently admitted to hospital with recurrent congestive cardiac failure. In 1949 she was known to have auricular fibrillation. In June, 1953, pulmonary infarction occurred and at that time ligation of the inferior vena cava was considered on account of intractable cardiac failure and the distress of constant orthopnoea. She had no angina or syncopal attacks.

Clinical Examination.—Deep cyanosis; poor peripheral circulation; pulse of varying volume from auricular fibrillation; blood-pressure 150–140/95–90 mm. Hg recorded over 4 years; strong heaving left ventricular impulse; systolic thrill in aortic area; harsh systolic murmur audible over the

precordium but maximal in the aortic area and well heard over the carotid arteries in the neck; faint, early diastolic murmur of aortic incompetence; intermittently at the apex a short rumbling mid-diastolic murmur, attributed to mitral stenosis; systolic murmur at the apex indistinguishable from that in the aortic area.

Radioscopy.—Gross cardiac enlargement due mainly to enlargement of the left ventricle; deep, low backward curve of barium-filled oesophagus in right anterior oblique view, probably secondary to enlarged left ventricle; aorta of normal size, slightly more pulsatile than normal and calcified; no calcification seen in aortic or mitral cusps.

Electrocardiography.—Pattern of severe left ventricular hypertrophy.

Operation and its Effects.—We recognised that operation on this patient would carry great risk, but her wretched state and the chance of some relief appeared to justify

it. Accordingly surgical treatment was advised.

The heart's action was unaffected by the intracardiac manipulation. From the cardiac point of view her post-operative condition was satisfactory; but for some obscure reason, possibly cerebral anoxia, she was disorientated and never fully co-operative. Her heart-rate was well controlled with digitalis and no sign of pulmonary congestion or cardiac failure appeared. She had, however, tenacious infected sputum which she could not expectorate properly and which necessitated repeated bronchoscopy aspiration. The pulmonary condition was thought to be aggravating her anoxia. Her general condition deteriorated and she died on the 5th post-operative day. Necropsy showed a heart enlarged by left ventricular hypertrophy. The commissures of the stenotic aortic valve had been widely opened. There was no calcification of the valve (fig. 6). The cusps of the mitral valve were sclerotic with mild stenosis.

Rheumatic mitral and aortic valvular disease are often combined, and when stenosis of both valves is sufficiently severe to warrant an attempt at surgical correction there is no *a-priori* reason why these two defects should not be treated at the same thoracotomy. In our first patient with this combination of valvular defects the decision to treat the mitral stenosis was taken before we had begun to treat aortic stenosis surgically.

Case 6.—E.F. was a woman of 32.

History.—At the age of 10 she had rheumatic fever. She

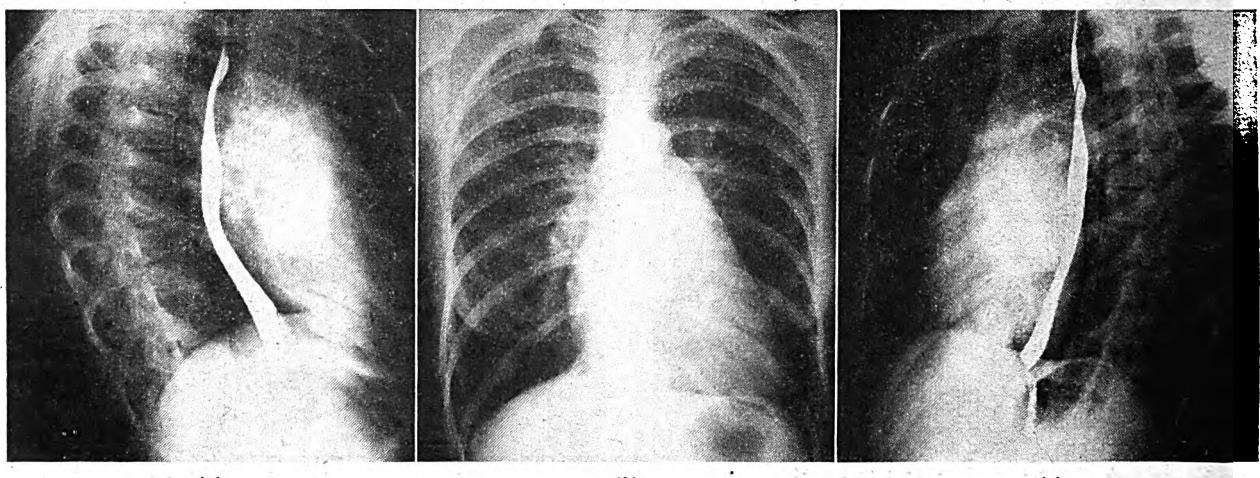


Fig. 7 (case 6)—Radiograph of patient with severe aortic and mitral stenosis showing enlargement of pulmonary artery and of left atrium and auricle. (a) Right anterior oblique (b) postero-anterior (c) left anterior oblique.

remained well until 19 when she first noticed dyspnoea on exertion. This was slowly progressive. With her third pregnancy at the age of 28, she became very breathless and was admitted to hospital and kept in bed from the 3rd month. She had a normal delivery. During the next year dyspnoea increased more rapidly and in addition she was inconvenienced by fatigue. Thereafter cough and palpitation became troublesome. When first seen in May, 1953, she was severely disabled by breathlessness on waking even on the level and with excitement. She had never had pulmonary oedema, haemoptysis, or congestive failure.

Clinical Examination.—General condition fair; thin and cyanosed; pulse regular and of very small volume; blood-pressure 100/80 mm. Hg; right ventricular heave but no left ventricular heave; aortic systolic thrill; loud, harsh systolic murmur maximal in the aortic area and also audible at the apex and over the carotid arteries; aortic second sound barely audible; faint aortic diastolic murmur; pulmonary second sound markedly accentuated; first heart sound accentuated at the apex; presystolic murmur; rumbling mid-diastolic murmur; clear opening snap. Wassermann reaction negative.

Radioscopy.—Slight general enlargement in postero-anterior view; aorta of normal size; pulmonary artery markedly enlarged; left atrium and auricle slightly enlarged; right-sided enlargement in left anterior oblique view but no definite left ventricular enlargement; no calcification of mitral or aortic cusps seen (fig. 7).

Electrocardiography.—Sinus rhythm; right ventricular hypertrophy.

Cardiac Catheterisation.—Resting mean pulmonary arterial pressure 65 mm. Hg; resting mean pulmonary capillary-venous pressure 44 mm. Hg; no exercise undertaken.

Operation and its Effects.—It was considered that she had severe aortic stenosis in addition to mitral stenosis, but, in view of the severe degree of pulmonary hypertension and right ventricular hypertrophy, most of her disability was attributed to mitral stenosis. She had in fact tight mitral stenosis and the commissures were divided with striking improvement in her exercise tolerance. 9 months later the signs of severe aortic stenosis noted before operation were unchanged. The pulse pressure had not increased (blood-pressure 100/80 mm. Hg). The electrocardiographic signs of right ventricular hypertrophy had regressed. Cardiac catheterisation was repeated and it was found that the mean pulmonary arterial pressure had fallen from 65 mm. Hg to 24 mm. and the pulmonary capillary-venous pressure from 44 mm. Hg to 22 mm. The aortic valve was found to be tightly stenosed and was satisfactorily divided.

In the next two cases of combined aortic and mitral stenosis both valvulotomies were performed at the same thoracotomy. The aortic valve was divided first.

In case 7 it was necessary to estimate the relative importance of four valvular defects. Physical signs of aortic stenosis and incompetence and of mitral stenosis and incompetence were present.

Case 7.—G.H. was a man of 43.

History.—He had had rheumatic fever 25 years before, and gave a history of undue dyspnoea on exertion for 5 years with rapid progression for 9 months. His disability was considerable but he had not experienced paroxysmal dyspnoea, angina, syncope, or cardiac failure.

Clinical Examination.—Radial pulse of full volume; blood-pressure varying from 120–125 to 55–60 mm. Hg; normal left ventricular impulse; harsh aortic systolic murmur and thrill conducted into the neck; long blowing early diastolic murmur at the left sternal border; aortic second sound not heard; first heart sound at the apex slightly accentuated; no opening snap; apical systolic murmur of different quality from that of the aortic systolic murmur; distinct rumbling mid-diastolic murmur.

Radioscopy.—Heart much enlarged in the postero-anterior view (cardiothoracic ratio = 60%), and all four chambers contributing to this; aorta of normal size with slightly excessive pulsation; gross calcification of aortic valve but none of mitral valve.

Electrocardiography.—Sinus rhythm; left ventricular hypertrophy.

Cardiac Catheterisation.—Pulmonary arterial pressure 60/28 (mean 45) mm. Hg, rising on exercise to 78 mm. (mean); capillary-venous pressure = 34 mm. Hg (mean).

Systemic Arterial Pressures.—Right brachial pressure 100/55 mm. Hg; right femoral pressure 125/60 mm.

Operation.—It was concluded that stenosis was the predominant defect in both the aortic and the mitral valve. First aortic valvulotomy was performed. The narrow calcareous orifice was widely opened. Mitral valvulotomy was then carried out. The valve was exceptionally rigid and the orifice, through which there was some regurgitation, just admitted the terminal phalanx of the index finger. The anterior commissure was completely divided.

It will be appreciated from this case that preoperative assessment may not be easy. This is a common problem and the most logical procedure in such instances would probably be to explore the mitral valve first and then to record simultaneous aortic and left ventricular pressures, a significant fall in pressure across the aortic valve being an indication to proceed to aortic valvulotomy.

Discussion

The treatment of aortic stenosis by valvulotomy is palliative; the cusps remain rigid and deformed and the myocardium is damaged; stenosis may recur. The operation carries a risk of death, of embolism, and of aortic regurgitation. Nevertheless it is clear that in advanced cases valvulotomy may alleviate symptoms to an extent not achieved by medical treatment. It is evident that our patients have undergone operation too late to derive maximum benefit. The decision to advise operation should not await the appearance of severe symptoms, and it may be that patients with uncomplicated aortic stenosis who are asymptomatic but have evidence of increasing left ventricular hypertrophy should be subjected to valvulotomy.

Summary and Conclusions

The symptoms and clinical signs and the radiographic, electrocardiographic, and phonocardiographic features of aortic stenosis are reviewed.

The diagnosis is often missed because even severe stenosis may exist in the absence of some of the classical signs.

Nine severely disabled patients were subjected to aortic valvulotomy. The operative procedure is described. One patient died. Eight are improved.

When mitral and aortic stenosis coexist both valvular defects may be treated at the same thoracotomy.

Aortic valvulotomy may offer material relief to severely disabled patients who can no longer respond to medical treatment, and surgical treatment should be advised before severe symptoms are manifest.

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"The prime requirement of an industrial democracy is that the work itself should be worthy of the dignity of a human being. Whether the product of work is useful, for example, making a drain, or socially desirable, for example, filling milk bottles; or even beautiful, for example, building a bridge, matters not. The incentive for doing the work, often very laudable, for example, keeping a widowed mother, is unimportant. What matters is the content of work. Is the work itself, neither for its product nor incentive, worth doing? Work must be its own incentive. . . Men can be conditioned to meaningless work, and judgments are there in humanistic terms of inter-personal relationships. The tragedy is that men, women and children should be content with so little. The perpetual chase of happiness to which they are condemned is self defeating. Problems of industrial organization and of productivity arise only because joy is no longer in work."—Prof. T. A. LLOYD DAVIES, F.R.C.P., in *Mental Health and Human Relations in Industry*, edited by Dr. T. M. LING, London, 1954; p. 202.

HYPOTENSIVE ACTION OF RESERPIN

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INDIAN pharmacologists have ascribed a hypotensive action to preparations of *Rauwolfia serpentina* (Bhatia 1942, Vakil 1949, Chakravarty et al. 1951). The plant has been used for treating arterial hypertension. In the United States Wilkins and Judson (1953) have reported a moderate hypotensive and symptomatically beneficial effect from rauwolfia preparations. Swiss workers have described the hypotensive activity of a pure rauwolfia alkaloid, reserpine ('Serpasil'), in laboratory animals (Müller et al. 1952, Bein et al. 1953) and its action in cases of high blood-pressure (Löffler et al. 1953). Löffler et al. (1953), in an investigation of 51 patients with high blood-pressure, found a rise of blood-pressure in 6 and no significant fall in 27. In 14 patients there developed a clear fall of blood-pressure which persisted only twelve days despite continued medication. In 4 patients a fall of blood-pressure was induced which lasted until their discharge from the clinic. Subjective improvement was noted in 16 cases. The dose used by these workers was usually 0·75-1·5 mg. of reserpine daily. It seemed that with these doses substantial hypotensive activity was infrequent.

Side-effects were comparatively slight with 1·5 mg. a day. Where the dose exceeded 1·5 mg., these workers found no improvement in the hypotensive activity, but 18 of 28 patients had side-effects: 17 experienced a striking degree of fatigue, 11 were depressed, 2 had a state of mental excitability, 8 had painful heavy feelings in the muscles of the four limbs, 5 had flickering in front of the eyes without objective findings, 2 had bradycardia, 1 had dryness of the mucosae, and 1 had mild miosis.

Wilkins and Judson (1953), using 'Serpina,' a preparation manufactured by the Himalaya Drug Company, of Bombay, got the general impression that it was a mild hypotensive agent working better in patients with labile hypertension and often ineffective in severe cases.

Patients with labile hypertension are particularly liable to exhibit falls of blood-pressure with placebos or with sedatives, and the difficulty in recognising the presence of more specific drug actions is increased when only moderate hypotensive activity is shown.

The object of the present investigation was to decide whether reserpine acts as a placebo or a sedative or exerts a definitive action on the blood-pressure. Also it was desired to investigate the claim that the hypotensive action only emerges after several days' administration. For these purposes it was decided to attempt to administer much larger doses of reserpine than have been recommended by most workers. 20 patients were studied.

Effects of Single Doses

The dose of reserpine usually recommended is 0·75-1·5 mg. daily. To study the effect of single doses we have used 2 or 3 mg. of reserpine by mouth not less than half an hour before a meal. It is evident that most patients with hypertension exhibit significant falls of blood-pressure when given such large doses of reserpine. The trough of the fall has, as an average, occurred about five hours after oral administration. In 6 of 9 patients, after single doses of reserpine, the systolic blood-pressure was reduced by 40 mm. Hg and the diastolic by 20 mm. Hg or more. The significance of this observation is sustained

by the larger falls of blood-pressure which were noted after repeated administration.

Effects of Repeated Large Doses

When 2 or 3 mg. of reserpine is given thrice daily, the blood-pressure usually falls on the first or the second day. In 4 patients the falls of blood-pressure were small and such as we have often observed during the administration of placebos. Systolic falls of more than 40 mm. Hg occurred in 16 patients, and of more than 60 mm. Hg in 12 patients out of the 20 tested. Diastolic falls of more than 25 mm. Hg occurred in 17 patients, and of more than 45 mm. Hg in 7 patients out of the 20.

The blood-pressure attained after the administration of reserpine at the trough of the fall were sometimes normal and occasionally subnormal. Evidently under certain conditions and in some patients the hypotensive activity of reserpine is potent; and, if adequate doses are administered, this alkaloid need not be relegated to the category of substances which only reduce the blood-pressure in labile hypertensives (see accompanying table). It will be seen that the lowest blood-pressure recorded was in most cases well below the basal blood-pressure, and well below anything ordinarily observed in similar patients with placebos.

In almost all instances the fall of blood-pressure was preceded by gross flushing, which gave ancillary evidence of a distinctive effect on the vascular system.

The large doses used—3 mg. thrice daily—produce, in most patients, other side-effects, such as conspicuous conjunctival injection, nasal blockage, sensations of fatigue and sleepiness, depression, shivering, and, occasionally, restlessness. Most patients, as well as flushing, experienced a distinctive sensation of heat within one or two hours after the administration of reserpine.

Usually after the administration of reserpine changes of posture had little effect on the blood-pressure; but occasionally, when the blood-pressure fell to a normal or subnormal level, a little postural hypotension was evident, though postural changes of blood-pressure were not of the magnitude observed after the administration of methonium compounds.

When, after the blood-pressure has been much reduced by reserpine, the drug is discontinued, a significant fall in blood-pressure often persists for twelve and sometimes for twenty-four hours. In our experience, however, significant falls of blood-pressure do not persist for a week or more; but our experiments do not enable us to comment on the suggestion (Wilkins and Judson 1953) that a mild hypotensive activity may last so long.

The prolonged action of reserpine, the absence of substantial postural hypotension, and the fact that

EFFECT OF REPEATED DOSES OF RESERPINE ON BLOOD-PRESSURE
(MM. HG)

Case no.	Total daily dose (mg.)	Casual B.P. before reserpine	Basal B.P. before reserpine	Lowest casual B.P. after reserpine	Maximum B.P. fall	Average daily casual B.P. after reserpine
114	8	204/108	194/110	188/102	16/6	200/110
183	5	208/120	156/96	164/90	44/30	185/108
194	5	260/160	250/164	140/98	120/62	180/105
269	9	230/142	188/116	168/98	62/44	200/118
277	9	198/118	174/114	164/78	34/40	188/100
288	4	204/130	128/96	110/78	94/52	160/100
293	9	232/124	178/100	138/76	94/48	148/90
363	4	170/110	136/94	118/68	52/42	130/80
376	9	214/118	200/122	184/98	30/20	210/118
729	9	238/118	194/108	188/90	50/20	210/110
733	3	192/118	138/88	130/86	62/32	152/88
755	9	198/126	168/120	112/88	86/38	150/90
765	5	182/110	176/114	120/172	42/38	140/88
766	3	214/138	166/116	102/58	112/80	115/62
767	9	228/130	166/14	166/92	62/38	190/118
768	9	206/128	156/98	112/66	94/62	130/75
770	6	196/124	160/106	130/90	66/34	150/98
771	9	254/140	158/114	130/80	124/60	140/82
772	9	230/140	164/120	92/64	138/76	135/90
778	4	204/138	174/114	170/118	34/20	190/120

dosage with reserpine need not be so critical as dosage with methonium compounds, would combine to make reserpine extremely useful were it possible to produce adequate falls of blood-pressure without important side-effects. This, however, we have failed to do in most patients with reserpine alone. Almost all our patients stated that, comparing effective falls of blood-pressure obtained with oral reserpine with those produced by injections of hexamethonium or of M. & B. 2050A, they were much more comfortable on the methonium compounds and preferred them even by injection.

It should be made quite clear that the last statement refers only to doses of reserpine that produced falls of blood-pressure to near normal levels or, failing this, as low as side-effects would permit. In 8 of 20 patients, despite high dosage with side-effects, the falls of blood-pressure were not comparable with those obtained after the administration of hexamethonium.

In our experience the small doses (0.75-1.5 mg.) usually recommended have not, by themselves, induced falls of blood-pressure which we regard as satisfactory for the treatment of high blood-pressure. A dosage of 3 mg. daily, or sometimes even as much as 3 mg. thrice daily, occasionally did not produce falls of pressure which could be distinguished readily from effects due to placebos or to sedatives. It should be pointed out here, however, that we are not accepting falls of 30-40 mm. Hg systolic and of 15-20 mm. diastolic as necessarily significant. By other methods of testing it may well be possible to demonstrate (and in fact it seems likely) that modest falls of blood-pressure may be obtained with smaller doses than we have used.

The extent to which reserpine may be used in combination with other substances, such as veratrum alkaloids and 1-hydrazinophthalazine, has not been tested by us in any detail.

In several patients we have noted that, when reserpine is administered in addition to either hexamethonium or M. & B. 2050A ('Ansolyse'), an additive effect is obtained. In 5 of these patients (A. E. Doyle, E. G. McQueen, and F. H. Smirk, unpublished) the combination appeared to be of practical value in that, with fewer side-effects, the blood-pressure was held at lower levels with less fluctuation.

Summary

Large doses (2-3 mg. thrice daily) of reserpine sometimes produce striking falls of blood-pressure, at times to normal levels, which start from four to six hours after oral administration and may persist to a significant degree for more than twelve hours after withdrawal of the drug. Postural hypotension is unusual.

Such large doses are unsuitable for routine treatment and should not be used, because they usually produce pronounced side-effects.

Striking falls of blood-pressure to well below the basal blood-pressure may occur in severe hypertensives whose basal blood-pressure are high.

The side-effects from overdosage which may be observed are flushing, nasal and conjunctival congestion, sleepiness, depression, mental excitement, dizziness, nausea, vomiting, and diarrhoea.

Usually the side-effects and the hypotensive action are equally mild with the doses ordinarily advocated (0.75-1.5 mg. daily); but occasionally fully satisfactory falls of blood-pressure are observed on reserpine alone.

In some patients an additive effect can be obtained when reserpine (3 mg. daily or less) and certain methonium salts are administered together.

We are indebted to Ciba Limited, Basle, for generous supplies of 'Serpasil.' The expenses of the research were defrayed in part by the Life Insurance Medical Research Fund of Australia and New Zealand.

References at foot of next column

ARTERIAL HYPERTENSION TREATED WITH RAUWOLFIA SERPENTINA AND VERATRUM VIRIDE

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RECOGNITION of the lethality of systemic arterial hypertension has been somewhat tardy, in part because of the undue significance accorded the systolic level and in part because prognosis has been largely based on the relatively benign course in the elderly. Furthermore, the uræmic termination in the young has in the past focused attention on the kidney (Volhard and Fahr 1914) rather than the diastolic level of blood-pressure. Leishman (1953), from the observation of 151 hypertensives, aged less than 60, over periods of two and a half to five years, recorded a death-rate of 51 (34%) and in men alone 44%. Mortality was highest where the diastolic level was above 130 mm. Hg and where galloprhythm, left ventricular strain, considerable albuminuria, and retinopathy were present. With such findings treatment is imperative, and, no matter what is the aetiology, simple lowering of the diastolic pressure is attended by dramatic improvement.

It has been our practice to treat such cases with hexamethonium subcutaneously, as suggested by Smirk (1953), and now rarely to advise lumbodorsal sympathectomy. But in the less severe hypertension with cerebral or cardiac symptoms, particularly in men, and in slowly progressive hypertension of the young or middle-aged a less drastic therapy is desirable. No measure currently available has been uniformly satisfactory. The difficulties and vexations of prolonged sodium restriction, the narrow margin between toxic and therapeutic levels with veratrum, the tachycardia and increased cardiac output with 1-hydrazinophthalazine, the acquired tolerance to dihydrogenated ergot, the ileus from hexamethonium, and, above all, the vagaries of intestinal absorption have too often blighted early therapeutic promise.

Consequently the reported action of an alkaloidal extract of an Indian shrub, *Rauwolfia serpentina*, as lowering the blood-pressure of 50% of patients on oral administration and without objectionable side-effects (Ford et al. 1953, Vida 1952, Arnold and Bock 1953) is of particular interest. Relative hypotension might take two weeks to develop and might persist for a time after the withdrawal of the drug. This slowly developing hypotension reported with rauwolfa raises the interesting possibility of a hormonal mechanism analogous to the depression of the adrenal cortex by thiocyanate (Davis et al. 1950, Bernstein et al. 1951). Additional effects were bradycardia and remarkable emotional calm.

Ford and Moyer (1953) have noted the additive or synergistic action of hexamethonium with 'Rauwiloid.' Wilkins (1953) also emphasises the additive properties of rauwolfa with other hypotensive drugs. The present

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TABLE I—STATISTICAL COMPARISON OF MEAN PULSE-RATES AND SYSTOLIC AND DIASTOLIC PRESSURES (MM. HG) IN 10 PATIENTS RECEIVING VERILOID (1 MG. PER 10 LB. BODY-WEIGHT) FOR EIGHT WEEKS, AND THEN VERILOID PLUS *Rauwolfia serpentina* (0.5 G. NOCTE) FOR A FURTHER EIGHT WEEKS

	Case 1			Case 2			Case 3			Case 4			Case 5			Case 6			Case 7			Case 8			Case 9			Case 10		
	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D
R ₁ ..	67	187	117	86	206	124	69	184	119	34	214	136	71	185	130	75	245	140	80	182	117	82	195	95	81	184	133	92	214	154
S.D. ¹ ..	3.8	9.4	1.9	11.4	6.2	4.7	5.2	10.2	2.5	4.7	8.5	2.5	4.5	8.7	8.1	1.8	20.3	4.0	6.8	2.9	9.5	4.2	23.4	4.0	2.5	9.4	5.0	5.2	15.9	7.4
R ₂ ..	59	187	117	77	210	119	56	171	109	77	227	141	66	176	129	67	229	129	68	166	107	64	173	81	73	136	88	68	166	120
S.D. ² ..	4.1	6.4	5.0	4.4	8.1	2.4	4.2	4.7	2.4	4.1	2.9	4.7	5.0	18.7	16.4	5.9	20.0	6.3	1.0	5.0	3.4	6.5	14.8	8.6	6.1	8.6	17.4	11.4	23.5	14.2
R ₁ -R ₂ ..	8	0	0	9	-4	5	13	13	10	7	-13	-5	5	9	1	8	16	11	12	16	10	18	22	14	8	48	45	24	48	34
S.E.D. ..	2.8	5.7	2.7	6.1	5.1	2.6	3.3	5.6	1.7	3.6	1.9	2.1	3.3	10.3	9.1	3.1	14.4	3.7	3.4	2.8	5.1	3.9	13.8	4.7	3.3	6.4	9	6.2	14.1	8

D, diastolic blood-pressure. P, pulse-rate. R₁, mean value of weeks 5-8. R₂, mean value of weeks 13-16. S, systolic blood-pressure.

observations are on a combination of a preparation of *Rauwolfia serpentina** with *Veratrum viride* ('Veriloid'**).

Method

Certain general considerations apply to the clinical trial of a therapeutic substance—namely, that only one variable should be studied; that observations should be multiple and made under constant conditions; that neither observer nor patient should know whether an active or similar but inert preparation is being administered; and that an identical control group should be simultaneously studied, or else the patient should be used as his own control.

With these premises we have studied 24 hospital outpatients, the criterion of selection being a chronically raised diastolic blood-pressure. All these patients underwent the usual preliminary clinical studies, including fluoroscopy, cardiography, chemical examination of urine and blood, and intravenous pyelography. The group consisted of 9 men and 15 women, aged 32-66, with a mean of 48. Aetiologically the hypertension was in 22 instances "essential" and in 2 associated with chronic renal failure.

All the patients were given veriloid 1 mg. per 10 lb. body-weight in three divided doses daily for a preliminary fortnight and throughout the trial. For eight weeks 12 patients (group A) received dummy tablets resembling those containing the preparation of *Rauwolfia serpentina*, and then for the next eight weeks the active substance 0.5 g. nightly. The remaining 12 patients (group B) were given the preparation of *Rauwolfia serpentina* 0.5 g. each night for eight weeks and 1 g. nightly for a further eight weeks. The cases were allocated to one or other group at random. In both groups a third period of eight weeks similar to the first was planned, but in view of the results obtained this was

not pursued. Throughout this period no other drugs or treatment were given.

Weekly observations of blood-pressure and pulse-rate after the patient had rested for five minutes, were made by the same observer (R. K.) without knowledge of the treatment received. Thus it was hoped that such variables as admission to hospital, rest in bed, dietary change, and alteration in sleeping habits were avoided and observer error reduced. We emphasise particularly that no sedatives or other drugs were given. That the readings of blood-pressure and pulse-rate so obtained were representative for the patient was deduced by comparing the readings obtained before treatment was started with those obtained at previous attendances as outpatients.

Results

Of the 24 selected patients 1 died from malignant hypertension with uræmia and 2 were admitted to hospital with left ventricular failure. 1 defaulted before the observations were complete, and 2 others were discovered to be obtaining drugs from other sources; their results are therefore not reported. 1 other patient's readings proved so quickly and widely variable as to be quite unreliable and he was withdrawn from the trial; yet another developed such severe pruritus that eventually the administration of *Rauwolfia serpentina* had to be stopped. The results presented in tables I and II apply to the remaining 16 patients.

Table I shows the mean values of pulse-rate and systolic and diastolic pressure obtained from 10 patients in the second four weeks of the control period (weeks 5-8) and treatment period (weeks 13-16). The second half of each interval was chosen because of the reported delay in the action of rauwolfia. It is seen that a significant ($p = 0.0125$) slowing of the pulse-rate is shown by 6 patients (cases 1, 3, 6, 7, 8, and 10) but that the order of change in all the cases is small and the slowest

* Supplied by Riker Laboratories Inc.

TABLE II—STATISTICAL COMPARISON OF MEAN PULSE-RATES AND SYSTOLIC AND DIASTOLIC PRESSURES (MM. HG) IN 6 PATIENTS RECEIVING VERILOID (1 MG. PER 10 LB. BODY-WEIGHT) AND *Rauwolfia serpentina* (0.5 G. NOCTE) FOR EIGHT WEEKS, AND THEN 1 G. NOCTE FOR A FURTHER EIGHT WEEKS

	Case 11			Case 12			Case 13			Case 14			Case 15			Case 16					
	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D	P	S	D
R ₃ ..	55	195	125	58	230	125	64	215	120	63	181	122	59	161	101	71	255	130			
S.D. ³ ..	3.8	8.2	2.9	6.3	12.0	4.0	1.6	11.5	7.4	10.2	12.4	2.6	8.9	8.5	2.5	2.9	30.9	4.0			
R ₄ ..	54	171	108	58	225	126	61	226	119	54	180	117	61	152	99	77	276	135			
S.D. ⁴ ..	4.0	13.1	2.9	4.2	10.8	9.4	2.3	16.9	7.5	5.1	15.7	6.4	7.3	13.2	2.5	2.0	24.1	15.7			
R ₃ -R ₄ ..	1	24	17	0	5	-1	3	-11	1	9	1	5	-2	9	2	-6	-21	-5			
S.E.D. ..	2.7	7.7	2.2	3.7	8.1	5.1	1.4	10.2	5.3	5.7	10	3.4	5.7	7.8	1.7	1.7	19.6	8.2			

D, diastolic blood-pressure. P, pulse-rate. R₃, mean value of weeks 13-16. R₄, mean value of weeks 21-24. S, systolic blood-pressure.

mean pulse-rate observed is 56. Changes of a similar order of significance are seen in the diastolic levels in 5 of these patients (cases 3, 6, 8, 9, and 10), but in only 3 patients (cases 8, 9, and 10) does it appear large enough to have significance clinically. There is concurrent lowering of the systolic level. Judged by "mean blood-pressure" cases 9 and 10 show a definite hypotensive effect. In 1 patient (case 4) the average diastolic pressure rose during the treatment period.

In table II the effects of increasing the dose of the preparation of *Rauwolfia serpentina* in 6 patients (group B) are shown. There is no significant slowing of the pulse-rate. In 1 patient (case 11) the diastolic blood-pressure is lowered ($p = 0.0125$).

An attempt was made in each case to decide clinically whether or not the active substance was being given. The observer (R. K.) did not know the total of the control group. The result was quite inconclusive. Certainly no particular tranquillity was noted.

Discussion

Our object was to assess the additive or synergistic effect of *Rauwolfia serpentina* and not its single action. The results so obtained refer only to the present small group of patients, and generalisation is unjustifiable; yet this group represents the main problem in treatment, the severe or moderately severe and, in most cases, progressive hypertension with symptoms, in which effective oral therapy is particularly desirable. The severity of the hypertension in the present series is indicated by the death of 1 patient and the occurrence of left ventricular failure in 2 others during the observation period. Perhaps in milder cases results would have been better.

From the results in group B (table II) it seems that there is little point in increasing the dose of the preparation of *Rauwolfia serpentina* above 0.5 g. daily; in no case was a striking fall in diastolic pressure so induced, although a statistically significant fall was seen in case 11. We emphasise, however, that results which are statistically significant, although they represent real pharmacological effects, do not necessarily imply clinical significance in terms of change in prognosis. Examination of table I (group A) with this in mind shows statistically significant lowering of diastolic pressure in 5 patients, in 3 of whom (cases 8, 9, and 10) it was judged of sufficient degree to matter clinically. A similarly significant degree of bradycardia was demonstrated in 6 cases, but in no case did it seem large enough materially to alter the outcome. But there is no doubt from these results that a mild pharmacological action leading to bradycardia and lowering of the diastolic pressure additional to that from veratrum does result in certain hypertensive patients from the concurrent administration of the preparation of *Rauwolfia serpentina*. No measurements of cardiac output or of peripheral blood-flow were made during the treatment, and no certain conclusions about the mechanism of the fall in blood-pressure can be drawn. Because the changes are seen chiefly in the diastolic pressure, decreased peripheral resistance appears likely.

No serious toxic effects were seen in these patients with the cited dosages. 2 patients in group B developed pruritus with urticaria, and in 1 it was sufficient to cause withdrawal of the drug. Nasal stuffiness in excess of that commonly met with was not often seen.

Conclusions

The preparation of *Rauwolfia serpentina* used in a dosage of 0.5 g. daily induced bradycardia and lowered the diastolic blood-pressure in certain hypertensive patients already under treatment with *Veratrum viride*. There was no evidence of a striking additive or synergistic action. Postural hypotension did not occur.

Summary

A clinical trial of *Rauwolfia serpentina* in 24 severely hypertensive patients under treatment with *Veratrum viride* is reported. 8 were withdrawn before the end of the trial.

Bradycardia was shown in 6 of the remaining patients. Lowered diastolic pressures were demonstrated in 6. 2 patients developed pruritus, which was severe in 1.

With this combination of drugs there was no clear additive or synergistic action.

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THE PULMONARY ALVEOLAR MUCOID FILM AND THE PNEUMONOCYTES

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Does a thin watery mucoid film provide a surface for the air spaces of the lung? Since all exposed areas of the endodermal tracts, alimentary and respiratory, are covered by a layer of mucus, it might be argued, a priori, that such a film, though of submicroscopic thickness (Frey-Wyssling 1953a) and in a much modified aqueous state, should overlie the attenuated epithelium (Low 1952, 1953) of the lung alveoli. At the 19th International Physiological Congress at Montreal on Sept. 4, 1953, I suggested that the interface between alveolar air and lung tissue is indeed of such a nature, and that it is formed from a hydrated secretion of the granular pneumonocytes. This was an elaboration of a view presented to the Royal Society of Canada some years ago (Macklin 1946).

The pneumonocytes are the characteristic cells of the lung, and are assumed to be of endodermal origin. They have also been called niche cells, septal cells, epicytes, alveolar epithelial cells, &c. The list is a long one, and it is high time that we had a suitable term for universal adoption. All the current names have drawbacks. The vague designation "alveolar cells" (Bertalanffy and Leblond 1953) has least to commend it, for there are many kinds of alveoli and they may contain many kinds of cells. "Pneumonocyte," a translation into Greek of the French term "la cellule pulmonaire" (Bratianni and Guerrero 1930) has all the advantages and none of the disadvantages. It is already recognised (Cowdry 1952). The subdivision of pneumonocytes into three varieties—granular, phagocytic, and membranous—is in accord with their morphology and physiology. It is understood that the granular type has no ingesta. Some of the phagocytic type have surviving granules, and some have lipid droplets. The membranous type is respiratory, and in its flattened form is the "nucleated squame" of the older pneumonologists. Low's electron micrographs have shown its attenuations clearly and convincingly. To me the subdivision into the miscegenations "vacuolated" and "unvacuolated" (Bertalanffy and Leblond 1953) has no virtue and many insubcurities.

Exocrinosity

The granular pneumonocytes have long been regarded as externally secreting cells. For instance, in cat lungs which had been, while fresh, washed internally with weak silver-nitrate solution (Macklin 1938b), I found that the air-surfaces of these cells were stippled with many fine golden-brown particles, while the large areas round them, on which no cells were visible, showed a scattering of these granules, having the same affinity for silver, which had apparently come from the pneumonocytes. This finding moved me to write: "It may be that it [the granular pneumonocyte] contributes something to the circumscribing fluid film of the alveolar capillary wall which is advantageous in external respiration" (Macklin 1946). von Hayek (1953, fig. 143) illustrates granular pneumonocytes with droplets on the air-surface which, he suggests, have emerged from these cells. Such a secretion is presumably derived from the granules of the pneumonocytes, which seem to be minute sacs of fluid that may be supravitally stained with toluidine-blue and other dyes, and, while fresh, show a brightly glowing periphery and a weakly luminous centre when viewed between crossed Nicol prisms. A study showed that the developing osmophil granules arise in the pneumonocytes amid clusters of cytoplasmic fluid pools; and, as the granules enlarge, the pools about them merge into a larger space or vacuoloid (Macklin 1953c). In newborn kittens hordes of such granules, apparently a surplus from the pneumonocytes, may be recovered in washouts from the respiratory tract.

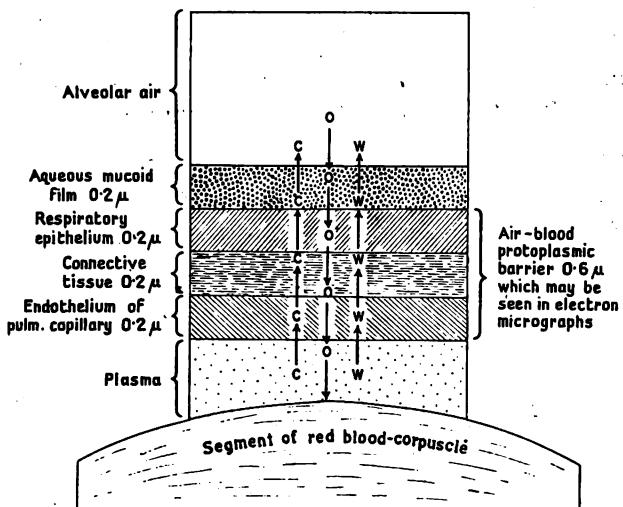
Argument

I have seen no direct evidence of material forming a smear over the alveolar wall as it emerges from the granular pneumonocyte, such as we see in the smear of mucus which has arisen from the mucin granules of the mucus-secreting cells of the bronchi or intestine. Many hints, however, point to the existence of an aqueous mucoid film clinging to the alveolar wall (see figure), and

to the granular pneumonocytes as its source. Terry (1926) reported that there was clear free fluid on living alveolar walls of cats and other animals. I have recently studied frozen sections of fresh mouse lungs mounted in physiological saline solution or in serum, often containing a dye, with conventional illumination and phase contrast, and have seen on the respiratory surface a thin line which marks the interface between air and alveolar wall tissue. The underlying substance often appears irregularly swollen, so throwing the surface film into sharp relief. The airface of the dog's alveolar wall is stained brilliantly blue by the modification of the method of Hale (1946) reported by Rinehart and Abul-Haj (1951), and the mucus overlying the bronchial epithelium in the same sections is similarly coloured by prussian-blue. This finding suggests that both have an affinity for colloidal iron and are acid mucopolysaccharides, and seems to justify the use of the term "mucoid" for the surface layer. The underlying collagen is definitely red. The fact that the mucoid layer can be seen at all when so stained, with the light microscope, implies an optical domination of the thin air-blood layer by the stained surface film. Perhaps Leblond and Bertalanffy (1951), in what they called the "surface reticulin membrane" on the alveolar wall of the rat lung, were really dealing, at least in part, with the mucoid layer. I have seen nothing by phase-contrast microscopy or by any other means in mouse or any other lungs that corresponds to their "internal reticulin membrane" connecting the two mural surface layers. They used P.A.S.-Hotchkiss staining. Leblond (1950) emphasised the outstanding ability of this staining combination to demonstrate mucopolysaccharides in secretions. Ham (1953) admits that a membrane of extracellular material may constitute the actual alveolar surface. If such a mucoid layer does not appear as a distinct entity in the usual electron micrographs, it is possibly because it does not throw an electron "shadow" or has become shrunken and blended with the underlying tissue, since it must consist predominantly of water, or because it has been dissolved away in the technical operations.

It ill becomes any worker in histological science to spurn aids to visibility in studying tissues, no matter how humble and unprepossessing, and perhaps formalin pigment, which to pathologists is a nuisance, will to histologists in some instances actually be a blessing. Thus I have deliberately invited the deposition of this material in the tissues of mice and cats.

Sjöstrand and Sjöstrand (1938) showed that dark-brown bodies appeared in granular pneumonocytes while they were being treated with an extract of blood and strong acid formalin (F.B.E.). I have used the Sjöstrand methods (Macklin 1953a) and feel that these crystalline aggregates are analogous to, if not identical with, the aforementioned formalin pigment or precipitate of the histologists and pathologists. Though the bodies are typically large and round, I found many small particles, often irregular in form. I shall provisionally call these bodies formalin-blood substance (F.B.S.). When they are dissolved by a saturated solution of picric acid in absolute alcohol they leave no vestige in the cytoplasm, and the last traces as they disappear are fine brown particles. The most interesting point is that they show a striking predilection for the cytoplasm of granular pneumonocytes (Macklin 1953b), appearing precociously in these cells, which then stand out so prominently that they give a striking impression of their density in the lungs, while showing hardly anywhere else in the early stages of the formalin-blood treatment. This propensity of certain loci in the cytoplasm of granular pneumonocytes to become resting-places for these bodies may indicate the presence in it of an enzyme or a catalyst, as the Sjöstrands suggested, which causes deposition of the crystalline pigment. It cannot be a random precipitation, at least



Ideal panel through effective air-blood intermediary complex of pulmonary alveolar wall showing its lamination and relationships with contiguous alveolar air and blood.

This complex is represented as consisting of a protoplasmic barrier with (from within outwards) endothelial, connective tissue, and epithelial strata reconstructed from electron micrographs of Low (1952, 1953), overlaid by an aqueous mucoid film. The various layers are arbitrarily drawn at a thickness of 0.2μ each, giving the total thickness of the complex as 0.8μ . The magnification is about 27,000 diameters. To convey an idea of relative sizes a small arc of the circumference of a red blood-cell at about the same enlargement is shown. Pathways of molecules of oxygen, carbon dioxide, and water are indicated by the arrows and letters O, C, and W respectively.

in the lung tissue as a whole in these early stages; but, if the treatment is prolonged, the precipitate is found almost wherever blood is present. Within the cytoplasm the precipitation determiners may be localised in cryostogenic centres; but I have never been able to identify these apart from the F.B.S. deposits.

An equally interesting manifestation of the preference of F.B.S. for a definite site is seen in the many F.B.S. bodies that lie from place to place upon the alveolar walls of these lungs after prolonged treatment with F.B.E. These bodies are usually small and often occur in minute clumps, which are particularly well marked on the rings of the alveolar ducts. Even where such particles are not visible, however, the margins of the alveolar walls, viewed on edge, sometimes appear as extremely thin dark lines in which very fine particles can be discerned. Both free granules and dark lines glow between crossed Nicol prisms, as do the F.B.S. bodies within the granular pneumonocyte. It may be inferred that a material from the granular pneumonocyte has become spread thinly on the alveolar walls and has brought about the precipitation there of a thin layer of F.B.S. This deposit on the airface is taken to mark the position of material excreted from the granular pneumonocyte. Again, this can hardly be a random deposit, and is regarded as having been formed in the mucoid layer, probably because it contains a catalyst from the granular pneumonocyte. It is admitted that the appearance of the dark lines by conventional illumination in the light microscope doubtless exaggerates the actual thickness of the mucoid coat because of the accumulation in it of granules of F.B.S., but even at that the layer is usually so thin in the lungs of mice and cats that probably only its densest parts are thus visible. An analogous thin line is seen in certain stretches of mouse alveolar wall after heavy osmiumisation.

Organology

This concept of the derivation of the alveolar mucoid lining assigns an exocrine glandular function to the granular pneumonocytes. Brodersen (1933) regarded them as secretory cells. The collective mass of the granular pneumonocytes constitutes a diffuse organ within the lung, whose volume in man has been estimated to equal that of the spleen (von Hayek 1942) but whose modus operandi, though often speculated on, remains in many ways a mystery. In human lungs it would manufacture a mucoid film which, if it could be pieced together as a continuous sheet, would measure as much as 100 sq. m. (von Hayek 1942). If it were even 0.2μ thick, its volume would be 20 c.cm. Such a mucoid film would lie upon an attenuated epithelium as recently interpreted by Low (1952, 1953) from electron micrographs (see figure), or possibly a layer of specialised connective tissue, as conceived, for instance, by Leblond and Bertalanffy (1951). We may postulate that it would be cohesive, flexible, and viscous. Phase-contrast microscopy seems to show that it wrinkles minutely when the wall is contracted. It transmits silver-nitrate molecules, which become segregated in the underlying silver lines. It would, of course, be readily penetrable by the molecules of oxygen and carbon dioxide (Terry 1945), and must retain its integrity and proportional water content under the high water-vapour tension of the alveolar air. It may be causally related to the myelin figures (Leathes 1925) which are seen by phase-contrast microscopy to emerge in great abundance from the surfaces of the alveolar walls in sections of fresh lung mounted in water or in physiological saline solution, for they are generated in hydrophilic material (Frey-Wyssling 1953b). It may have something to do with the inhibition of bubble formation, for in life no air-bubbles are normally formed in the alveoli. If they were so formed, in quantity, the effect would be disastrous. They are often seen after death. The mucoid film may be responsible for the maintenance of constancy in the surface tension of the alveolar wall

(Macklin 1946)—a matter of paramount importance. After complete and prolonged collapse of the lung, such as that produced by Loosli et al. (1949), the mucoid film may prevent adhesion of the alveolar walls, which would be expected if the approximated surfaces were formed of naked connective tissue. In oedematous thickening of the alveolar walls it may help to retain the augmented contents, and thus would be functionally represented in specimens such as those illustrated by Short (1950). In lungs of mice subjected while alive to drastic intrabronchial decompression (Macklin 1953a) I have noted that the extravasated blood in certain swollen walls that have been broken down interiorly is confined on either side by a thin layer that corresponds to that described and figured by Short. The alveolar wall should not be looked on merely as a capillary plexus. The capillaries occupy the *milieu interne*, but are supported on either side by an independent confining layer of relatively stable character that has a fluid mobile air-surface, the mucoid film. These confining layers persist after the capillaries have been broken down; and it is between these layers that the growing rays of adenoma, such as those of urethanised mice, infiltrate.

The mucoid film may undergo a slow drifting movement toward the mural phagocytes (Macklin 1951a), so transporting fine foreign particles to eliminational areas. Experience with carmine particle insufflation in mice supports this conjecture (Macklin 1951a). What may be rudimentary cilia have been noted on granular pneumonocytes (Macklin 1950a) which would be expected to promote such a drift. Leblond (1950) has emphasised the viscosity or stickiness of most polysaccharides, and it is easy to see how this property in the mucoid coat would arrest foreign particles gaining entry to the alveoli in contaminated air. Such an ability to trap and transport offending fine material, alive or dead, is a very important function of this muciform lining. This function is not perfect, because fine silica and other particles may pass through it (Macklin 1950b). Possible antiseptic or bacteriostatic virtues in it should not be overlooked. It is undoubtedly dynamic, not static. It would be expendable, of course, continually breaking down and being renewed. Fine and almost invisible wisps of substance that may be cast-off parts of it are often found in the alveoli. In F.B.E. cases they have been seen with particles of F.B.S. entangled in them.

Ability to maintain in itself a constancy of volume and of concentration of water and solids, is assumed as inherent in the productive mechanism of the mucoid film. Salt crystals, for instance, do not appear in it even after a lifetime of evaporation. Disturbances in its constants, however, may occur. There may be a form of alveolar oedema due to an over-accumulation of water in it. The 400 ml. of water daily eliminated by the lungs of a sedentary adult in a temperate climate (Evans 1949) must mainly enter and leave the mucoid film. It is one of Nature's marvels that the alveoli do not fill with water. How speedily they are filled by aqueous fluid when damaged by noxious gases—e.g., phosgene—is common knowledge. Perhaps, on the other hand, the mucoid film may sometimes become deficient in water. Possibly such a desiccation is a fundamental ingredient in the pathology of so-called medical emphysema. Polycard (1942) conceived of a relatively thick layer of transudate lining the alveoli which he regarded as spaces of interstitial emphysema having no epithelium. When the protein content became rich this fluid was to him like the exudate of pneumonia. He thought it was excreted by lymph vessels. I have been unable to find that alveolar exudates such as those following exposure to chlorine and other war gases are significantly eliminated by lymph vessels. Polycard's alveolar fluid seems to have little in common with that herein described.

Phagosity

Many other functions have been assigned to the granular pneumonocytes, only a few of which can be mentioned. Pathologists have too often dismissed them as phagocytes, though they contain no ingesta under usual conditions. It is admitted that they are sister cells of the phagocytic pneumonocytes or dust cells (Macklin 1949), but the latter are, in the normal mouse at least, much less numerous (Macklin 1951a). Like human civilians, the granular pneumonocytes can, it seems, undertake military (phagocytic) duties on occasion. In gathering in the dust particles that impinge on the alveolar wall they have, as has been noted, the co-operation of the mucoid layer (Macklin 1946). This synergy is essential, for under ordinary conditions the phagocytic pneumonocytes are pegged into the alveolar wall and do not wander about as many pathologists seem to think (Macklin 1951a). Foam cells (Schaumzellen) are often found in the lungs, and sometimes superficially resemble the mural granular pneumonocytes. Brodersen (1933) thinks they represent a different functional state of these cells. They may occur free in the alveoli, often contain ingesta, and under pathological conditions are numerous and large. In urethanised mice their numbers and size are increased. The cytoplasm then abounds in small droplets of refractile lipid material which is definitely osmophilic. They are then often called lipoid cells, and may have no characteristic granular-pneumonocyte granules. F.B.S. bodies were seen in them only after prolonged exposure to F.B.E. and were sparse. When they are recovered by the "washout" method (Macklin 1949, 1951a) and examined, while fresh, by phase-contrast microscopy in an aqueous medium, striking myelin figures emerge from the periphery while none are noted in the interior; and it is suggested that the cells have acquired a coating of mucoid while moving about in the alveoli, and that it is this that gives rise to the figures. They may be looked on as a fourth variety of pneumonocyte, the lipoid pneumonocytes, but seem to be a special type of phagocyte.

Endocrinosity

Sjöstrand and Sjöstrand (1938) have brought forward interesting findings that suggest that the granular pneumonocytes play an endocrine rôle having to do with the formation of haemoglobin. von Hayek (1942) suggested that they may be cellular furnaces, producing heat from the combustion of particles of fat and ready oxygen, and found that from a half to four-fifths of the cell surface is closely applied to the neighbouring capillaries. Perhaps, like hepatocytes and other cells, they have more than one function. It is this versatility that moved van Hayek (1952) to emphasise "die vielseitige Funktion der Alveolarepithelzellen." I have never seen membranes extending from bona-fide granular pneumonocytes over the contiguous capillaries, and thus they do not seem to be respiratory cells, in contrast to their sister cells, already referred to, the membranous pneumonocytes.

Fecundity

I have admitted that the granular pneumonocytes have mitotic potency (Macklin 1938a, 1946), though in uncolchicinised normal mice no mitotic figures were seen either in them or in what may be looked on as their precursors in the alveolar wall; and this is said after an inspection of many sections from hundreds of animals. Thus the finding in "alveolar cells" of colchicinised mice of 4·52% of arrested metaphases to total alveolar wall cells (Bertalanffy and Leblond 1953) seems surprisingly high; but this estimate is based on only one six-hour period. I have tacitly questioned the reliability of colchicine as an indicator of mitotic activity in lungs (Macklin 1951b). In normal mice I look on the bona-fide granular pneumonocytes as relatively long-lived cells, though it is well known that, when stimulated, as with

the fumes of osmium tetroxide (Macklin 1938a and b), they proliferate by mitosis. The usually fewer phagocytic pneumonocytes (mural dust cells) are normally subject to constant loss as they succumb in their phagocytic labours; but even here, in the healthy mouse, there does not seem to be a need for such a high rate of cell division as that reported—judging by the limited number of such spent cells that are found free in the alveoli or on the surface of the air tract (Macklin 1951a).

I have noted many small cells containing a nucleus that seemed to be dividing directly, and these may be precursors of the phagocytic and granular pneumonocytes. Guiyesse-Pellissier (1920), Clara (1936), and others have recognised an amitotic form of division in these cells. Such presumably young granular pneumonocytes, in fresh mounts, supravitally stained with toluidine-blue and other dyes, showed a perinuclear investment of fine basophilic granules, often bearing polar conical or cylindrical projections. In more advanced stages this granular mass was seen to be broken up by metachromatic fluid pools in the cytoplasm, which were no doubt engaged in the formation of the definitive granules of the granular pneumonocytes already described. Absolutely nothing that could be construed as a mitotic figure was seen in the many such preparations made from over two score mice.

I have never observed, in healthy animals, the great numbers of large free vacuolated cells in the alveoli and on the ciliated air tract that were reported by Bertalanffy and Leblond (1953) in the rat. I have, however, found this condition in the diseased rat, and attributed it to a mild form of pneumonitis in this animal (Macklin 1949) which I feel is common. I have also found large numbers of such free cells (foam cells) in the recoveries from a bronchiectatic area in a lobectomy specimen of a human lung (Macklin 1949). Such a cytorrhœa seems to be evidence of a pathological condition that would call for regenerative proliferation. There is little reason for the multiplication of the large vacuolated "alveolar cells" since they apparently are speedily eliminated.

Substratum

As regards the layer of living tissue that underlies the mucoid film (see figure), Low (1952, 1953) has described an electron "shadow" layer on the surface of the alveolar wall which resembles closely that cast by the endothelium of the alveolar capillaries underneath. It is obviously continuous with the perinuclear cytosomes of certain rather large surface cells of the wall which are fusiform in profile, and which he thinks are epithelial cells. With this classification I am inclined to agree. I have often seen them by phase-contrast microscopy, and they are often seen on the rings of the alveolar ducts, where their bed is firm and does not allow them to sink into a depression. They are prominent, for the same reason, on the free edges of the alveolar walls; indeed they often project bluntly into the air space, as Low has shown. They appear to be covered by the mucoid layer, which sometimes may be separated under the oil-immersion phase-contrast lens from a thinner layer underneath that seems to be the cell membrane. Bertalanffy and Leblond (1953) call them "endothelium-like cells," and evidently have confused them with ordinary endothelial cells, which are more common; but they are related to the air spaces rather than to the blood spaces of the capillaries, and are clearly distinguishable from endothelial cells, the nuclei being larger and more lightly staining and not appearing as if partly wrapped round the capillaries. Their cytosomes are disc-shaped and lie flat on the surface. Low has also described a more rounded cytosome which lies in an indentation of the wall, and it similarly gives rise to an attenuated surface layer like that of the flat form. This cuboidal or columnar cell corresponds to the "epicytes" which I have

described (Macklin 1946, figs. 1 and 2) and to the alveolar epithelial cells which von Hayek (1953, fig. 121) has shown. When the neighbouring capillaries are distended, the cytosome takes the shape of a carafe when seen in profile. This form is found on the general alveolar wall rather than on the rings of the alveolar ducts and the edges of alveolar walls; and because of its cryptic situation it is not so readily discerned as is the flat form, but it is functionally the same cell. Since both varieties of these membranated cells seem to be epithelium they may be designated "membranous pneumonocytes" as already suggested, for they are sister cells to the granular and phagocytic pneumonocytes.

It should be admitted, however, that other workers have regarded such elements as specialised mesenchymal cells, somewhat analogous to those lining the synovial and serous cavities. Their attenuated layers closely resemble those of the underlying endothelial cells, which are mesenchymal. Perhaps, as some workers think, the epithelial cells, which once covered the alveolar walls completely, have relinquished most of the surface area, but their places are taken by specialised attenuated mesenchymal cells, covered by the mucoid membrane, a secretion of the surviving epithelium. In that case we would have a coating, really of epithelial origin, taking the place of the cells themselves. The well-known silver lines on the alveolar wall might perhaps be harmonised with either hypothesis; but I find this network to agree better with the endodermal than the mesodermal hypothesis, because it is linked with that of the bronchiolar and bronchial epithelium (Macklin 1938b). The granular pneumonocytes occupy the small heavily circumscribed areas, whereas the membranous pneumonocytes with their attenuations doubtless have as their domains the larger and more faintly outlined "bare areas," so called because on them, with the light microscope, no cells are seen. Carleton (1934) has published convincing evidence that the phagocytic pneumonocytes are of endodermal origin, and it seems reasonable to regard their sister cells, the granular and membranous, as of the same lineage. The basement membranes seen in Low's electron micrographs speak for either hypothesis.

Pneumonologists will rejoice that Low, with his electron microscope, has gone far to explain "the riddle of the lung," for "Tidy minds demand that there be a barrier between it [the tissue fluid of the alveolar wall] and the air-cavities" (*Lancet* 1947). We know now that the capillaries are not "naked," but that there is a specialised membranous layer covering them. There is no reason to suspect that any part of the alveolar wall remains uncovered by Low's "attenuation." For instance, when a mural phagocyte drops out, the evacuated socket has the form of a short tunnel through the wall or "pore," and it seems that the attenuated epithelial layers immediately grow in to provide a surface for this tunnel, perhaps after the manner described by von Hayek (1953, p. 150). Indeed it is likely that this clothing process takes place as the phagocyte is loosening; hence no raw surface ever exists. The silver lines which Macklin (1938b) found in the walls of the pores would be the linear junctions of these attenuations. It is fitting that a mucoid coat, thin, aqueous, and ordinarily invisible though it be, should overlie these delicate tissues, guarding them against desiccation (Macklin 1950b), and serving in many other ways, some of which have been mentioned.

Summary

From a-priori reasoning there ought to be a thin aqueous cohesive flexible film on the pulmonary alveolar walls, in constant slow movement toward the phagocytic pneumonocytes and bronchioles, in course of continual renewal as its expended solid remnants are cast off, and incapable of self-adhesion. Its normal total volume in the human lungs would be at least 20 c.cm.

Certain light-microscope evidence from fresh and fixed and stained lung tissue under conventional, phase-contrast, and polarised illuminations supports this conception of a dynamic mucoid alveolar microfilm and suggests that it contains acid mucopolysaccharides and myelinogens.

This mucoid film has been credited with performing vital functions, such as assisting in the removal of fine living and dead particulate matter, the maintenance of a constant favourable alveolar surface tension, the facilitation of gaseous exchange, the protection of the underlying tissue from desiccation, and the suppression of invading micro-organisms. Its mechanism of production normally insures a constancy of volume, thickness, water and solid content, and other features.

There is evidence pointing to the granular pneumonocytes as the originators of the secretion which composes this film.

The water is contributed constantly by the blood-plasma of the pulmonary capillaries in an amount (in man) of about 400 ml. a day. This evaporates as fast as it is produced, but solids in the film are never increased.

This mucoid film is visualised as supported by the attenuated epithelium of the membranous pneumonocytes which Low has reported from his electron microscopic studies.

The pneumonocytes comprise three forms—granular, phagocytic, and membranous—and all are regarded as specialisations of the original endodermal epithelium of the lung. Observations on cytogenesis and granulogenesis are given.

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Addendum

Since this paper was written I have made some further observations.

DRAINAGE OF SURPLUS ALVEOLAR FLUID AND INTERCEPTION OF PARTICLES IN IT

A hint of what happens to any alveolar fluid that is not evaporated is given by the conspicuous accumulations of dust in the reticulo-endothelial cell clumps in the walls of respiratory bronchioles and alveolar ducts as seen, for instance, in dog and human lungs. These dust concentrations obviously were brought about by phagocytosis of loose particles which had drifted in with the residual alveolar fluid, and as it percolated along a devious channel that suggests the sinus of a lymph-gland. It is concluded that this "overflow" of aqueous mucoid fluid is drained away via the lymphatic system. It gains entry to these dust traps through certain epithelial plaques that are clearly marked in the dog lung, and that seem to correspond to the stomata of earlier writers (e.g., Sikorsky 1870). Perhaps the mucoid fraction is skimmed off at these points and added to the sheet of mucus that rides outward upon the bronchial cilia.

There is no evidence whatever that phagocytic pneumonocytes (alveolar endodermal dust cells), that dispose of most of the alveolar dust, ever leave the air tract to enter the loose tissues of the lung or the lymph channels; but, on the other hand, there is every indication that these cells are disposed of by way of the glottis (Macklin 1951a). The dust that has evaded them enters the lung tissue and lymph channels as above described but is not really eliminated, for there is no proof that it ever leaves the body. Much of it that is not intercepted as above is incarcerated in the hilar lymph-nodes, and some may even enter the blood to be trapped in reticulo-endothelial cells at remote points. Its presence in tissues of the lung and beyond is thus adventitious and is a sort of by-product of the action of the drainage system for the surplus alveolar fluid, which represents probably most of the lymph coming away from the lung.

It seems likely that bacteria—e.g., *Mycobacterium tuberculosis*—are arrested in the above-mentioned dust traps, which

would then form the initial lesions of disease, as tubercles. In this light the topography of tubercles is determined by the anatomy of the carry-off system for surplus alveolar fluid.

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TUBERCULOUS MENINGITIS IN CHILDREN TREATED WITH STREPTOMYCIN AND P.A.S.

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WITH the advent of streptomycin in 1947 it became possible to treat patients with tuberculous meningitis. Since then there have been many modifications in the treatment, but there have been four main stages in its evolution.

In the first stage, in 1947, streptomycin alone was available, and no-one knew the best way to use it.

In the second stage, from 1948 to 1950, streptomycin treatment was more standardised and consisted in prolonged and uninterrupted intramuscular courses, with shorter and often interrupted intrathecal courses. Alternative routes were introduced for the intrathecal administration of streptomycin in spinal blocks and other obstructions in the pathways of the cerebrospinal fluid (C.S.F.). Major neurosurgical procedures were attempted occasionally. Adjuvants such as 'Sulphetrone' and streptokinase were tried but found to be of little value. Towards the end of that period intrathecal tuberculin was introduced by Smith and Vollum (1950).

The third stage in the treatment of tuberculous meningitis is described here. It is characterised by the routine use of oral *p*-aminosalicylic acid (P.A.S.) and the selective use of intrathecal tuberculin in conjunction with streptomycin treatment, and ends with the introduction

of isoniazid in April, 1952. That date marks the beginning of the fourth stage, which is still in progress.

Several British centres have already reported their results relating to the first two stages. The combined results of five major English centres, including our own, were recently analysed statistically (Lorber 1954); 549 patients of all ages admitted to those centres between 1947 and 1950 were observed for a minimum of two years, and many of them for five years or more. Observation for two years was useful for the assessment of results because deaths were relatively frequent up to that time but

TABLE I—AGE-DISTRIBUTION ON ADMISSION

Age (yr.)	No. of cases
Less than 1	
1-11 ^{1/2}	8
2-2 ^{1/2}	3
3-4 ^{1/2}	7
5-9 ^{1/2}	15
10 or more	2
Total	38

very exceptional afterwards. These results form a baseline for comparison with newer methods of treatment. The two-year survival-rate of the whole series was 46.1%. In 1947 the results were indifferent, 32% having survived for two years compared with almost 50% in 1948-50. The results were the same in each of the three years 1948, 1949, and 1950.

The most important prognostic factor was the stage of the tuberculous meningitis on admission. In 1948-50, 74% of the patients admitted in an early stage survived, compared with 54% of those in an intermediate stage, and only 25% of those in an advanced stage. Most of the survivors of those admitted in either an early or an intermediate stage were in good condition and without neurological sequelæ. The survivors of those admitted in an advanced stage often had permanent physical or mental damage. Children aged less than 3 years and those with miliary tuberculosis fared less well, but the most important prognostic factor was the stage of the tuberculous meningitis on admission.

The results in our first 82 cases (Illingworth and Lorber 1951) showed an over-all one-year survival-rate of 44%. After the completion of that series our routine treatment was altered in several respects. I report here the results in our patients who were admitted in the twenty months from August, 1950, to March, 1952. All the patients have been observed for two years or more, and all completed their course of treatment more than a year ago.

Material

38 consecutive cases of tuberculous meningitis in children were admitted without any selection. No patient was refused treatment. Most of the patients were referred from other hospitals. The series includes 3 children who had been unsuccessfully treated elsewhere for several weeks. 1 other child is not included, because he received no treatment; he was brought to hospital in status epilepticus and died an hour after admission.

TABLE II—STAGE OF TUBERCULOUS MENINGITIS ON ADMISSION

Stage	Present series. No. of cases	First 82 cases (Illingworth and Lorber 1951). No. of cases
Early	9 (23.7%)	9 (11.0%)
Intermediate	16 (42.1%)	37 (45.1%)
Miliary developing meningitis	2 (5.2%)	10 (12.2%)
Advanced	11 (28.9%)	26 (31.7%)
Total	38	82

Nearly two-fifths of the children were aged less than 3 years, and only 2 were aged more than 10 years (table I). Of the 38 children 26 were boys.

The classification suggested by the Medical Research Council (1948) was again used for assessing the stage of tuberculous meningitis on admission. About a quarter of the patients were in the early stage, over two-fifths in the intermediate stage, and nearly a third in the advanced stage and unconscious. Only 2 patients developed meningitis while under streptomycin treatment for miliary tuberculosis (table II). The treatment of 1 of these was started in another hospital, and he developed meningitis before he was transferred to us.

Miliary tuberculosis was shown by radiographs of the chest in 10 children (26%) (table III); 5 of these had choroidal tubercles. In 5 other children the initial radiograph of the chest suggested miliary tuberculosis but was insufficient to enable a firm diagnosis to be made. Of these 5 children 2 died, and miliary tuberculosis was confirmed at necropsy. In another fatal case miliary tuberculosis was found at necropsy but had not been detected during life. In view of our experience (Emery and Lorber 1950) that miliary tuberculosis may often be missed during life, the total number of children who had miliary tuberculosis was probably more than the 16 definite or probable cases.

Bacteriological confirmation was obtained from the c.s.f. in life in 35 (92%) of the 38 patients. The organism was of the human type in 22 of the 23 cases in which typing was successfully done.

In 3 children no bacteriological proof was available. All survived and all had a positive tuberculin test and a characteristic c.s.f. 1 infant, aged 1 year, had miliary tuberculosis of the lungs. The 2nd, a boy aged 5 years,

TABLE III—TYPE OF CASE, AS DETECTED DURING LIFE

	No. of cases
Meningitis alone	23 (60.5%)
Miliary and meningitis	10 (26.3%)
Possible miliary and meningitis	5 (13.2%)
Total	38

developed permanent optic atrophy and intracranial calcifications. The 3rd, a girl aged 5 years, had miliary tuberculosis of the lungs and choroidal tubercles. The diagnosis in these 3 patients is felt to be supported sufficiently by indirect evidence.

Treatment

Streptomycin

(a) Intramuscular streptomycin was given in two divided doses (20 mg. per lb. body-weight daily) either for a minimum of six months or for a minimum of two months after the last intrathecal injection of streptomycin, whichever period was the longer. If the patient's clinical condition, the state of the c.s.f., or the radiographic appearance of the miliary lesions in the chest was unsatisfactory, intramuscular treatment was continued for as long as necessary. Of the 28 survivors 26 received a single course. In 13 this lasted for the minimum period of six months; in 8 it lasted for seven months; and in 4 it lasted up to twelve months. None were treated for more than a year. In 1 child treatment was abandoned after three months because of extreme hydrocephalus and decerebrate rigidity; she nevertheless survived. The 2 other survivors completed one course of treatment (six and seven months) but relapsed three and a half and four and a half months later and were treated for another six months in each case. All the deaths took place within four and a half months of admission.

The total duration of treatment was substantially shorter than in our earlier series, in which 7 of 36 survivors were treated for more than a year, and 2 for more than two years.

(b) *Intrathecal streptomycin* in daily doses of 25 mg. or 50 mg. was given for forty-five injections in the first two months of treatment, a day's rest being allowed each week in the first four weeks and two days' rest each week in the next four weeks. Intrathecal treatment was continued beyond this period without interruption if tubercle bacilli had been recovered from the c.s.f. during the preceding six weeks, or if there were other signs of an active meningeal process, judged by the clinical condition or by the state of the c.s.f. If intrathecal treatment was discontinued after forty-five injections it was resumed if tubercle bacilli were again found in the c.s.f.; or if the c.s.f. cell-count did not fall below 100 per c.mm. soon after intrathecal treatment was stopped; or if the c.s.f. cell-count did not show a progressive fall after that period or showed a sudden or sustained rise, especially in association with a falling c.s.f.-sugar and a rising c.s.f.-protein level. If any of these conditions was found, further similar courses of forty-five injections were given as often as necessary.

In none of the fatal cases were more than fifty intrathecal injections given. Of the surviving 28 patients 10 had fewer than fifty injections, 9 had between fifty and a hundred, and 9 had between a hundred and one and a hundred and thirty-five; none had more than a hundred and thirty-five injections. The number of injections given was much smaller than in our previous series.

Spinal blocks developed in 2 patients, of whom 1 survived. The diagnosis was confirmed by the methods reported elsewhere (Lorber 1950), and the treatment was given by the cisternal route. This incidence of spinal blocks—2 (5%) out of 38—was much less than in our previous series: 20 (24%) out of 82. 1 other patient was treated by the cisternal route because of tuberculosis of the lower thoracic vertebrae.

The ventricular route was used for streptomycin injections in 4 patients: in 3 because of either high c.s.f. pressure or gross papilloedema, and in the 4th because of extensive tuberculous involvement of several vertebrae.

Para-aminosalicylic acid

P.A.S. was given by mouth in divided doses three-hourly (0.5 g. per kg. body-weight daily). No P.A.S. was given between 9 P.M. and 6 A.M., but the 9 P.M. dose was doubled. P.A.S. treatment was continued until the child's discharge from hospital two or three months after the discontinuation of streptomycin treatment. This treatment was well tolerated.

Intrathecal Tuberculin

Purified protein derivative (P.P.D.) was given selectively to 9 patients in the advanced stage of tuberculous meningitis on admission after a short period of observation on streptomycin treatment, and to 3 patients in the intermediate stage on admission who showed definite and progressive deterioration despite the routine treatment. Free access to the lateral ventricles was considered essential during this treatment, and anterior burr-holes were made in all the cases in which the fontanelle was already closed.

Intrathecal Streptokinase

A controlled trial of intrathecal streptokinase was in progress in 1950 (Lorber 1951a) and the first 8 patients belonged to that trial; 3 of them received streptokinase, 2 of them surviving.

Relapse

The 2 patients who relapsed after the completion of streptomycin treatment were treated again as if they were new patients.

General Treatment

In all the cases general supportive measures were used, as in the earlier series. Emphasis was placed on the earliest possible mobilisation out of bed and on play therapy.

Method of Follow-up

The method of follow-up was the same as in our earlier series. All the children attended a special clinic and were examined and supervised by one person throughout. Intelligence and hearing were tested regularly by the same independent experts not connected with the department or with the treatment of the children. All the survivors remain under observation.

Results

Of the 38 children 28 (73.7%) survived, and 10 (26.3%) died. The minimal follow-up was two years. Of the survivors 9 have been observed from two to two and

TABLE IV—RESULTS OF TREATMENT OF 38 CASES OF TUBERCULOUS MENINGITIS

Condition on admission	No. of cases	Survivors
Conscious	27	25 (92.6%)
Unconscious	11	3
Total	38	28 (73.7%)

Period of observation 2-3½ years.

a half years, 11 from two and a half to three years, and 8 from three years to three years and eight months. This survival-rate is almost exactly double the two-year survival-rate in our previous series, if deaths are included which took place after our report in 1951. All the survivors in this series have been observed for more than thirteen months after the completion of streptomycin treatment, and 26 of the 28 for more than eighteen months.

PROGNOSTIC POINTS

Tables IV and V show the importance of early diagnosis. Of the 27 patients who were conscious on admission 25 (92.6%) recovered. Neither of the 2 deaths was due to tuberculous meningitis. None of the 9 children admitted in the early stage of tuberculous meningitis died. The only death among the 16 children admitted in the intermediate stage was in a boy aged 7 years, four and a half months after the beginning of his treatment. By that time his C.S.F. was practically normal, and no gross meningeal lesions and no hydrocephalus were found at necropsy. He had seven carious vertebrae with paravertebral cold abscesses, a tuberculous knee-joint, ulcerative tuberculosis of his kidneys, and diffuse calcifying tuberculous lesions in his spleen. All these lesions were present on admission. His death was due to advanced cachexia.

The other child who was conscious on admission and died was a boy, aged 4 months, who had been admitted

to another hospital with miliary tuberculosis and massive consolidation of the right upper lobe.

His C.S.F. was normal. Streptomycin treatment was begun, but meningitis developed within a fortnight, and he was transferred to us. His response to treatment appeared satisfactory for nearly four months. His C.S.F. returned to normal, and the miliary shadows and consolidation could no longer be detected in radiographs of the chest. His fever, however, returned, and a radiograph of the chest unexpectedly showed a gross pericardial effusion. The effusion was tapped, and pneumococci were grown from the thick pus obtained. In spite of penicillin treatment the boy went downhill and died suddenly after two days. At necropsy a further unexpected finding was an extensive pneumococcal meningitis. There was evidence of healing disseminated tuberculosis on histological examination. There had been no clinical indication of acute meningitis; and, when the C.S.F. was last examined three days before his death, the cell-count was 9 per c.mm., protein 40 mg. per 100 ml., and sugar 58 mg. per 100 ml.

The 25 survivors who were conscious on admission are all in excellent general condition; none are mentally affected, but 2 are deaf, 1 is partially deaf, and 1 is partially blind. 21 (84%) of the 25 are without any neurological sequelæ. 1 of them, however, is still in an orthopaedic hospital receiving treatment for tuberculous spondylitis. All the 3 deaf children received more than ninety intrathecal injections. The need for prolonged intrathecal treatment was probably a factor in the causation of their deafness (Lorber 1954). None of our patients received dihydrostreptomycin.

Patients who were unconscious when treatment was started responded poorly. Of 11 children admitted with advanced tuberculous meningitis only 3 survived. None of the 3 survivors are free from sequelæ, 2 being hydrocephalic idiots with gross neurological defects. The 3rd child recovered without any subjective defects, although he had a severe paraparesis in flexion during treatment, associated with ectopic ossifications in his psoas-major tendons, which are now resorbing. This case, together with 4 others of ectopic ossifications, has already been described (Lorber 1953).

Compared with our first series, the quality of the survivors has shown great improvement. Altogether 75% of the survivors in the present series are free from any defect (grade 1), compared with 61% in the previous series. The sequelæ in the remainder were less severe in this series: 18% have some physical disability (grade 2), against 11% in the previous series, and only 7% have grave mental and physical sequelæ (grade 3), against 22%. 10 of the first 19 survivors have developed some intracranial calcification, but it requires a little longer period of observation to assess its final incidence. In our previous experience intracranial calcification developed in about two-thirds of all the children who recovered from tuberculous meningitis (Lorber 1952).

Of the deaths of the 8 children admitted in the advanced stage 6 took place within a month, 1 on the forty-eighth day, and the last on the sixty-third day after admission. 1 of these children had a double meningitis, pneumococci and tubercle bacilli being obtained from the C.S.F.

The child's age appeared to have an influence on the prognosis. Of the 14 children aged less than 3 on admission 8 (57%) survived, including the 2 decerebrate children. Of the 24 aged more than 3 years 20 (83%) survived, and none of them suffered mental damage. The influence of age, however, is only apparent, and is directly connected with the stage of the tuberculous meningitis on admission. Of the 14 children aged less than 3 years 7 were in the advanced stage; 5 of them died, and the other 2 are decerebrate. Of the 7 who were conscious on admission only 1 died—the infant, aged 4 months, who developed pneumococcal meningitis and pericarditis. The 6 other children are in good health, 1 being deaf. Only 4 of the 24 children aged more than

TABLE V—RESULTS IN RELATION TO THE STAGE OF DISEASE ON ADMISSION IN 38 PATIENTS

—	Stage				Total
	Early	Miliary developing meningitis	Intermediate	Ad-vanced	
Recovered:					
No sequelæ	7	1	13	0	21
Moderate sequelæ	2	0	2	1	5
Severe sequelæ ..	0	0	0	2	2
All survivors ..	9	1	15	3	28
Died ..	0	1	1	8	10
Total	9	2	16	11	38

3 years were in the advanced stage, and 3 of these died. Therefore the less favourable prognosis in young children was directly due to delayed diagnosis, as in our first series.

The presence of miliary tuberculosis did not adversely affect the prognosis. 8 of the 10 children recovered, and the 2 who died were those in whom the cause of death was not directly attributable either to the miliary tuberculosis or to the meningitis. The appearance of miliary tuberculosis in the radiograph of the chest disappeared in all 10—in 7 within three months.

Of the 12 patients who were given P.P.D. 6 died, but we gave P.P.D. selectively to the patients with the poorest prognosis. Of the survivors 3 were in the intermediate stage on admission but did not respond to routine treatment. 1 of them became unconscious before P.P.D. was started. After a very stormy course this boy, aged 4 years, made an excellent recovery. He was the first child in our experience who recovered in spite of becoming unconscious during routine treatment. Intrathecal tuberonin probably helped in these 3 cases. Without P.P.D. there might have been only 12 recoveries instead of 15 out of the 16. P.P.D. seemed to be of little benefit in most of our 9 advanced cases in which it was used. Only 3 of the 9 children survived, and 2 of them are decerebrate. In 1 of the fatal cases death was possibly accelerated by the P.P.D.

Discussion

These results represent a considerable advance over our previous figures. The over-all two-year survival-rate is much higher (73.7% against 46.1%) than in the large combined English series relating to 1947–50 and representing five important centres in the country (Lorber 1954).

They are the highest long-term survival figures published in this country. These results were obtained with shorter courses of intramuscular treatment and fewer intrathecal injections of streptomycin than in the previous series. Fewer children had relapses, and many fewer developed a spinal block. The incidence of hydrocephalus was much less, although exact figures cannot be given because encephalography was no longer a routine procedure. Encephalograms were made only as a guide to treatment if progress was unsatisfactory, if complications were suspected, or if a decision was required about abandoning treatment (Lorber 1951b). Treatment was abandoned in 1 case only. The condition of the survivors was better, more are free from sequelæ, and fewer became decerebrate. There have not been any late deaths.

The whole of the improvement in the results was obtained in children who were conscious on admission. The two-year survival-rate in these children was 92.6% (25 of 27), compared with 43.6% (24 of 56) in our first series. The results in children who were unconscious on admission were still very bad. The moral of this is obvious. All possible efforts must be made to avoid delay in diagnosis.

Increasing experience undoubtedly played a part in the improvement in the results. The outstanding difference, however, is the elimination of deaths after the second month of treatment. The prevention of the development of streptomycin-resistant organisms by the adjuvant action of P.A.S. was probably responsible for this. No resistant organisms were found in this series. Debré et al. (1952) presented evidence that streptomycin-resistant organisms played a large part in the late mortality in tuberculous meningitis.

There is another major point concerning the absence of late deaths. We have never continued with intrathecal treatment until the c.s.f. returned to normal. Indeed, the c.s.f. usually did not return fully to normal for from nine to fifteen months with this method of treatment.

So long as the c.s.f. showed a steady tendency to improve, it did not seem to matter and did not lead to late deaths. This policy spares the patient much pain and reduces the risk of deafness. Possibly a further reduction of intrathecal treatment might not be reflected in poorer results now that isoniazid is available. The risks, however, in disregarding the good results with the method described might be serious and need careful consideration.

It is also apparent that the routine use of intrathecal tuberculin is unjustifiable. Of our 27 conscious patients 22 recovered without it, and we were able to use it in good time in those 3 who were thought to be in need of it. The last 2 deaths were not due to the tuberculous meningitis. The value of P.P.D. in advanced cases has not yet been fully determined.

In conclusion, the chances of dying from tuberculous meningitis are very small if the treatment described above is followed and if the patient is conscious when treatment begins.

Summary

Between August, 1950, and March, 1952, 38 consecutive children admitted with tuberculous meningitis, 14 being aged less than 3 years, were treated with intramuscular and intrathecal streptomycin and oral P.A.S. 12 selected patients with a poor prognosis were given intrathecal tuberculin.

The results of this treatment were compared with our previous results and with the results of a large combined English series relating to 1947–50. Considerable improvement was noted. Of 27 conscious children on admission 25 (92.6%) recovered, and the 2 deaths were not due to tuberculous meningitis. Of 11 children admitted with advanced tuberculous meningitis only 3 survived—2 with severe sequelæ. The total survival-rate was 73.7% with a minimal period of observation of two years from the beginning of the treatment and thirteen months from the end of the treatment.

The worse prognosis of infants in this series was directly due to delayed diagnosis. Young children who were conscious on admission did as well as older children.

Intrathecal tuberculin appeared to benefit 3 children in the intermediate stage on admission who did not respond to routine treatment.

There were no late deaths in this series. This is probably due to the elimination of streptomycin-resistant organisms by the combined action of streptomycin and P.A.S.

It was not found necessary to continue with intrathecal treatment until the c.s.f. returned to normal.

I have much pleasure in thanking Prof. R. S. Illingworth for his criticism; my colleagues Dr. M. G. Philpott, Dr. D. G. H. Stone, and Dr. D. M. G. Beasley, who supervised the daily management of many of the patients; our house-physicians, Dr. N. Cole, Dr. A. George, Dr. M. Hunter, Dr. D. Judson, Dr. J. Owens, the late Dr. V. Radcliffe, Dr. K. A. Halliday-Smith, Dr. E. Sutherland, Dr. A. Turycyn, and Dr. M. Wylie, who did so much of the clinical work; Dr. J. L. Emery, Miss Sheila Stewart, and Miss E. Finch for the pathological, bacteriological, and biochemical work; Dr. T. Lodge and Sister Mallinder for the radiographs; Dr. M. C. Taylor and Mr. N. E. Whilde for the psychometric assessment of the children; Mr. G. C. Arnold for the audiometric examinations; and the many consultants and general practitioners who referred cases to us.

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VENOUS COOLING A NEW METHOD OF COOLING THE BLOOD-STREAM

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HYPOTHERMIA is likely to play an important part in the further development of cardiac surgery, and promises opportunities for unhurried and deliberate operations within the dry heart. The method of cooling should be efficient and easily controlled, while at the same time the extra time required to reduce the body-temperature should be reduced to a safe minimum.

Surface cooling by immersion, or with ice packs or refrigerated blankets, has the virtue of simplicity and has been widely used (Lewis and Taufic 1953, Swan et al. 1953, Bailey et al. 1954), sometimes in combination with chlorpromazine (Dundee et al. 1953, Ripstein et al. 1954). This method involves exposure of the skin to temperatures of about 0°C for a long time, and this may damage the skin, subcutaneous tissues, and nerves (Behnke 1953). A case of subcutaneous fat-necrosis has been reported following thirty-four minutes' exposure of the skin to ice packs (Collins et al. 1953). In dogs deep anaesthesia or a combination of drugs is required to suppress the troublesome shivering caused by surface cooling (Hegnauer and Penrod 1950). Moreover, the rate and depth of cooling are difficult to control. A further drop of temperature is usual on removing the source of cold (Alexander 1946) owing to the relief of peripheral vasoconstriction and perfusion of the cold surface tissues (Eichna 1948). This uncontrolled "after-drop" is likely to be a serious factor where cooling has to be stopped unexpectedly.

Cooling of the arterial blood in an extracorporeal circuit (Boerema et al. 1951, Delorme 1952) is a means of cooling all the body tissues with maintenance of their thermal gradients, and without subjecting any tissue to

a very low temperature (fig. 1). In dogs under light thiopentone anaesthesia, the method causes little shivering and the depth of cooling can be quickly controlled by clamping the artery supplying the cooling coil : after disconnecting the cooling circuit, any further fall of temperature is unlikely. This technique has been applied in 130 dogs and has supplied useful information (Ross 1954). It does, however, involve cannulation of a major artery ; and, though this is no disadvantage in dogs, where the artery can be tied off, the superficial femoral artery has subsequently thrombosed in at least two of our human cases in spite of excision of the damaged area and careful end-to-end arterial suture.

In addition, the efficiency of the cooling coil decreases progressively as the cardiac output falls and circulation through the coil slows ; hence the temperature drop below 30°C is likely to be slow. Finally, the effect of the

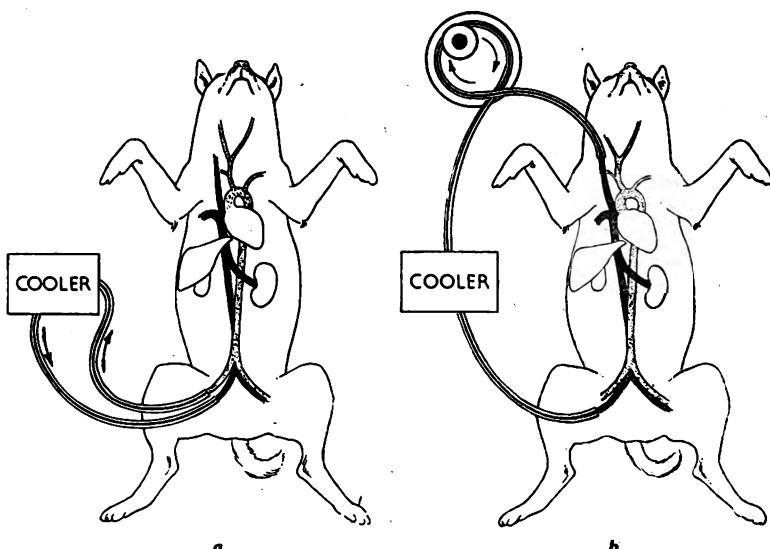


Fig. 2—Course of blood in *a*, arterial cooling ; *b*, venous cooling.

arteriovenous fistula is to cause a small but significant fall of diastolic pressure when measured manometrically, and in cases of congenital heart-disease this is likely to accentuate or to precipitate a right-to left shunt.

By cooling the blood in only the venous system these drawbacks can be surmounted while the advantages of cooling the blood-stream are maintained.

Apparatus

The apparatus consists of a coil of 'Polyvinyl' tubing ('Portex') about twelve feet in length and with a capacity of about 60 ml., surrounded by a circulating refrigerant solution exactly as described for arterial cooling (Delorme 1952, Ross 1954) (fig. 2). A simple rotary pump drives the venous blood through this coil and back into the venous system. No form of anticoagulant is used, but the tubing is siliconised, and joints and irregularities are reduced to a minimum.

Technique

The external jugular vein is exposed through a small skin incision in the neck, and the sucking cannula is gently manipulated into the superior vena cava. The cooled blood is returned via a similar catheter inserted into the femoral vein through the saphenous vein on the same side (fig. 2b).

Cooling begins as soon as the pump is set in motion, and can be stopped at any stage. The temperature falls promptly and is uniformly maintained, with a tendency to rise slightly when cooling is stopped, after which it

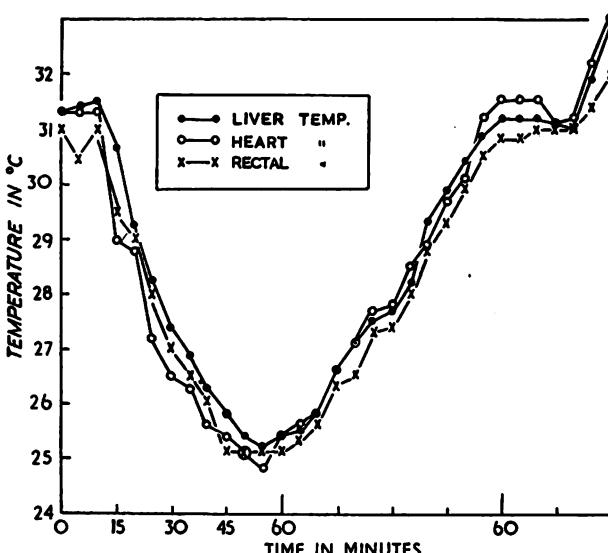


Fig. 1—Chart showing uniformity of cooling of various tissues during cooling of blood-stream.

becomes more stable and rises very slowly for several hours (fig. 3). As soon as the temperature has fallen to the desired level the cannulae are removed and then the whole cooling apparatus is removed, leaving a clear field for the subsequent operation.

With this technique dogs of an average weight of 20 kg. have been cooled to about 25°C in from twenty to thirty minutes. In addition one adult patient weighing 60 kg. was cooled to 26°C in an hour and has made an uncomplicated recovery after closure of an atrial septal defect.

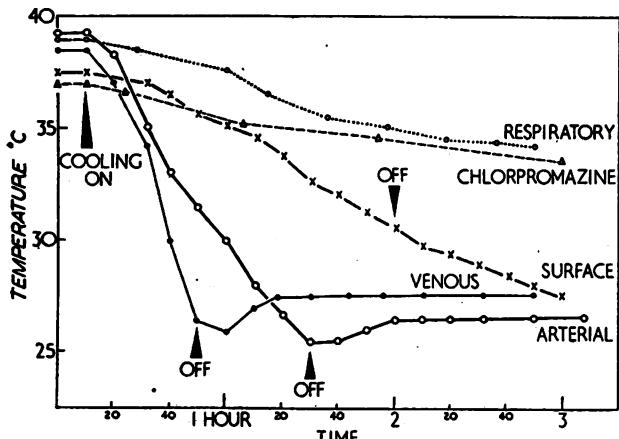


Fig. 3.—Comparison of cooling-rates with different techniques of cooling. Note how temperature continues to fall after surface cooling has been stopped. Respiratory cooling was brought about by cooling inspired air.

Summary

A new method of cooling the blood-stream is described. Blood is withdrawn from the superior vena cava, cooled, and pumped back into the saphenous vein on the same side.

This provides rapid and uniform cooling of the tissues and aims at avoiding the disadvantages of arterial cooling.

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"... a vast experience of international arbitration and International Courts has been effected; but the governments of the world still feel themselves to be under the necessity of expending enormous resources of labour, blood, and treasure in the service of the historic form of decision by cruelty, decision by war. Even in the most strictly 'justiciable' issues states are far too reluctant to use the machinery of the International Court of Justice, though any issue is open to decision by the judgment of independent men if the contestants would agree.... It is possible—that man, along with superb endurance and courage, has an implacable ability to suffer and inflict cruelty—that the potentialities of modern warfare will cause national statesmen slowly but mutually to realise that the form of decision to which the centuries have accustomed them is no longer a form of decision that can be tolerated."—L. HARVEY MOORE, hon. secretary general, International Law Association, 3, Paper Buildings, The Temple, London, E.C.4.

CHROMOSOMAL SEX IN TRANSVESTITES

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The cell nuclei in many species have a distinctive morphology according to sex (Barr et al. 1950, Graham and Barr 1952, Moore and Barr 1953). The nuclei of females contain a special mass of chromatin, the sex chromatin, which is rarely seen in nuclei of males.

Several lines of indirect evidence suggest that the sex chromatin of females is derived from a fusion of heterochromatic portions of the two X chromosomes—i.e., regions of the chromosomes which remain compact in the intermitotic nucleus. For reasons that are not entirely clear, although the small size of the Y chromosome may be partly responsible, the XY sex-chromosome complex of male nuclei does not produce a mass of sex chromatin of comparable size. Moore et al. (1953) showed that human epidermal nuclei are quite suitable for this work. In most epidermal nuclei in females, but not in males, there is a mass of sex chromatin which appears typically as a planoconvex body lying against the inner surface of the nuclear membrane. Moore and his colleagues suggested that the skin-biopsy test of chromosomal sex might be applied profitably to cases of hermaphroditism and reported the findings in two such patients. Since then one of us (M. L. B.) has studied skin-biopsy specimens from thirty additional cases of hermaphroditism. The method shows promise of being a useful aid in the differential diagnosis of the main types of hermaphroditism—i.e., female pseudohermaphrodites caused by adrenal cortical hyperplasia, and male pseudohermaphrodites.

The skin-biopsy test of chromosomal sex has been extended to several cases of transvestism. Our interest in these patients arises from the theory that the male transvestite may represent an extreme type of intersexuality or sex reversal, in which an embryo with the XX sex-chromosome complex is diverted in the male direction at a very early stage of embryonic development.

The Transvestite

Hamburger et al. (1953) have summarised the main features of transvestism and published a detailed case-history. Hamburger (1953) also describes the difficult problems which confront these patients.

Transvestism, or eonism, is a comparatively rare sexual deviation in which a person has an overwhelming desire to assume the attire, and be accepted as a member, of the opposite sex. Most students of sexual deviation feel that transvestites should be distinguished from homosexuals, in whom the urge to wear clothes or adornments of the opposite sex is a consequence of the direction of the sexual urge. Similarly, the transvestite is to be distinguished from the fetishist, who concentrates on one or more articles of dress as the result of a neurotic obsession. In contrast to the homosexual and the fetishist the intense desire of the transvestite to appear in clothes which are contrary to the somatic sexual development is the primary manifestation of the abnormality.

The male transvestite feels that he is in fact a female who has, through some fundamental error in development, acquired the anatomical features of a male. He detests his male sexual organs and may implore a surgeon to make such alterations as are possible to correct the error which he feels Nature to have made. The impelling urge to

dress in feminine attire is a natural consequence of his desire to be a woman. In the same manner, the transvestite would prefer to engage in feminine occupations. This extends into the domestic sphere, even to the point where there may be a wish to bear children. However, the sexual urge, as regards physical intercourse, is seldom a prominent feature. Such sexual desire as may be present is likely to be ambivalent, as would be expected from the conflict between psyche and soma.

Epidermal Nuclei in Transvestites

Skin-biopsy specimens were studied in five cases of genuine male transvestism. Sections were stained by the Feulgen method, with haematoxylin and eosin, and were of excellent quality technically. In each case the epidermal nuclei had a typical male morphology, whence it is inferred that these five patients bear the male XY sex-chromosome complex.

Discussion

Goldschmidt (1931) made a detailed study of intersexuality in the gipsy moth (*Lymantria dispar* L.). He demonstrated a series of female intersexes—i.e., moths bearing XX chromosomes—beginning with normal females and leading through increasing gradations of intersexuality to complete sex reversal and apparently normal males. A corresponding series of male intersexuality, with XY sex chromosomes, led from normal males through all grades of intersexuality to apparently normal females. The degree of intersexuality in the gipsy moth depends on the stage of development at which sex differentiation is disturbed. Should this crucial point (Goldschmidt's *Drehpunkt*) be reached very early in development, the end-result is complete sex reversal. On the basis of Goldschmidt's work Hamburger et al. (1953) made the interesting suggestion, as a working hypothesis, that the male transvestite may be an intersex of the highest degree. According to this suggestion the male transvestite would bear the female XX sex-chromosome complex; the factor causing the sex reversal would exert its influence at a very early stage of embryonic development, producing a person with a male soma, with the feminine psychological manifestations remaining as the only indication of the patient's chromosomal constitution. A similar suggestion has been made by Witschi and Mengert (1942) regarding the more pronounced types of homosexuality.

Contrary to the theory mentioned above, the present observations indicate that the male transvestite bears the male XY sex-chromosome complex. This result agrees with current work on hermaphroditism, since all male pseudohermaphrodites studied to date have typical male-type epidermal nuclei and presumably XY sex chromosomes, regardless of how closely their general anatomy may approach the female type (Barr 1954). Though it is now reasonably certain that male transvestites have XY sex chromosomes, this by no means rules out the possibility that the abnormality may have a genetical basis, since the ability to detect alterations at the gene level lies far beyond our relatively crude method of studying intermitotic nuclei.

Summary

The skin-biopsy test of chromosomal sex was applied to five cases of genuine male transvestism.

In each case the epidermal nuclei had a typical male morphology.

It is inferred that these persons bear the male XY sex-chromosome complex.

We are greatly indebted to our colleagues who made the material available for this study. Correspondence with Dr. Christian Hamburger, of Copenhagen, has been especially helpful. This work was supported by the National Health Grants Administration (Mental Health Division) of Canada.

References at foot of next column

POISONING BY SEWER GAS WITH UNUSUAL SEQUELAE

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POISONING by sewer gas is now rare in this country, but a number of accidents of this kind, some of which were fatal, were reported in the latter half of last century by Haldane (1896), Holden and Letheby (1861), Kite (1850), Johnson (1888b), and others.

The present case emphasises the need for constant precautions to prevent such accidents, and was remarkable for some unusual neurological and cardiovascular symptoms.

Case-report

A foreman sewer-worker, aged 46, was admitted to Upton Hospital on July 10, 1953. His mate stated that the patient had descended a 20-ft. manhole to investigate an obnoxious smell. As soon as he reached the bottom he remarked to the mate (standing at the top) that it was "the foulest smell I have ever come across." He coughed and spluttered immediately, said he felt dizzy, and began to ascend. When he got to within 3 ft. of the top he lost consciousness and fell to the bottom, landing on his feet in a crouched position. His mate said that the patient did not strike his head during the fall. The patient was in the gaseous atmosphere for at least 30 minutes before he was brought to the surface.

Condition on Admission

When admitted to hospital he was unconscious, cyanosed, and unresponsive to stimuli. He was having generalised tonic spasms, each lasting 10–20 seconds and occurring every 2 minutes. During the spasms the teeth were tightly clenched and risus sardonicus was present. The accompanying apnoea persisted after the spasm had passed, and the patient only started rhythmical shallow breathing when artificial respiration had been given after each spasm. Between spasms there was generalised muscular twitching. There were a few abrasions over the limbs, but no evidence of injury to the bones. At this stage the pupils were dilated and reacted sluggishly to light, and all reflexes, including the corneal and plantar responses, were absent. Pulse-rate 88 per min., regular; blood-pressure 140/90 mm. Hg; heart sounds of normal quality; lungs clinically clear.

Immediate Treatment and Response

He was given 95% oxygen with 5% carbon dioxide, with artificial respiration, and also two pints of strong coffee by rectal drip, and 3000 units anti-tetanus serum intramuscularly. After 20 minutes he was placed in an oxygen tent. Tonic spasms continued to occur at intervals for two hours and then became gradually less frequent and less severe. Regular respiratory rhythm was established when the spasms ceased, but the respiratory excursion remained shallow, with a chest expansion of only 1 inch.

Re-examination at this stage revealed bilateral extensor plantar responses. Tendon-reflexes were present, normal, and equal. The level of consciousness slowly improved, and 5½ hours after admission the patient could obey simple commands though he could neither speak nor swallow. Tongue and palate movements were absent, jaw-jerk was brisk. Convergence was poor, and the pupils reacted slug-

PROF. BARR, PROF. HOBBS : REFERENCES

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Fig. 1—Blackened coin from patient's pocket.

gishly to light. No abnormal physical signs were found in the cardiovascular system or in the abdomen.

Blackened coins (fig. 1) were found in the patient's pocket.

Investigations

Neither carboxyhaemoglobin nor sulphhaemoglobin was found on spectroscopy of the blood. A blood-count showed red cells 5,250,000 per c.mm.; white cells 13,300 per c.mm. (polymorphs 81%, lymphocytes 14%, eosinophils 1%, basophils 1%, monocytes 3%); Hb 115% (Haldane); packed-cell volume 48%, mean corpuscular volume 91 c.u., mean corpuscular Hb 34 µg., and mean corpuscular Hb concentration 37 g. per 100 ml.

Lumbar puncture next day produced clear colourless cerebrospinal fluid under a pressure of 60 mm. and containing 3 lymphocytes per c.mm., protein 25 mg. per 100 ml., chlorides 742 mg. per 100 ml., and sugar 48 mg. per 100 ml. The urine was normal. The erythrocyte sedimentation rate was 7 mm. in 1 hr. (Wintrobe). Radiography showed nothing abnormal in the chest and skull but there was marginal lipping of the lumbar spine. The Wassermann and Kahn reactions of the blood were negative.

Subsequent Course

Nasal feeding was instituted on the 2nd day and continued for 3 days while movements of the jaw, tongue, and palate were gradually regained. Articulation was slow to improve, but after 2 days the patient could say a few words with difficulty, though it was several days before he could say a short sentence. He could move his limbs against gravity, but power in all muscles was greatly diminished. Co-operation was excellent. There was no demonstrable loss of sensation. Owing to muscular weakness, co-ordination was difficult to test. Movements of the respiratory muscles gave rise to anxiety for several days, and the use of a mechanical respirator was at one time considered. After 2 days the tendon-reflexes were pathologically brisk and both plantar responses extensor. After 6 days the patient could swallow with ease and the respiratory excursion was adequate. He could say

a few short sentences in a scanning monotonous voice, with great effort, and could write slowly.

A week after admission he complained of tightness in the chest and substernal pain. Electrocardiography showed evidence of a recent small anterolateral infarct and right bundle-branch block. No special treatment was given for this, the patient being already at complete rest because of his neurological disability.

A month after admission neurological examination showed generalised exaggeration of reflexes and a slight increase in tone of the limbs, with a positive jaw-jerk, poor movements of the palate, and impaired convergence of the eyes, suggesting pseudobulbar palsy. The planter responses were now flexor, but this was not thought inconsistent with this diagnosis. In addition he had attacks of cerebellar inco-ordination (gross intention tremor in both hands), which came on spontaneously and lasted only a few minutes. He was developing immobility of the facial muscles.

When seen as an outpatient 3 months after his accident he was walking normally but had anginal pain on severe exertion. The neurological signs remained unchanged. Electrocardiography showed right bundle-branch block only (fig. 2).

Discussion

The gaseous hazards in sewers are due either to asphyxiants such as carbon dioxide, nitrogen, and methane, or to poisons such as carbon monoxide and hydrogen sulphide. It is generally considered that hydrogen sulphide is the main hazard. Haldane (1896) stated that sewage ordinarily met with in well-built sewers did not contain hydrogen sulphide, and that this gas was only evolved when there was contamination with acid. In the present case a quantity of sulphuric acid had been allowed to escape into the sewer on the day of the accident, and probably the resulting liberation of hydrogen sulphide caused the accident. This is borne out by the following extract from the analyst's report on samples of sewage sent to the Counties Public Health Laboratories, London.

"The sample taken at the inlet to the Sewage Disposal Works indicated quite clearly the cause of the accident. This sample is highly acid, the acidity being due to sulphuric acid, and it smells strongly of sulphuretted hydrogen. There can be no reasonable doubt, therefore, that the odour of the sulphuretted hydrogen was correctly recognised at the time, and that this arose from the acid condition of the sewage acting on the sulphide. Blackened coins found on the patient also bear this out."

Blood spectroscopy did not reveal sulphhaemoglobin. Smith (1948) states that in moderate concentrations the gas does not form this pigment, the haemoglobin recombining with oxygen to form oxyhaemoglobin; hence no changes are found in the blood.

There are very few references to chronic illness following poisoning by hydrogen sulphide, but these include persistent albuminuria (Johnson 1888a and b), acute nephritis (Vachell and Paterson 1894), and delirium (Wiglesworth 1892). Dr. René Sand, quoted by Sir Thomas Legge (1934), describes the case of a man, aged 38, who developed progressive sclerosis of the spinal cord and polyneuritis, which he attributed to chronic hydrogen-sulphide poisoning. Cardiovascular degeneration has also been described as an occupational hazard in sewer-gas workers (Bell 1953).

The present case exhibits both neurological and cardiovascular changes. It seems likely that hydrogen sulphide was responsible for the neurological changes, although hypoxia may have been a contributing factor (Stegemann 1951). In any event hypoxia must have contributed to the myocardial ischaemia. The neurological findings are probably attributable to a demyelinating lesion in the mid-brain, possibly in the corpus striatum.

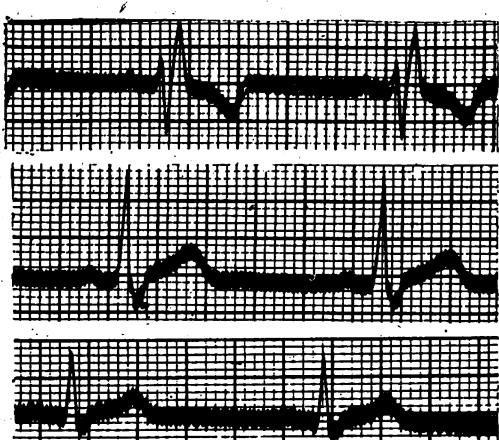


Fig. 2—Electrocardiogram showing right bundle-branch block.

To prevent accidents in sewers it seems necessary to emphasise the need for continuous caution by sewer-workers. The simple tests recommended by the Ministry of Health (1934) should always be carried out: they include the ventilation of the sewer before the man enters, and testing for hydrogen sulphide with lead-acetate paper. In addition, asphyxiating conditions should be tested for with a safety lamp, and inflammatory gases with a suitable detector lamp. Had these precautions been taken, this accident would not have happened.

It also seems desirable that such accidents should be made notifiable to the Ministry of Health, because less serious cases of poisoning may be more common than is generally appreciated.

Summary

Poisoning by sewer gas had neurological and cardiovascular effects probably caused by hydrogen sulphide and hypoxia.

Precautions should always be taken before entering a sewer.

Cases of suspected poisoning should be notified to the Ministry of Health.

We should like to thank Dr. John Lister for permission to publish this report and for his help and encouragement. Great credit is due to the nurses of Upton Hospital who nursed the patient. Also we are indebted to Dr. G. M. Hobbin, medical officer of health for the Eton Rural District, for his report; and to the Counties Public Health Laboratories for their analysis of the sewage.

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TONSILLAR CALCULI

P. R. R. CLARKE
M.B. Lond., F.R.C.S.

LATE SURGICAL SPECIALIST, MINISTRY OF HEALTH,
SUDAN GOVERNMENT

ALTHOUGH small calculi are often seen in the tonsils, large ones are uncommon. Tonsillar calculi have been recognised for many years. Terillon (1886) cited cases reported in the sixteenth, seventeenth, and eighteenth centuries.

Weller (1924) found more than a hundred references to published reports and gave details of the sixty-seven which he was able to study. In a thousand pairs of tonsils examined by him there were small concretions in eighty. He found that concretions can arise in any part of the tonsil, but that it is only in the crypts that they can reach such a size that they become clinical tonsilloliths. He stated that these calculi are formed round nuclei which may be colonies of organisms, keratohyalin, food debris, inflammatory exudate, desquamated epithelium, or old blood from haemorrhage.

Gibb (1860) thought that healing tuberculous foci could act as starting-points for the development of calculi.

Castellani (1927) was of the opinion that calculus formation could be a sequel to granular mycosis of the tonsil, and stated that the causal organisms could be fungi of the genus nocardia, leptotheices, spirochaetes, amoebae, or flagellates.

CASE-REPORT

A man, aged 35, from the Yemen, was admitted to hospital on Dec. 17, 1952, with right basal pneumonia, for which



Fig. 1—Radiograph showing calculi in right tonsil.



Fig. 2—Calculi after removal (actual size).

he was treated with penicillin and sulphathiazole. On Dec. 31 he was referred to the surgical department because of a sinus in the right side of the neck and a lump in the throat. He stated that a year previously he had had severe pain in the right side of his throat, and that the lump had been present since that time.

On examination was found, on the right side of the neck half an inch below the angle of the mandible, a small sinus from which oozed creamy pus. A hard lump as big as a walnut lay under the sinus. The patient's breath was exceptionally foul. The mucosa of the anterior pillar of the fauces on the right side was stretched over a swelling, and in this covering layer of mucose were three sinuses. A probe, passed through the sinuses, grated on something hard and stony. Radiography showed opaque material in the region of the tonsil (fig. 1).

Operation.—On Jan. 15, 1953, under chloroform anaesthesia a Boyle-Davis gag was inserted and a vertical incision was made through the anterior faucial pillar. Four calculi (fig. 2) were removed with lithotomy forceps. The wound in the mouth was left open, and the patient was given systemic penicillin and peroxide mouth-washes.

Postoperatively the sinus closed on Jan. 20, and the patient left hospital on Feb. 5.

Pathology.—Chemical analysis of the four calculi, which together weighed 13.3 g., showed that they were composed of calcium phosphate and traces of albuminous material.

SUMMARY

A case is described in which four calculi weighing a total of 13.3 g. were removed from a faucial tonsil.

I wish to thank Dr. P. H. Abbott and Dr. Abdel Moneim Wasfi for referring this case to me; Mr. B. G. Pendleton, of the department of clinical pathology, Newcastle upon Tyne General Hospital, for the chemical analysis of the calculi; and Dr. H. Richards, O.B.E., Director of Medical Services, ministry of health, Sudan government, for permission to publish.

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Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION

THE association's annual meeting was held at Buxton on May 6-8, under the presidency of Prof. BRYAN MCFARLAND.

Arthroplasty

A debate was held on the motion that all methods of arthroplasty of the hip have failed to achieve their purpose.

Mr. K. I. NISSEN (London), proposing the motion, based his attack on hip arthroplasty on four counts : (1) the serious postoperative complications that can occur ; (2) the early deterioration of the results ; (3) the expense of the seemingly endless physiotherapy required ; and (4) the faulty conception of the operations, due to ignorance of the true pathology. One concept of vascular degeneration in the femoral head had been exploded in recent Oxford work. Any pain-relieving operation reduced the blood-supply of the hyperemic head, but the arthroplasties interfered with it too extensively. McMurray's displacement osteotomy, Girdlestone's pseudarthrosis, or arthrodesis could be relied on to give equivalent or better results, and the reason why these were not in favour with younger surgeons was that they had little experience of them, the result being permanently good and not necessitating the patient's return to the surgeon. In most arthroplasties of all types the head eventually disappeared, leaving some form of pseudarthrosis.

Mr. W. A. LAW (London) opened against the motion. After saying that there was no universally applicable hip operation, he enumerated the essential requirements of a good arthroplasty : (1) a joint must be made ; (2) the pain of the arthritic joint must be alleviated and that produced later from over-fatigue of the controlling muscles must be limited ; (3) fixed deformity must be corrected ; (4) the new joint must be stable ; and (5) an adequate range of movement must be produced, though a stable joint with small range was greatly preferable to an over-free joint where muscle control was poor and fatigue-pain was therefore great. With these criteria he maintained that cup arthroplasty was a good operation, the good results of which lasted better than was suggested by Mrs. Shepherd's investigation [see below]. Patients asked him to do an arthroplasty on their second degenerating hip five to ten years after one had been done on the first hip. But careful selection of patients was essential ; obesity was not a contra-indication, but one must be satisfied that the patient had the morale to pursue the necessarily arduous aftercare (he mentioned private patients favourably in this connection). Patients must be warned of, and understand, the limitations of the benefit to be expected. The essential exercises could perfectly well be done at home, but circumstances often made prolonged supervision in the physiotherapy department essential. He did not look on cases needing revision as "failures," which was suggested by Mr. Nissen as the proper description, but considered revision an essential part of the treatment of the rheumatoid hip.

Mr. NORMAN CAPENER (Exeter) seconded the motion. He said that we had not yet overcome the difficulties of certain essential mechanical conditions : (1) the new joint surfaces must have not only congruity but conformity of hardness ; (2) there must be proper lubrication ; and (3) the problems of leverage and adequate power must be solved. Our present methods were incompatible with the above requirements. He estimated the cost to the nation of an arthroplasty at £200, which he looked on as very expensive for an operation doomed to failure. According to Mrs. Shepherd's figures deterioration set in five years after a cup arthroplasty and two years after insertion of an acrylic head, which on the basis of

the life-expectancy charts of insurance companies should confine the former operation to the over-80s and the latter to the over-90s.

Mr. LLOYD GRIFFITHS (Manchester), seconding for the opposition, denied that the traditional British operations relieved pain, and compared their results with those obtainable by taking the local waters. Arthroplasty was in a state of rapid evolution, and even the best of operations (like aeroplanes) were liable to temporary "grounding." He considered the results even now well worth while and pointed out that little progress would be made if surgeons must always await exact pathological elucidation of the problem.

Mr. R. G. TAYLOR (Oxford) said that good results could be obtained in a properly done Girdlestone's pseudarthrosis. Mr. W. E. TUCKER (London) thought it advisable to make patients write down their preoperative complaints as objective evidence for comparison with their later troubles ; and Mr. H. OSMOND-CLARKE (London) said that there was no place for arthroplasty in the young patient.

Prof. MERLE D'AUBIGNÉ (Paris) said he thought that all the failures of arthroplasty were due to technical errors. It took perhaps 200 arthroplasties to learn the art. He reported a much lower failure-rate than the British figures, and emphasised the importance of providing the right length of neck and of correcting anteversion. He thought that the results on the whole did not deteriorate in later years ; indeed some cases classed as only "fair" a year after operation became "good" with further passage of time. Mr. K. H. PRIDIE (Bristol) remarked on the advantages of the d'Aubigné type of prosthesis. Sir REGINALD WATSON-JONES (London), while maintaining that arthrodesis was incomparably the better operation in the young, said he would vote against the motion as it was worded. Mr. JOHN CHARNLEY (Manchester) spoke of the advantages, essentially of principle rather than technique, of central dislocation of the hip, and thought that arthrodesis was a good operation even in the elderly—particularly those of wiry build.

Dr. ROBERT JUDET (Paris) gave figures to illustrate the good results of acrylic-head arthroplasty and recommended the new prosthesis with an oblique base. He pointed out that the crushed cancellous bone around the stem of any prosthesis was in a state comparable to a bone-graft and that therefore weight-bearing should be delayed two months until revascularisation of the trabeculae was advanced. He thought that acetabular changes resulted from incongruity of the prosthesis, which should be of exactly the right size. Fractures of the prosthesis were now seldom seen in France, owing to the use of a better acrylic resin. Mr. J. H. MAYER (Tunbridge Wells) thought that the poor results were due to failures either of the surgeon or of the material, and advocated the use of metal prostheses rather than acrylic resin.

Mr. LAW, in summing up for the opposition, said we should continue to aim at the ideal of a mobile hip even in the young ; and Mr. NISSEN summed up for the motion. This was lost by a substantial majority.

Syme's Amputation

Mr. J. H. SHELSEWELL (Stanmore) had reviewed Syme's amputees from the material available at Roehampton. Of 534 cases the 302 done before 1939 were chosen for assessment, and 66 of these were followed up. Two-thirds had had no significant trouble ; 23%, including immediate failures, needed re-amputation. (Mr. LEON GILLIS pointed out that this rate is no higher than that after the standard below-knee amputation.) The operation had no place in the neuropathic limb, nor in those with vascular failure ; and it was seldom indicated in women, who had no means of concealing the necessarily bulky and obvious ankle-joint in the prosthesis. But for the working man it was a most satisfactory operation, enabling him to stand and walk for long hours and even to

play games. It was particularly advantageous for the double amputee, and Mr. Shelswell concluded that a properly done Syme's amputation was an excellent and long-lasting operation.

Arthroplasties of Hip

Mrs. M. M. SHEPHERD (Birmingham) reviewed 650 arthroplasties of the hip, followed up for a maximum of six years from operation, which in almost all cases was either of the 'Vitallium'-cup or acrylic-head type. Excepting loss of pain, stability and satisfactory unconscious control of the hip were of greatest value to the patient, but the better the range the better on the whole was the result. Even so the mobility index (Gade) was not much worse in the poor than in the excellent results. With regard to durability, cup arthroplasties went on improving for up to four years, when 45% had good or excellent results; after five years 54% had poor results. The Judet arthroplasty was characterised by quicker recovery, but the result deteriorated sooner and progressively. Not all arthroplasties deteriorated in later years. Mrs. Shepherd believed that arthroplasties with no inserted foreign material lasted best, then those with unfixed inserts (e.g., cups), and lastly those with fixed prostheses. The percentage of good results was higher in unilateral than in bilateral cases, and in the latter it was higher when only one hip was operated on.

Broken Acrylic Head

Mr. PRIDIE expressed his dissatisfaction with the Judet arthroplasty, which he maintained should be reserved for those with a brief expectation of life. In his hands 5-10% would fracture their prostheses. Even at a year distinct flattening and wear of the head was to be seen, and he thought that when flattening was not evident the prosthesis was rotating in the femoral neck. In his survey 20% had loose prostheses, though these might become fixed again by a period of plaster fixation. As an alternative to replacing the head when fracture or a poor result necessitated further operation he considered the Girdlestone "pseudarthrosis" satisfactory.

Kyphoscoliosis

Mr. J. I. P. JAMES (London) called attention to the lack of British work on kyphoscoliosis. Apart from that occasionally seen in Pott's or Scheuermann's disease (where the scoliosis was usually mild), he classified his 27 cases into: (1) congenital; (2) associated with otherwise typical idiopathic scoliosis; and (3) associated with neurofibromatosis. In the first group radiography or operation displayed the malformation, but even early films of the second group showed no vertebral abnormality. Congenital cases occurred usually in the lumbodorsal region, but occasionally in the cervicodorsal region. The deformity was progressive and severe, and might cause paraplegia. Early operation was indicated, but fusion was difficult.

Wedge Excision for Scoliosis

Mr. R. ROAF (Liverpool) described an operation of wedge excision of the vertebrae for scoliosis. He pointed out that ordinary "correction" affected the transitional vertebrae at each end of a curve but left the central fixed portion unchanged. There had been fear of direct operation, because of the difficulties encountered in attempting excision of hemivertebrae. With experience of anterolateral decompression, skilled anaesthesia, and plaster work of the highest order, he had found no great difficulty in doing what was really a lateral osteotomy of the spine. At the apex of the curve the posterior parts of two ribs were removed; from the two underlying vertebrae were removed the transverse processes, pedicles, intervertebral joint, and part of the laminae on one side. Aiming at a subperiosteal enucleation, a wedge of bone was then removed from the bodies of the two vertebrae, including in the wedge the intervening disc. A few days later correction was obtained in a Risser jacket, and treatment proceeded on usual lines. Ideally bony union between the vertebral bodies occurred, but in the event of failure later spinal fusion might be needed. This was not an easy operation for routine use, but was offered tentatively for those curves not responsive to other methods.

Control of Prostheses

Dr. JACK JOSEPH, Mr. A. NIGHTINGALE, and Mr. C. K. BATTYE demonstrated the prototype of an invention of Prof. JAMES WHILLIS by which in amputees the electromyographic currents in the stump could be made to work a switch and thus electrically motivate a prosthesis.

Fractures of Femoral Neck

Mr. C. M. M. MURRAY (Portsmouth) presented a review by Mr. G. N. GOLDEN (Guildford), Mr. A. G. ORD (Portsmouth), and himself of 60 cases of fractured necks of femur treated by primary replacement with Judet's acrylic prosthesis. There was no immediate mortality, but 7 patients died while still in hospital. Later complications included 2 dislocations, 2 fatal cases of infected haematoma, 1 broken prosthesis, late ossification in the capsule, and late varus deformity. At eighteen months over 80% had a satisfactory result, and he recommended the operation for the older age-groups, especially those with high or vertical fractures.

Mr. J. C. F. CREGAN (Manchester) reviewed 65 cases of high fracture of the femoral neck similarly treated. In contrast to the satisfactory immediate results, by the third year 85% suffered increasing pain and disability, and by the fourth year results were even worse. He thought that the integrity or otherwise of the region of the calcar femorale had an important bearing on these results.

Mr. PRIDIE pointed out that with a Smith-Petersen nail 50% of patients at five years had a hip indistinguishable from normal, and deplored the use of an acrylic head in immediate treatment—a view supported by Prof. D'AUBIGNÉ.

Hand Wounds

Prof. MICHAEL MASON (Chicago) discussed the importance of primary closure of wounds of the hand, the only exceptions being those due to bites, and war wounds where early evacuation was necessary.

Injuries of Hand

The demonstrations included one by Mr. R. G. PULVERTAFT (Derby) of the results of treatment of injuries of the hand. The principles of his methods embodied: (1) immediate toilet of the wound; (2) fixation of fractures by internal methods when necessary; (3) primary tendon repair when there were no doubts regarding the cleanliness of the wound; (4) late nerve suture; (5) complete closure of the skin covering; and (6) reduction of the reactionary swelling.

ROYAL SOCIETY OF MEDICINE

Stammering

THE section of psychiatry met on May 11, with Dr. E. B. STRAUSS, the president, in the chair, to discuss Stammering.

Dr. LEOPOLD STEIN said that the fundamental symptom of stammering was the rhythmical sound like "wa-wa-wa-wa, pa-pa-pa-pa," which seemed funny and childish because it corresponded to the baby's babbling. To explain how this symptom arose it was necessary to expound the nature of this pattern first. Speech was made up of two components—vocal sounds and oral noises added to this. The breath-stream component took three main forms, technically known as "attacks" from the Italian *attacca* (start or onset): (a) the aspirated attack produced by air escaping between the vocal cords and setting them in vibration (e.g., the sigh of relief); (b) the soft attack in which sound followed gentle approximation of the cords, producing a grunt; and (c) the hard attack or glottal stop, an explosive sound produced by escaping air forcing open the closed glottis. If marked, this sound was aesthetically unpleasing, whereas the two preceding ones were pleasant. These "attacks" were probably developed from biological needs, the first two to counteract sudden deflation of the lungs and, by closing the glottis, to prevent the intrusion of foreign bodies (in the first instance, food).

The second main component of speech was derived from the oral sucking noises—technically termed "clicks"—which were part of the rhythmic vegetative mechanism that enabled the infant to suck by creating successive vacua in the mouth. The "attacks" by their expulsive protective nature came to symbolise anxiety and warding-off an intruding "bad object," while the "clicks" from their origin in sucking symbolised union with the mother and primitive social erotic contact.

To begin with, these two types of sound were independent, but later they became integrated. When this integration of the expulsive and sucking components was complete, it might be said to represent the normal give-and-take between mother and child. At a later stage the sucking element in speech was given up—it was found in adult speech only in some primitive tribes—and the "clicks" were reversed into consonants. At this stage the child began to realise that the people around him also made vocal noises and that by this means they got others to do things for them. Striving to emulate this, he made use of his babbling, and this gradually evolved into speech; baby-words such as "boom-boom" and "kokopumpum" were shortened and the child said "book" and "chocolate pudding." Inhibition of the pleasurable reiteration, which was one of the baby's primitive erotic gratifications, was the price paid by him for obtaining better control over his environment by speech. Independent words were later arranged by the child in sequences of his own, to express his various individual thoughts—a process which went on all through his life.

In stammering the most highly developed level of speech first broke down—that of coöordinating mental patterns with verbal motor patterns. The preceding level was thus released, and the child or adult under conditions of stress reverted to the pleasurable rhythmic speech pattern of babbling—e.g., in "lalalamp" for "lamp." At first this was not noticed by the stammerer; but if he were ridiculed or checked, both he and his listeners unconsciously resenting the erotic exhibitionism symbolised by his babbling, the next stage would follow: the clonic repetitive babble would be inhibited and a tonic stage ensue. Rage at this frustration showed itself in tonic stammerers by facial gestures, such as baring or grinding the teeth, and by kicking or hitting movements. With greater frustration conscious speech phobias became commoner, and at the next stages complete "freezing-up" would take place. This might take the form of bodily rigidity and a long silence, after which the stammerer would say "I don't stammer but it takes me a long time to get my words out." At this level the babbled utterances might split into their original components—"attacks" and "clicks." When the infantile crying level was reached regression was complete and the stammerer felt himself surrounded by a hostile world: he concealed his anxiety and his aggression by evasive tricks, avoiding difficult words and using meaningless stop-gaps ("also, also—as well, as well—also—I beg your pardon"). He masked his depression by an air of unconcern, aloofness, and superiority. The apparent ease of speaking in stammerers at this stage should not tempt us to think the symptom unimportant.

Mrs. MARY WILLIAMS had taken the histories of 100 male stammerers aged 16–50. (Women stammerers were not studied because their numbers were so few.) What had impressed Mrs. Williams most in taking these case-histories was the rarity of anything unusual; one might say almost that a stammerer had no history. Partly this was due to the long childhood amnesia, extending up to the 11th year in some cases, partly to the fact that the patient appeared unobservant of other people and usually described everything and everybody in his life-story as "all right"—except for his stammer. Treatment was almost invariably sought from motives of ambition. Nearly all the patients could do their work and pass examinations but had difficulty with their superiors and therefore feared they would be passed over for promotion. Most of them blamed their lack of success on the stammer, but a few realised that even apart from this they could not take responsibility. Questioning was difficult because any topic causing mental conflict made the stammer much worse; it was

found that a "shock and soothe" technique was best: if a direct request for the expression of the patient's own opinion produced shock, he would often respond with relief to a question asking him what somebody else would think on the topic.

The attitude to the parents was characteristic. Only 5 gave unqualified praise of their father; the others described the father either as strict and forceful or as cold and remote. 23 expressed unqualified praise of their mother; most often she was described as worrying or fussy, and 20 said she had "nerves." The stammerers usually described the home atmosphere as one of tension. 25 said they had a happy home despite previous remarks—e.g., about their father's harshness—which obviously contradicted this statement. 17 came from broken homes, but economic and social insecurity did not seem to be a major factor. As regards siblings, they usually felt jealous or envious or had "nothing in common" with them in earlier years, but later became "friends." 18 gave a family history of stammering, usually on the father's side, and 10 had fathers who had stammered but who were said to have got over it. The onset of the stammer was often attributed to an accident or shock; but this was substantiated in only 18 cases, and mostly it was through admission to hospital in early life. It more often started on first going to school. 20 had other psychosomatic disorders, such as asthma, migraine, eczema, dyspepsia, and bed-wetting; these presented a more neurotic picture. Many of them overcompensated by excelling in sport and in scholastic subjects, especially English and art. They had a wide variety of occupations, noticeably not of the kind leading to isolation. There were signs of attempts by the father to get the son to follow his trade or profession, but if the boy did, he tended to fail. 44 served in the Forces, most of them efficiently, but they were doubtful risks in battle. 43 described themselves as sexually normal, but 20 felt they were lacking in libido. The remaining 37 admitted various difficulties—11 had disturbances of potency, 13 were inhibited or afraid of women, 9 complained of masturbation, 6 had homosexual tendencies, and 3 had other perverse tendencies. 32 were married and 27 said their marriage was happy. They described their wives as active, lively and capable, and it seemed that they chose wives who were protective and rather dominating.

Miss THEODORA ALCOCK said that as a child psychotherapist she did not claim to have had much experience of stammering, but she regarded it as an ego-defence symptom. It was related to oral conflict and to the infant's desire to make contact with the mother's breast. In a primitive African tribe among whom she had lived stammering was unknown, and she thought this was related to the habit of giving the breast to the child until it showed no further desire for it. Stammering was the antithesis of the condition referred to as verbal diarrhoea, and she had noticed that stammerers often suffered from chronic constipation. It was another form of magical control of their aggressive impulses directed towards the mother.

The PRESIDENT reminded the meeting that over 60% of stammerers showed signs of right-sided cerebral dominance, often associated with left-handedness and crossed laterality. Other syndromes, such as tics and word-blindness, were associated with stammers. Might not a neurogenic basis be the simplest explanation and might not the psychological factors be secondary to this?

Dr. GERALD GARMANY agreed that crossed laterality was important and pointed out the strong familial tendency. He thought that many stammerers had no psychiatric abnormality as ordinarily assessed, and were not socially or economically disabled by their stammer. Some stammers were simply due to mimicry or to an intelligent child thinking faster than it could speak.

Dr. J. A. HOBSON said that the stammerer often had difficulty in bodily coördination as a whole. A stammer had some value to the patient; removal by hypnosis or suggestion might release psychotic tendencies.

Replying to the debate, Dr. STEIN said that the stammer of patients recovering from aphasia and of soldiers suffering from blast injuries were the only types that could be explained in a neurological framework.

Reviews of Books

The School and the Site

A Historical Memoir to Celebrate the Twenty-fifth Anniversary of the School. London School of Hygiene and Tropical Medicine Memoir Series, no. 9. CATHERINE M. CLARK, M.A., JAMES M. MACKINTOSH, M.D. London: H. K. Lewis. 1954. Pp. 105. 21s.

THE 25th anniversary of the opening—not the foundation as stated in the preface—has properly occasioned the publication of a historical memoir. It is in three parts: the site and its earlier history; the school on the site; and appendices with details of the governing bodies, staff, and statutes.

The history of the site at the corner of Keppel Street and Gower Street covers, first, the open land, with tales of duels behind Montague House; next the building development at the end of the 18th century by the fourth Duke of Bedford's widow; then the dwelling-house period, when Constable, Trollope, and Parnell lived in Keppel Street; then clearance, at the beginning of the 20th century, with abortive proposals for the Shakespeare Memorial Theatre, and a Y.M.C.A. hut for soldiers during the first world war; and finally redevelopment by the school, made possible by a grant of \$2 million by the Rockefeller Foundation. The early administration, the different departments, including the Ross Institute, the Bureau of Hygiene and Tropical Diseases, the field station near St. Albans, and the related hospital facilities, are described fully; but, seeing that the school has been described as one of the best examples of modern architecture in London, one would have liked more than a reference to the architect, V. O. Rees, and his problems. With its lavish maps and photographs the memoir is a most worthy memorial, which makes us regret the lack of almost contemporary publications on the early history of other London medical institutions.

Oral and Facial Deformity

C. KERR MCNEIL, PH.D., L.D.S., senior lecturer, University of Glasgow. London: Sir Isaac Pitman. 1954. Pp. 127. 25s.

IT is an unfortunate fact that surgical treatment of cleft palate, though it may succeed in its primary object, often deforms the arch of teeth. This contraction of the maxillary arch, which is not seen when the condition is untreated, has now become tacitly accepted as an unfortunate but unavoidable sequela. Kerr McNeil has suggested, as a new approach, the application of orthodontic principles and methods, and claims that growth of bone in the region of the cleft in the hard palate can be obtained in this way. A good historical survey of the subject is followed by a discussion of congenital abnormalities of the face and jaws. The importance of getting the upper lip forward, by means of an appliance, at the earliest possible stage after operation for cleft palate and hare-lip, in order to disguise the characteristic facial deformity with its associated psychological disturbance, merits more emphasis than he gives it. Many of the devices shown for retaining appliances in position in difficult cases are of novel and ingenious design, but it would have helped considerably if the photographs, which are good, had been more fully explained in the text. Though not everyone will agree with all his conclusions, controversy stimulates thought, and Kerr McNeil is to be thanked for suggesting a fresh approach to an old problem.

Handbook of Tropical Dermatology and Medical Mycology

Vol. II. Editor: R. D. G. PH. SIMONS, senior lecturer, dermatological clinic, University of Leyden. Amsterdam and London: Elsevier Publishing Company. 1953. Pp. 1705. £5.

THE second volume of this work covers diseases caused by animal parasites, fungi, malnutrition, metabolic disturbances, and tumours. It has been written by 58 contributors, many of them distinguished in their fields, others less well known. As in the first volume, the aim has been to cover "every tropical skin affection with a completeness never before achieved in a single work." This can fairly be stated to have been done, though critical selection of material would have been a better aim. The section on nutrition and the skin is exceptionally good, and the illustrations are profuse and uniformly excellent. The standard, however, is uneven, and there are many loose statements and inaccuracies: for example, the treatment recommended for patients harbouring *Enterobius vermicularis* is "one gram tablets of gentian violet three times daily before meals for a two weeks period." Not only is the value of gentian violet in this infection doubtful, but the correct dose is 1 grain, and even this small quantity should be given in a keratin-coated tablet. A dose of 1 gramm causes very severe vomiting and purging, which in children might have grave results. Such errors tend to undermine confidence in a work which generally reaches a high standard. It contains a wealth of information drawn together from sources not usually readily available.

Pain Syndromes and their Treatment

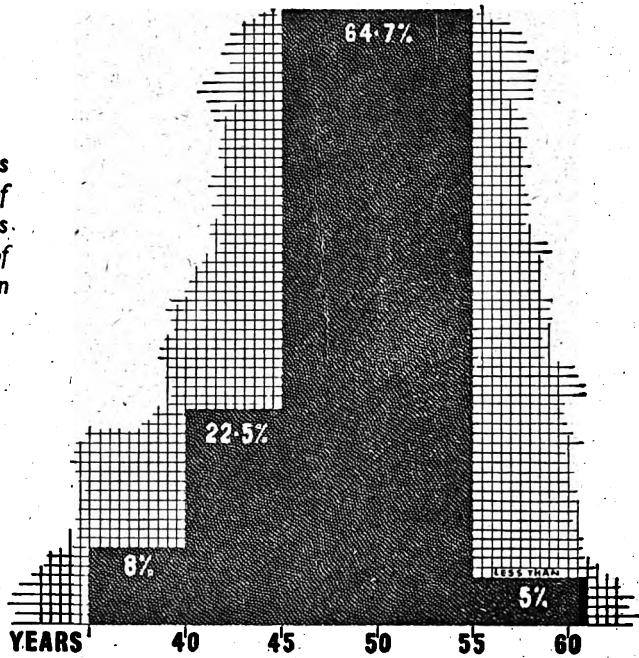
With Special Reference to Shoulder-arm Pain. JAMES M. TABSY, M.D., chief, arthritis clinic, University Hospital, New York. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953. Pp. 591. 86s.

THE tail, not the head, of its title justly describes this book, which is not concerned with pain syndromes in general, or with the place of pain in diagnosis, but is an elaborate study of shoulder-girdle, upper thoracic, and arm pain, mainly of arthritic or mechanical origin. It sets out to analyse the pain itself, the anatomical, pathological, and aetiological basis of each pain syndrome, and the clinical signs to be elicited in the conditions responsible. The extreme complexity of the subject is amply shown, and the book is likely to appeal more to the rheumatologist, or perhaps the orthopaedist, than to the more general clinician, who may find himself more bewildered than enlightened. After considering pain generally and regionally the authors discuss all available means and methods of treatment, without apparent bias; but this section, too, is for the expert—especially when it comes to handling the long-needed syringe—rather than for the general clinician or even the surgeon.

In this, as in many other books from the United States, a contrast is evident between the skilful use of pen and camera in diagram and photograph and the relatively unskilful use of words. Neglect of the art of writing makes for heavy reading.

Your Rheumatism. What you can do about it (London: Cassell. 1954. Pp. 173. 10s. 6d.).—Mr. Robert Potter, an American journalist, was executive director of the 7th International Congress on Rheumatic Diseases held in 1949 in New York, and he undertook "to turn the medical manuscripts into a layman's volume on rheumatism." He has done his work well, expounding technicalities with skill, not slurring hard facts, and presenting claims with moderation. But cortisone and corticotrophin are the main theme of ten out of twenty-four short chapters, and though their shortcomings and dangers are not concealed they are given an important place in curative treatment. In the present state of knowledge, opinions will differ on whether it is well to give the public this favourable view, at a time when these hormones may become more widely available for the treatment of rheumatic patients.

Graph showing percentages of average age of onset of menopause, drawn from figures compiled by the Council of Medical Women's Federation in England.



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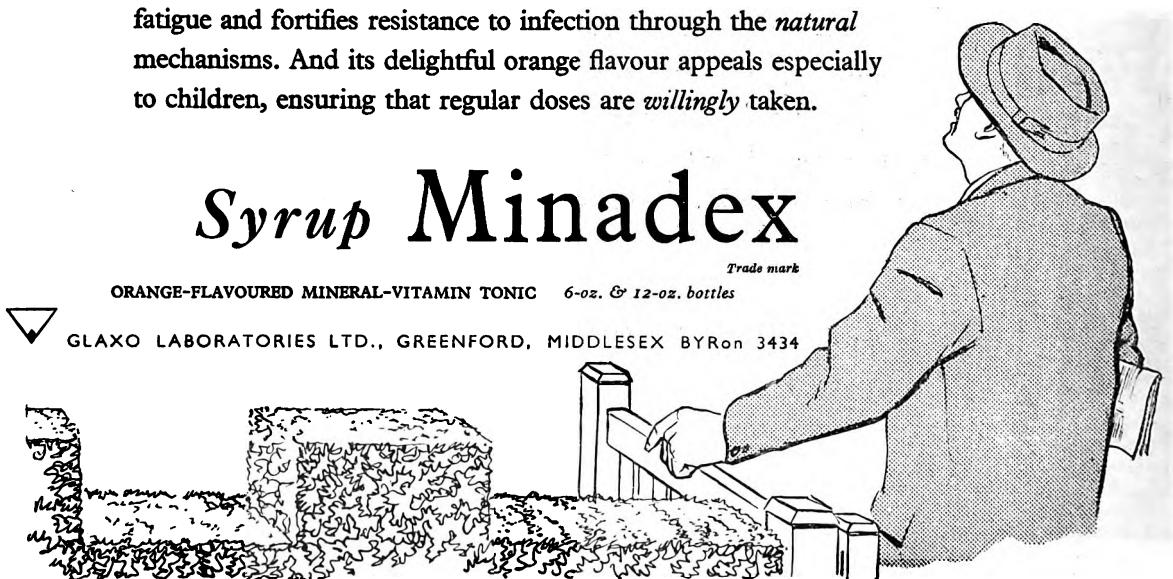
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THE LANCET

LONDON : SATURDAY, MAY 29, 1954

Mental Care: a Different Pattern?

In the last official statement, the degree of overcrowding in our mental hospitals was put at 14·7%, the highest figure yet reached. Indeed, it looks as though, after spending some decades in persuading patients to come into the mental hospitals for treatment, we must now find ways of persuading them to stay out, or anyhow to leave earlier. Nor are these things impossible, given the necessary adjustment of mind and practice.

In his important contribution which we published on May 1, Dr. J. A. R. BICKFORD points out that, though mental hospitals mostly cater well for the acute recoverable case, they certainly do not favour remission of the longer illness and in fact must often postpone such remission. BICKFORD rightly takes the profession to task for getting such poor results with long-term mental cases, and suggests that more interest in them and a more energetic programme of reablement would allow many chronic patients to return to the outside world, and some to take up work again. All psychoses, he believes, remit in time; and anyway the mere possession of delusions is not a bar to life in the community, provided the patient does not act on them in a way to endanger himself or to harm or annoy others. Yet many people who have reached this stage of adequate social recovery remain in the wards because, in the course of their long illness, they have outgrown the concern of their friends and relations: they have nowhere to go. If attention to their needs had continued after the first few months, some of them would have recovered sooner and would not have lost touch with their former lives. Even at this late stage, many could, as BICKFORD says, be transferred from the hospitals to outside hostels, run by mental nurses, from which some of them could go out daily to appropriate work. Apart from the relief of overcrowding in the chronic mental wards, this plan would have a therapeutic effect on many apathetic and despairing people who see no hope of getting out into the world again.

Moreover it would release more beds for patients who are acutely ill. But are we in fact sure that we need so many more beds? On another page Dr. T. M. LING argues that admissions and readmissions to hospital could be reduced, and he cites the experience of Amsterdam in showing how much patients can be helped, and hospitals relieved, by early outpatient care, steady home visiting, and aftercare of those discharged. This experience has been described by QUERIDO,¹ who explains that when the municipal medical service of Amsterdam was reorganised after the 1914-18 war a psychiatrist was appointed to

advise on the admission of patients to mental hospitals. Soon the psychiatrist was asked to undertake the supervision of the "socially unfit"—a term covering patients with mild chronic psychosis, epilepsy, mental defect, and organic nervous disease. Given favourable surroundings, many of these patients could contribute to their own livelihood, and it became necessary to find foster-homes and to see that sheltered workshops were available. From this it followed naturally that, when admission to a mental hospital was sought, the psychiatrist would investigate the home circumstances and decide whether treatment in hospital was essential. This was the beginning of preventive care for adults, and before long the department had to be enlarged and strengthened so as to be able to offer a system of psychiatric first-aid. A centre was set up, where there was (and is) a psychiatrist always on duty, day and night; and anyone needing help or advice about a patient can get into touch with this centre. Those seeking such help include general practitioners, specialists who decide that a patient can no longer be kept at home, factory managers whose employees are taken ill at work, and the police when they have doubts about the mental condition of someone taken into the police-station or under arrest. (In all cases of sexual offences, and with all offenders over 70 years of age, the police seek this help as a routine.) Except when the call is from a specialist, the psychiatrist goes at once to see the patient—which usually means that he sees him in his home surroundings and so can assess the share these have had in determining a breakdown. Amsterdam, QUERIDO says, abandoned many years ago the practice of taking a patient into hospital before investigating his case.

Some patients, of course, do need to be admitted direct to hospital; but, as the experience of the department's staff has increased, the proportion of these has fallen. Many patients can stay at home if suitable advice is given and if the family are supported by visits from the psychiatrist and his social workers. The very fact of demonstrating to other members of the household that the patient can be quieted and handled in a reasonable way is of great educational value. Often the patient's excitement is largely an emotional reaction to financial troubles, quarrels at home, loss of a job, arrest by the police, or some other situation which threatens his security. Such things may provoke a hysterical or psychopathic outburst taking the form of a suicidal attempt, motor excitement, drunkenness, or maniacal or confused episodes. It does not benefit such a patient, QUERIDO finds, to admit him to a mental hospital, even for a short time. The hospital only too easily becomes a haven from his troubles; and, when he is discharged, any new difficulties he encounters inspire him to seek the same solution. It is much better that he should be made to face his difficulties at the first interview and that the "outlet" into hospital should be kept firmly closed: he should be offered help, sympathy, and understanding, but not an easy line of escape. This turns our own ideas topsy-turvy—but perhaps (as Dr. LING thinks) none too soon.

When QUERIDO wrote his report in 1950, Amsterdam had a population of 850,000 with about 400 psychiatric beds at its disposal, and the number of people under the department's supervision was then some 3000. Their homes are regularly visited, at longer or

1. Querido, A. *Int. Hlth Bull.* 1950, 2, 13.

shorter intervals as their case requires, either by a psychiatric social worker or by a psychiatrist, and always the aim is to teach the family to live with the patient, and the patient with the family—no other treatment being given. To many in this country this system of home visiting will recall the one developed by the National Association for Mental Health during the war but afterwards discontinued. Under the National Health Service Act the local health authorities now have power to provide similar services, but so far only about thirty of them have begun to use these powers. Of these, the London County Council has started a scheme which is expected to grow; and already its three psychiatric social workers are being asked—usually by general practitioners—to visit people who have not reached the stage of going to a mental hospital. Thus it may be said that the seed of a preventive service is in the ground, and even germinating. But equally it is evident that we have nothing that yet performs all the functions of the Amsterdam service; and before we commit ourselves to a vision of the future consisting in more (as well as better) mental hospitals we ought to consider very carefully, as in general medicine, whether the hospital should occupy so much of the picture.

Cytotoxic Therapy for Reticuloses

UNTIL quite recently the treatment usually recommended for the reticuloses, including the leukæmias and Hodgkin's disease, was exposure to X rays. Yet even in the heyday of radiotherapy some physicians were looking for other methods of treatment. X-ray treatment has its disadvantages: the exposed area is likely to become scarred or even burnt; and aplastic anaemia is liable to ensue even when the dose seems safe. Moreover it is hardly rational to expose a single organ or a group of organs to the rays and to leave all the other affected areas untreated—for example, to treat the enlarged spleen of a patient with chronic myeloid leukæmia but do nothing about the bone-marrow. Radiologists themselves were aware of this, and methods of whole-body irradiation were proposed; but these never became popular, perhaps because the local methods were so often successful. The only chemical rival to X rays was benzene for chronic leukæmia, but this proved so difficult to control and so liable to cause aplastic anaemia that its use soon ceased. The present application of cytotoxic chemicals to the treatment of leukæmias and Hodgkin's disease springs from the clinical trials with nitrogen mustards by WILKINSON in this country in 1942 and corresponding trials by American workers in the succeeding years. Nitrogen mustard is given as the di- or tri-chloro-ethylamine; the former has been more widely used, because it was commercially available, but WILKINSON prefers the trichloro form, and this too may now be had. Both these forms are notably effective in the treatment of chronic leukæmias and Hodgkin's disease, but are ineffective against acute leukæmias, and are less effective than X rays against lymphoreticuloses such as the Brill-Symmers syndrome. WILKINSON¹ found that among 70 patients with chronic myeloid leukæmia splenomegaly was completely relieved in 32, partly relieved in 34, and unrelieved in only 4; while among 48 patients

with chronic lymphatic leukæmia lymphadenopathy was completely relieved in 15, partly relieved in 29, and unrelieved in 4. In Hodgkin's disease the trichloro form brought about shrinking of swollen lymph-glands in all except 9 of 54 cases. The main disadvantage of nitrogen mustards is that, to be effective and safe, they must be administered intravenously in a running saline drip; furthermore a few hours after the injection there is sometimes really troublesome nausea and vomiting, which is difficult to control; in some patients repeated doses eventually lead to sclerosis of accessible veins, and this may have serious repercussions if blood-transfusion becomes necessary; and finally the results show that nitrogen mustard is less effective in lymphatic than in myeloid leukæmia.

BEATTIE and HOWELLS² have described some of the efforts to find better drugs. They end their review in 1952, and it is a measure of the activity—if not of the progress—in this field that most of the information they give is even now of historical interest only. A compound that did appear promising was triethylene-melamine (T.E.M.)³. This was found to have the cytotoxic action without the mustard activity; it could be given intravenously in small volumes of fluid without causing local phlebothrombosis, or it could be given orally; and it gave promising results in the treatment of lymphatic leukæmia and the other lymphoreticuloses that were relatively less responsive to nitrogen mustards. But extended experience with T.E.M. has brought to light serious disadvantages. MEYER and his group⁴ treated 67 cases and confirmed that the best results were in lymphatic leukæmia; but in Hodgkin's disease it was disappointing. They noted that it was very difficult to find a suitable dose, since individual variation was great—from 15 to 165 mg. in different patients. The margin of safety was very small, and it was distressingly easy to produce leucopenia or irreversible pancytopenia owing to damage to the marrow. SILVERBERG and DAMESHEK⁵ found T.E.M. by mouth effective in Hodgkin's disease, even sometimes where the disorder had become resistant to radiotherapy. Vomiting occurred in about half their patients; and they too remark on the risk of bone-marrow hypoplasia. PATERSON et al.⁶ administered the drug in enteric-coated tablets, in an attempt to overcome the individual variation in effective dosage. This device did enable them to assess doses more closely on the basis of body-weight; thus for Hodgkin's disease 0·2–0·3 mg. per kg. given in divided doses spread over two or three days, or as a single undivided dose, was usually effective, and for chronic lymphatic leukæmia 0·1–0·2 mg. per kg. was recommended. But, like other workers, they found that haemopoietic tissues were very sensitive to T.E.M., and lymphocytes were affected along with other cells. PAVLOVSKY and VILASECA⁷ in the Argentine also thought that T.E.M. was most effective

2. Beattie, J. W., Howells, L. H. *Quart. J. Med.* 1954, 23, 231.
3. Karmofsky, D. A., Burchenal, J. H., Armistead, G. C. jun., Southam, C. M., Bernstein, J. L., Craver, L. F., Rhoads, C. F. *Arch. intern. Med.* 1951, 87, 477.
4. Meyer, L. M., Schwartz, S. O., Sawitsky, A., Bergers, M. R., Ritz, N. D., Brahn, C., Diefenbach, W., Kleinschmidt, W., Friedman, I. *Acta med. scand.* 1952, 144, suppl. 272.
5. Silverberg, J. H., Dameshek, W. *J. Amer. med. Ass.* 1952, 148, 1015.
6. Paterson, E., Kunkler, P. B., Walpole, A. L. *Brit. med. J.* 1953, 1, 59.
7. Pavlovsky, A., Vilaseca, G. C. *Sang.* 1953, 24, 578.

1. Wilkinson, J. F. *Proc. R. Soc. Med.* 1953, 46, 685.

in chronic lymphatic leukaemia. AXELROD et al.⁸ confirmed the general effectiveness of T.E.M. in lymphoreticuloses but reported that in chronic lymphatic leukaemia hypersensitivity occurred occasionally, so initial doses needed to be very small. They added to the list of possible complications renal and hepatic damage, haemolytic anaemia, and hyperuricæmia due to rapid breakdown of leucocytes. Though these reports gave qualified approval to triethylene melamine, this has not superseded nitrogen mustard. The reasons were made clear in a discussion at the Royal Society of Medicine last autumn. Thus NABARRO,⁹ though he found that oral T.E.M. was an effective palliative in Hodgkin's disease, declared that it was a dangerous drug liable to cause aplasia of the bone-marrow; great care was needed in planning courses of treatment, which had to be widely separated. HADDOW¹⁰ was no less cautious.

At least three other compounds of the mustard group are now on trial. KIMURA and his co-workers¹¹ at Nagoya have proposed the use of the N-oxide of methyl-bis-chloro-ethylamine ('Nitromin'), which is claimed to have a comparatively low toxicity and few side-effects. Doses of 50–150 mg. daily were given intravenously in 20–40 ml. of glucose saline; good results were claimed in 6 patients with chronic myeloid leukaemia to whom total doses of 1050–1450 mg. were given. The drug was of no value in acute leukaemias. SHAY et al.¹² have used triethylene-thiophosphoramide. This substance can be given intramuscularly or intravenously; orally it is effective but causes nausea. Doses of 10–20 mg. weekly have so far produced no toxic effects, and good results are claimed in chronic myeloid leukaemia, chronic lymphatic leukaemia, and Hodgkin's disease. Finally 1 : 4 dimethanesulphonyloxybutane ('Myleran'), which was devised by HADDOW and his colleagues¹³ for the treatment of chronic myeloid leukaemia, has proved effective given orally, though this effectiveness may be limited to single courses. A quite different substance lately on trial is 6-mercaptopurine. This substance was tested in the course of a general trial of purine and pyrimidine compounds allied to the folic-acid antagonists, which have sometimes proved effective against acute leukaemias. Mercaptopurine is given orally; in toxic doses it depresses all bone-marrow cells, but otherwise it is remarkably free from undesirable side-effects. BURCHENAL et al.¹⁴ found that results were best in the acute leukaemias of children; of 45 patients treated, 15 had remissions, some of which were in cases resistant to folic-acid antagonists. The only other disease influenced by mercaptopurine was chronic myeloid leukaemia in adults. Mercaptopurine is not a very effective drug; it is relatively slow-acting, and apparently in acute leukaemia therapeutic resistance develops fairly quickly. But the moderate effectiveness of such a compound indicates that the group of purine and

pyrimidine derivatives should be further explored. The latest drug to be tested is phenylbutazone. ROTTINO et al.¹⁵ administered this in Hodgkin's disease. Not unexpectedly it did not clearly act on the disease itself, but it proved useful in controlling the fever and the pain that some patients have, and in some it relieved the distressing pruritus; the dose used was 600–1200 mg. daily by mouth.

The chemotherapists are trying hard to find drugs to control the reticuloses. HADDOW,¹⁰ who has contributed much to these researches, has said that none of the agents at present in use is likely to gain a permanent place in therapeutics. He thinks that we have not fully exploited our present knowledge, and he looks forward to the time when these diseases will "come under the influence of chemical agents immeasurably more powerful and specific than any we have at our command today."

Arthroplasty v. Arthrodesis

THE British Orthopaedic Association gave a good deal of time at its annual meeting (reported on p. 1113 of this issue) to examining the question whether arthroplasty of the hip has succeeded in its purpose. From the growing mass of information it appears that the high hopes held by the advocates of both cup and acrylic-head arthroplasties are not being fulfilled, and not unnaturally there is a reactionary trend towards the older-established methods of arthrodesis, displacement osteotomy, and even the earlier forms of arthroplasty which did not involve metallic or synthetic inserts.

The variety of methods of arthrodesis reflects the difficulty of producing certain fusion of the hip-joint: and most operations of this type have to be followed by prolonged splintage, which is a burden both to the patient and to the hospital service. But the need for such long immobilisation, which may cause the knee to stiffen, has been largely overcome by new methods, including BRITAIN'S V-arthrodesis and CHARLEY'S technique of central dislocation, where splintage is either unnecessary or does not include the knee-joint. Once fusion has taken place the patient has a strong, painless, stable hip, the condition of which does not deteriorate except occasionally in growing children. A man can often return to his heavy work, a woman to her housework and shopping. It is true that sitting upright is possible only in a high chair, and that putting on shoes and stockings may be difficult for the elderly: but these are minor objections. In the young and middle-aged arthrodesis is vastly preferable to any form of arthroplasty; but in the elderly arthrodesis can be undertaken with no great confidence, since the increased strain on the lumbar spine may cause incapacitating low-back pain. AUSTIN BROWN¹⁶ believes, however, that this risk is negligible if the hip is fused in neutral abduction-adduction, by which hip movement is replaced almost entirely by flexion-extension movements of the lumbar spine; this being the normal movement in this region, progressive degeneration need not be feared.

There are obvious advantages in a mobile hip, and we should surely not accept arthrodesis as the best

8. Axelrod, A. R., Berman, L., Murphy, R. V. *Amer. J. Med.* 1953, 15, 684.
9. Nabarro, J. D. N. *Proc. R. Soc. Med.* 1953, 46, 696.
10. Haddow, A. *Ibid.* p. 692.

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possible measure. Mrs. SHEPHERD's review (mentioned on p. 1114) showed that the results of cup arthroplasty had commonly deteriorated after five years, when about half were unsatisfactory ; but many patients still retained extremely good function and could do far more than those with a fused hip. Patients with an acrylic head obtained good function earlier, but this deteriorated sooner ; and they were liable to their own peculiar complications from fracture, wear, or loosening of the prosthesis in its socket. It is easy to enumerate the essentials of a good arthroplasty—relief of pain, mobility, stability, durability—but it must embody what CAPENER has called congruity and conformity of hardness, together with maintenance of proper lubrication and adequate power, which itself depends on the leverage provided. We have not yet attained these ideals. In normal articular cartilage, and perhaps in the fibrocartilage that forms by metaplasia of fibrous tissue over the raw bony surfaces after arthroplasty, there is a critical load per unit area ; if this is regularly exceeded degeneration

ensues. Thus the perfect congruity which is the goal of present arthroplasties seems desirable ; the "business" surfaces of all cups and prostheses are parts of spheres, and accordingly the load is spread over the greatest possible area. But no normal joint surface has the same radius of curvature over all or even most of its area. Articular cartilage is compressible and has peculiar elastic properties similar to those of a sponge, and probably waves of compression passing to and fro over a joint surface during movement are partly responsible for the proper nutrition of the cartilage, fluid being squeezed out of this on compression and re-imbibed on release. Perhaps, for durability, prostheses and cups should also have slightly changing curvature.

Arthroplasty of the hip is not merely desirable : in bilateral hip disease it is often essential. Certainly no method yet devised gives consistently good and lasting results, but this is no reason to give up the battle. Success may be as likely to come from study of successes as from analysis of failures.

Annotations

"FAMILY MEDICAL CENTRE"

"Among the general practitioners in this country we have a wealth of craftsmanship which is being only half used. Capable men and women, who are willing to take responsibility, are spending too much of their time shifting this responsibility elsewhere because in some places they lack a few simple facilities to enable them to diagnose and treat their patients themselves."

WITH this challenging statement Dr. J. G. Ollerenshaw and Dr. J. H. Hunt open an article, in the May issue of the *Medical World*, which deserves attention from all those interested in the renaissance of general practice. Despite wide agreement that what the general practitioner needs is direct access to radiological and pathological facilities, nursing and secretarial help, and a closer liaison with the consultant and the public-health services, we wait upon ways and means. Health centres have proved expensive, and group practice, as usually undertaken, is not a complete solution of the problem. What Ollerenshaw and Hunt propose is a modified health centre serving all the family doctors in the neighbourhood. Such a centre could be created in converted buildings, or attached to a general-practitioner hospital, or adapted from an existing local-authority clinic. It would be provided, equipped, and maintained by the local health authority, with contributions from the regional hospital board and the local executive council, and it would be administered by a house-committee representing all who use it, not least the patients. The size, scope, and equipment of different centres would differ according to local needs. " Ideally the Family Medical Centre will provide every doctor with the opportunity to give his patients, near their homes, the simple treatment that every junior houseman can give in hospital." Nurses would be in attendance to assist with dressings, injections, minor casualties, and minor surgery ; a secretary would help with records, letters, and the telephone. A laboratory technician, under the supervision of a visiting pathologist, would provide the limited range of investigations necessary to the day-to-day work of the family doctor, and in the larger centres simple radiography would be undertaken. Combining some of the features of a diagnostic centre, treatment centre, and local-authority clinic, it is not meant to replace either the doctor's surgery or the hospital outpatient department, but to be a help to both.

Very important, in Ollerenshaw and Hunt's opinion, is that the family medical centre would be a common meeting-ground for members of all branches of the health service. General practitioners, consultants, and the staff of the local authority, who at present are often unaware of each others' aims and difficulties, would meet informally and casually in their work. More problems are solved and more trust and respect engendered over cups of coffee than round the committee table. By providing a congenial climate in which the family doctor could meet his colleagues, the family medical centre would do much to bridge the gaps that now exist between those who should be working constructively together for the patient's good. Regular visits by consultants, to see patients with whom the general practitioner can deal himself if given the right help, would help the family doctor to preserve interest in and knowledge of medicine. For the patient, it is suggested, the family medical centre would offer the advantage of nursing and diagnostic services brought near to his home and given under the care of his family doctor rather than by a stranger in some distant and overcrowded hospital.

Readers who have taken an interest in the centre lately opened at Corby¹ will be struck by the resemblance between Ollerenshaw and Hunt's "family health centre" and the Nuffield Trust "diagnostic centre." The need for this pattern of centre arises most obviously, we think, in places where the nearest hospital outpatient department is a long way off ; but it is of course capable of becoming a far more congenial medical focus than the ordinary outpatient department, and one can imagine that even a city hospital might usefully transfer some of its outpatient services to one or more local outstations of this kind, where people in all three branches of the service could work and meet. As most of the practitioner's work would still be done in his own surgery, where conditions of practice might still be bad, this type of centre would not necessarily lead to the same degree of environmental upgrading as was expected from health-centre practice ; but it could, at relatively low cost, do several things that would greatly encourage better practice.

MANHOLES AS MANTRAPS

IN an article in this issue, Dr. Hurwitz and Dr. Taylor draw attention to some unusual features of poisoning by sewer gas, and in doing so they emphasise that sewer-workers should be continually on their guard against the risk of this rare but violent poison.

1. *Lancet*, April 24, 1954, p. 871.

Another and perhaps less well-known danger in sewers is simple oxygen lack. There have been reports of two accidents in the United States in which 3 men lost their lives from asphyxia immediately after descending into manholes. In the earlier report¹ the accident occurred in a sewer manhole which was wet and situated in silty loam soil. In the more recent incident,² in Minneapolis, the manhole, 9 feet deep, was dry, was lined with concrete and mortar, and contained nothing more sinister than a water-main junction. Michaelsen and Park, who investigated this accident, found that mice lowered into the manhole sometimes died in about 20 seconds, and that the oxygen content was on some occasions as low as 3·2% at 5 feet and nil at 9 feet. The carbon-dioxide concentration was higher than normal. Since it is known that symptoms of anoxia appear at oxygen concentrations below 16% and that life cannot be sustained at concentrations below 6%, the deaths were clearly due to oxygen depletion. But the manhole had been entered twice daily without mishap for some time before the accident and there was no obvious explanation for the rapid loss of oxygen. The investigations that followed included continuous analysis of air-samples from the manhole under ordinary conditions, after blowing out with fresh air and after replacement by nitrogen. It was found that the local soil, sampled from the floor of the manhole, had a very high oxygen demand, and that the rate of gaseous diffusion and oxygen depletion could be remarkably rapid. Changes in barometric pressure had some, probably minor, influence on the rate of absorption. From extended observations on other manholes in Minneapolis it became evident that the dangerous sites were in low or swampy areas where the subsoil contained a large amount of organic matter. Most of the 19 manholes in such areas had a deficiency of oxygen at the time of sampling, 4 containing less than 16% and 2 less than 6%. None of the 25 on higher ground, mainly in sandy subsoil, had less than 17·3% of oxygen.

These accidents draw attention to a hazard associated with closed manholes, wells, or silos not naturally aerated. Such places should not be regarded as safe until they have been blown out with fresh air or tested for the presence of sufficient oxygen—for example, by lowering a safety lamp into them.

MASS CHEMOPROPHYLAXIS OF MENINGOCOCCAL DISEASE

In the second world war simultaneous mass prophylaxis by sulphonamide drugs was used with considerable success to check epidemics of meningococcal meningitis in relatively closed communities, such as residential schools and large Army camps. Evidence was finally obtained that sulphadiazine in a single dose 2·5 g. by mouth, given simultaneously to the whole of the group or population concerned, greatly reduced the carrier-rate for at least three weeks and substantially reduced or even put an end to clinical cases within the group.^{3 4} This method is not applicable to a large civilian population, in which the administration of the drug to everyone on one particular day is impracticable. But Machiavello and his colleagues⁵ have successfully applied it to parts of four isolated village communities in the Sudan, apparently protecting to a significant extent the groups (varying from 30 to 90% of the village populations) which received the drugs, though not checking the development of the epidemic in each village. These workers have also shown that a single injection of depot penicillin gives results equal to those derived from a single dose of sulphonamide.

1. Raschka, G. I., Uber, W. J. *Sewage industr. Wastes*, 1952, 23, 802.

2. Michaelsen, G. S., Park, W. E. *Publ. Hlth Rep., Wash.* 1954, 69, 29.

3. Painton, J. F. *Milit. Surg.* 1943, 95, 267.

4. Phair, J. J. et al. *Amer. J. publ. Hlth*, 1944, 34, 148.

5. Machiavello, A., Omar, W., El Sayed, M. A., Rahman, K. A. *Bull. World Hlth Org.* 1954, 10, 1.

The most suitable dosages were found to be 4 g. of sulphadimidine (or its equivalent) for adults, 2·5 g. for children aged 5–15 years, and 1·5 g. for children under 5 years of age; or, alternatively, 150,000 (or preferably more) units of procaine penicillin G in oil with 2% aluminium monostearate (P.A.M.) for adults, and 75,000 units for children under 5. There was no indication that either of these drugs in such doses was preferable to the other, but P.A.M. was more popular with the villagers and slightly less costly. The tabulated figures strongly indicate that the results were not due to chance, and Machiavello et al. advocate the extension of the method in the Sudan.

In these trials of simultaneous but subtotal mass prophylaxis it is not clear why the treated groups were not subsequently reinfected, since they remained in close contact with the highly infected untreated groups. (Likewise in earlier trials it was found that the carrier-rate after administration of sulphonamide remained low for at least three to six weeks, although the direct effect of the drug could not have lasted much more than forty-eight hours.) Possible explanations offered by the Sudan workers are: (1) that the chance of reinfection was reduced in the villages with low percentages of untreated population; (2) that low-grade immunity developed in the previous carriers who received the chemoprophylaxis; or (3) that infectivity decreased pari passu with the natural waning of the epidemic.

VIEWS ON POLIOMYELITIS

THE first report of the W.H.O. Expert Committee on Poliomyelitis¹ covers many aspects of the subject.

The all-important symptomless infections and minor illnesses are discussed under three headings: silent or inapparent infections, which are probably the commonest form; abortive poliomyelitis, a minor illness which usually lasts only 24–48 hours; and non-paralytic poliomyelitis, a more severe illness with definite signs of meningeal involvement but not progressing to paralysis. Spinal and bulbar paralyses and encephalitic manifestations are taken to be infrequent complications of a rather common infection. The host factors which might influence the development of paralysis include genetic constitution, pregnancy, associated infections, injuries, over-exertion, intramuscular injections, dental extractions, and tonsillectomy.

The virus enters the body via the mouth, and a primary site of infection is established in the pharynx and in the lower alimentary tract. During the first 10–14 days after onset almost every patient excretes virus in the faeces, and, in some, excretion may continue for as long as 12 weeks. Virus multiplies actively in the alimentary tissues, and in a small proportion invasion of the nervous system follows; but whether spread to the nervous system takes place along nerve-fibres or via the blood-stream cannot yet be decided. Immunity after infection is best studied by antibody determinations in various age-groups of the population. In areas where infection is highly prevalent paralytic cases are usually limited to the lower age-groups, and serum antibodies and effective immunity are acquired early in life. In countries with more advanced hygienic conditions, serum antibodies and effective immunity are acquired later in life, and paralytic infections are increasingly common in older children and young adults. The virus is spread by the transfer of intestinal and pharyngeal secretions of infected people, and intimate association with an infected person is probably necessary for the spread of infection. In communities such as ours, spread within the family may form foci with a high density of infection, which then tends to follow lines of movement of human beings from infected

1. Expert Committee on Poliomyelitis: First Report. *Tech. Rep. Wld Hlth Org.* 1954, no. 81. H.M. Stationery Office. 3s. 6d.

households and institutions. There are usually 10-100 inapparent infections to each clinical infection, and in some circumstances the proportion may be even higher.

Although epidemic outbreaks were not reported until about a century ago the disease is worldwide in its distribution today. In many tropical countries there is a low reported incidence of paralytic cases but a widespread incidence of subclinical infections. In areas such as the Eastern Mediterranean and North Africa where the local population is largely spared from paralytic attacks the disease may nevertheless be a serious hazard for recently arrived immigrants, such as troops from Europe and North America. Situations like this raise the difficult question of control measures. Theoretically one might expect that the standard public-health measures of isolation and quarantine might reduce the spread of infection; but, with the present inadequate facilities for laboratory diagnosis of inapparent infections, it is not surprising that little benefit has hitherto come from these methods. (If it were indeed possible with vastly improved diagnostic resources to recognise and isolate effectively every infected individual in this country for example, our population might eventually be highly susceptible to poliomyelitis infection and liable to severe epidemics as a result of the introduction of virus from an endemic area.) These considerations underline the need for developing effective vaccines which may help us to make our peace with the virus by learning to live with it. Nevertheless during an epidemic certain precautions in regard to isolating patients and imposing limited quarantine precautions are advisable. Patients should be nursed with the routine applied to other enteric infections; family and intimate contacts should be considered as probably infected; and children who have been in intimate contact with a case should be confined to their homes and avoid over-exertion. If a case occurs in a day-nursery or nursery-school the school should be closed. Unchlorinated swimming-pools should be closed; adequately chlorinated pools need not be closed but should not be overcrowded. Many simple precautions, such as avoiding over-exertion, tonsillectomies, and irritating intramuscular injections, and careful treatment of all minor infections arising in an epidemic period, are included in the committee's recommendations.

The administration of gamma-globulin is discussed in some detail. In a recent evaluation² of its use in the prophylaxis of poliomyelitis in 1953 it was concluded that gamma-globulin did not protect family contacts of patients with poliomyelitis; so further trials are required before firm recommendations can be made. It is hoped that vaccination against poliomyelitis may become feasible in the not too distant future, but such vaccination is still in the experimental stage.

The European Association against Poliomyelitis, when it met in Paris on April 8-10, considered poliomyelitis from the aspect of hospital care of patients in the acute stage. It recommended that such patients should be treated in special units, each associated with a central urban hospital. These centres should hold a reserve of material and should have trained medical and nursing staff. The later stages of treatment should be carried out elsewhere; but patients in whom the diagnosis is confirmed, whether the disease is paralytic or non-paralytic, will need to stay in the special centre for at least three weeks; and the centre should have resources for starting the treatment of muscular disabilities. "There is cause," the association concluded, "to regard poliomyelitis as an infectious disease, the patient constituting a potential source of infection, although cross-infection among the attendants on acute poliomyelitis is unusual. The usual measures for individual and collective protection in hospital must be applied."

2. Report of Committee for Evaluation of Gamma Globulin. *J. Amer. med. Ass.* 1954, 154, 1086.

TEACHING MEDICINE

THE best way of turning out good doctors has doubtless been a subject of debate among teachers of medicine ever since the days of Hippocrates. It can never be finally settled; for the river of medicine is always changing its banks, and those swimming in the tide are not in the best position for judging the set of the currents. Most will agree with Dr. R. D. Lawrence¹ that it is better to teach the student how to think in an orderly manner than to cram him with miscellaneous facts. But how to do it? Lawrence has some practical suggestions to make. The student arriving at hospital knows hardly anything about diseases, and most of our teaching hospitals now start him off on an introductory course, whose function is to teach not the details of diseases but the methods on which diagnosis depends—namely, the collection of accurate data and their interpretation and synthesis into syndromes. Techniques for collecting data must, of course, be taught and practised—a straightforward programme for both teacher and student. To teach how to interpret findings, however, is much more difficult; and Lawrence recommends to the student three honest serving-men of his own, "Where, What, and Why."

"Why," of course, covers the whole of aetiology, which he classifies under the headings physical, chemical, and biological. Under physical causes of disease he puts trauma, environment (covering temperature, altitude, occupation, poverty, housing), old age, mechanical disorders (such as obstruction by calculi), and congenital abnormalities. Under chemical causes come inorganic and organic poisons, drugs, mineral imbalance, and antigens. Biological causes cover viruses and bacteria, larger organisms such as spirochaetes and filariae, cysts and parasites, benign and malignant new growths, and degenerations or sequelæ resulting from any of these.

"Where" and "What" he groups together under the title of "systems and syndromes," and classifies these under seven heads: (1) cardiovascular and blood diseases; (2) respiratory; (3) alimentary; (4) urogenital; (5) nerve diseases, organic, and psychosomatic or functional; (6) nutrition and metabolism, including deficiencies, lack of vitamins, endocrine disorders, and allergies; and (7) the locomotor system, skin, and special senses.

The student who gets the habit of thinking his way through these two classifications when he examines a case will be safeguarded against many errors of omission. But nothing but hard work, and hard reading round his cases, can supply him with the facts on which to make his judgments. Lawrence counsels against the swallowing of textbooks whole: the descriptions of diseases should be read not in a vacuum but when a patient suffering from the disease is clearly in the student's mind. As for the teacher's part, Lawrence thinks there is a good deal to be said for teaching teachers how to teach; and he proposes some rather agreeable weekend conferences in pleasant surroundings at which this might be done. Here the "students" would be registrars and junior consultants, who would be invited to deliver short papers to seniors chosen as censors or preceptors. The manner, not the matter, of the lecturers would then be criticised publicly, with attention to diction, delivery, and arrangement of material. The best of such a conference—as of all conferences—would be informal discussions between members in the intervals of the arranged programme. "What a glorious prospect," he comments enthusiastically: "It must happen."

WE have to record the death on May 26 of Sir JAMES SPENCE, professor of child health at Newcastle upon Tyne.

1. Clinical Medicine. Some Principles of Thinking, Learning, and Teaching. London: H. K. Lewis. 1954. Pp. 64. 7s. 6d.

Medical Conferences

AMERICAN COLLEGE OF SURGEONS

A SECTIONAL meeting of the American College of Surgeons—the first in this country—was held at the Royal College of Surgeons of England on May 17-19. A full programme included panel discussions on massive gastro-intestinal haemorrhage, preoperative and postoperative care, hand surgery, and intestinal obstruction; symposia on cardiovascular surgery, gynaecology, and cancer; papers on many diverse subjects; and visits to hospitals. In addition a Moynihan lecture and a Hunterian lecture were given by two of the visitors.

This peaceful invasion of Lincoln's Inn Fields enabled British surgeons to listen to American workers who are well known here by name. The meetings, some of which are briefly outlined below, were conducted in a refreshingly brisk and forthright style.

Massive Gastro-intestinal Haemorrhage

Moderator : Prof. FRANK GLENN

The proceedings of this lunch-time meeting opened in earnest somewhere between the peach melba and the coffee. The panel were first allowed a little rein to speak in general terms on different aspects of the subject. In contrast to the teaching that persists in many textbooks, panel members insisted that haemorrhage from acute ulcers, as well as from chronic ulcers, can be dangerous to life. All were in favour of the indwelling oesophageal tube in the management of massive haemorrhage from the stomach, as a means of indicating the earliest moment at which haemorrhage recurs after having ceased.

Prof. WALTERMAN WALTERS (Rochester, Minnesota) pointed out the need for a thorough search of the whole intestine when operation was undertaken for haemorrhage, where there was no obvious lesion in the stomach and duodenum.

Mr. NORMAN TANNER expressed the view that oesophageal varices bleed as the result of ulceration of their surface, rather than from traumatic rupture. He had had 41 cases in the last ten years: up to 1947 two-thirds of the patients had died, but since then the mortality had been reduced to one-third with more vigorous treatment. This consisted in two stages: (1) immediate arrest of the haemorrhage by traction on an intragastric balloon which was distended by means of an oesophageal catheter; and (2) if haemorrhage recurred on removal of the balloon after a time-limit of two days, division of all veins round the cardia followed by subcardial transection and re-suture of the stomach, whereby the oesophageal varices were completely separated from the portal system. Most cases of gastro-intestinal haemorrhage were due to a gastric or duodenal lesion, and unless the diagnosis was obvious from the history or signs it was his practice to gastroscope the patient, since a bleeding lesion in the stomach or indeed in the oesophagus could be more easily seen by the gastroscope than by any other method.

Prof. C. F. W. ILLINGWORTH thought that the massive haemorrhage from a submucosal vessel might possibly be due to the actual rupture of the vessel as a primary lesion and might not necessarily be due to an acute erosion. He complained that, whereas formerly he had had difficulty in getting the cases from physicians early enough for operation, it was now difficult to hold them back from surgery, and he felt that they ought to learn to treat their patients medically—which he meant the use of the indwelling aspiration tube. When the cause of the bleeding could not be ascertained at operation, even after opening the stomach for inspection, he

was in favour of blind gastrectomy on the ground that 70% of acute erosions were in the pyloric half of the stomach.

Mr. IVOR LEWIS recoiled from the advocacy of blind gastrectomy, holding that the lesion must be identified if necessary by gastrotomy. In the case of duodenal ulcer it was his practice to open the duodenum, underrun the bleeding-point, and proceed to partial gastrectomy, or, if this was not possible, to gastro-enterostomy. He warned against leaving the bleeding artery in the duodenal stump untied merely because it appeared to be sufficiently occluded by clot. In his experience of 2 patients in whom ligation had been considered unnecessary for this reason, 1 had died from recurrent haemorrhage and the other had barely escaped with his life.

After these preliminary skirmishes came the real encounter—question and answer by the panel.

By what criteria was "massive" haemorrhage held to justify operation?

Professor WALTERS : If the patient is older than 45 years, especially if he has had pain or a known ulcer, and particularly if the haemorrhage has recurred.

Professor ILLINGWORTH : Never operate at first haemorrhage. Patients do not die from it if they have got to hospital. Operate only if the bleeding continues as indicated by the indwelling tube.

Mr. TANNER : At St. James's Hospital 55% of the cases were aged over 60; so on the whole they were suitable for surgery. If surgery seemed to be indicated anyhow, he would operate even after a single severe haemorrhage. The rest were gastroscoped and the site of the bleeding lesion was identified. Operation was undertaken on these only in the event of recurrence of the haemorrhage.

Mr. LEWIS emphasised the great value of the indwelling tube, which enabled operation to be undertaken before a rising pulse-rate indicated a general collapse.

What do you do if you operate for massive haemorrhage and fail to find the bleeding-point?

Professor ILLINGWORTH : Do a blind gastrectomy.

Mr. TANNER did not often find himself in this position because he gastroscoped the patients first, but he would do a blind gastrectomy.

Mr. LEWIS would never do a blind gastrectomy. Why, the next step would be for someone to report doing a blind gastrectomy because he could not find a perforation!

Professor WALTERS would do a blind gastrectomy because severe bleeding could come from multiple acute erosions which could be neither seen nor felt at operation, but which could be seen afterwards in the specimen under the microscope. He mentioned work in the U.S.A. which indicated that in fact bleeding seldom recurred after blind gastrectomy in these circumstances.

Is it sufficient to underrun the bleeding vessel and not resect the stomach?

Professor ILLINGWORTH : No.

Mr. TANNER : No, except for stomal ulcers. In 10 duodenal cases he had simply underrun the bleeding vessel and added a gastro-enterostomy. 2 bled again; 1 died.

Mr. LEWIS : No, except in some cases of duodenal ulcer.

Professor WALTERS : No, except in some cases of duodenal ulcer when it is unsafe to do a partial gastrectomy, but gastro-enterostomy should be done instead.

Would you resect the stomach for a bleeding ulcer in a child of 15?

Mr. TANNER : Yes; but he had no experience of such cases.

Mr. LEWIS : No experience, but he had done this in an 18-year-old patient.

Professor GLENN : Do a partial gastrectomy.

Professor ILLINGWORTH : No experience.

Is radiology useful to find the site of a bleeding ulcer?

Mr. LEWIS : No, because you are no better off if the result is negative.

Professor WALTERS : Yes, if carefully used.

Professor ILLINGWORTH : Yes, to exclude varices.

Can massive haemorrhage occur from stomal ulceration?

Professor WALTERS : Yes.

Professor ILLINGWORTH : Yes, but not usually dangerous.

Mr. TANNER : Yes, but rarely really massive.

Mr. LEWIS : Yes, but usually only from acute ulcers.

If the massive haemorrhage is found at operation to be due to oesophageal varices with portal hypertension, is immediate portacaval anastomosis indicated?

Mr. TANNER : No ; porta-azygos disconnection (by gastric transection) is better.

Mr. LEWIS : No. He would temporise by the compression balloon.

Professor ILLINGWORTH : No experience.

Professor GLENN would control bleeding by traction bag, close the abdomen, resuscitate the patient, and prepare for a portacaval shunt if the haemorrhage recurred when the bag was released.

Can massive bleeding arise from diverticulitis in the colon?

Professor ILLINGWORTH : No experience.

Mr. TANNER : No experience.

Professor WALTERS : No experience.

Mr. LEWIS had treated one case successfully by resection of the colon.

Has vagotomy any place in the treatment of massive bleeding from duodenal ulcer?

Mr. TANNER : No. Only useful afterwards.

Mr. LEWIS : No.

Professor ILLINGWORTH : No.

Professor WALTERS : No.

Are local agents, instilled through an indwelling gastric tube, of use to control haemorrhage from the stomach?

Mr. LEWIS had used adrenaline but was sceptical of its value and had given it up.

Professor WALTERS : No.

Professor ILLINGWORTH : No.

Mr. TANNER : No.

What lesions of the small gut can cause massive haemorrhage?

Professor WALTERS : Do not forget to search the second and third parts of the duodenum for a tumour—usually leiomyosarcoma.

Have you ever resected the stomach for massive haemorrhage from a Curling's ulcer after burns or trauma?

Professor WALTERS : No experience.

Professor ILLINGWORTH : No experience.

Mr. TANNER : No, but one patient had died from haematemesis after burns. Necropsy had shown a gastric ulcer.

Professor GLENN had seen one patient bleed to death on the tenth day after a burn. This patient should have been operated on.

This good-humoured cut-and-thrust was strictly refereed by Professor Glenn, who made the panel stick to the point of the question. It was an agreeable change from the usual formal discussion of a technical subject.

Preoperative and Postoperative Care

Moderator : Prof. WALTER G. MADDOCK

Prof. F. A. R. STAMMERS, commenting on the importance of fluid and crystalloid balance, contrasted the resilience of the young, healthy patient with the sensitiveness of the elderly, who withstand disturbances of fluid balance poorly. Particularly in this group it is important to restore "physiological balance" before operation. Professor Stammers declared that the treatment of fluid and electrolyte disturbances is the responsibility of the surgical team, and emphasised the size of the deficits that may develop in conditions such as intestinal obstruction, and the value of clinical examination and simple urine tests in the management of these cases. He recommended a daily intake of 2.5 litres of water containing 8-12 g. of sodium chloride and 2-3 g. of potassium chloride, and indicated the dangers of water intoxication from indiscriminate administration of fluid subcutaneously or rectally. Finally he referred to potassium deficiency and the need for accurately charting the patient's intake and output.

Prof. J. GARROTT ALLEN (Chicago) discussed the problem of a "man-made disease"—homologous-serum jaundice. In a large series he found that this condition occurred once in every 200 blood-transfusions, but 20-50 times in every 200 transfusions of pooled plasma; and the mortality-rate of those affected varied, in different series, from 5 to 28%. In Professor Allen's view pooled plasma should no longer be used, but should be replaced by liquid plasma stored at room-temperature; this never gave rise to jaundice. Viruses could survive long in dried or lyophilised plasma, but only for a few days in cell-free plasma, which was stable and remained fit for use for at least three years. Plasma alone did not suffice for anaemic patients, who also needed blood-transfusions.

Prof. MACLEOD DOUGLAS discussed the prevention of abdominal-incisional herniae in the obese. He contended that the main strength of an incision derived from its fascial, aponeurotic layers, and that these should always be sutured with fine, interrupted, non-absorbable sutures. He described experiments showing that healing in fascial tissue takes some ninety days, and that until that time the tensile strength of the wound depends largely on the sutures. If possible self-opposing incisions should be made, and in general transverse abdominal incisions were preferable to paramedian.

Professor MADDOCK explained that the source of the gas causing postoperative abdominal distension, or "wind," was swallowed air. Apparently many patients become aerophagists for a few days after an operation; even if these patients belched frequently they never returned as much air as they swallowed. Professor Maddock described experiments showing that swallowed air was passed down the alimentary tract very rapidly, reaching the caecum in ten minutes and the rectum in twenty-five to thirty minutes. He strongly recommended prophylactic continuous gastric suction after major abdominal operations, to prevent the development of "wind," and insisted that the abdomen should never be closed over distended intestines, which should first be emptied by aspiration.

Hand Surgery

Moderator : Prof. MICHAEL L. MASON

Introducing this panel discussion, Professor MASON spoke of the great increase in the scope of hand surgery. Not many years ago it was concerned mainly with infections, whereas now interest was centred on reconstruction after injury.

Mr. PATRICK CLARKSON first referred to the common minor injuries of the hand which are treated in casualty departments. He described the arrangements at Guy's Hospital, and said that although special accommodation and equipment were necessary these were of a simple nature. He emphasised the importance of teaching the principles of traumatic surgery on these cases and of the planned delegation of responsibility.

Dr. GEORGES E. CLOUTIER (Montreal) described the primary repair of hand and finger wounds, and also spoke of the importance of proper facilities and technique. Complete debridement of the wound was more important than the administration of antibiotics. Conversion of the open wound to a closed wound by suturing or grafting was an essential part of the primary treatment. Full-thickness skin-grafts gave the best results, but he thought that split grafts were safer with contaminated wounds. For pedicled flaps he sometimes used the side of the neck, while the local flap which he favoured was the cross-finger flap. When skin was avulsed it could sometimes be replaced as a full-thickness graft after careful removal of the fat.

Mr. W. C. GISSANE dealt with closed fractures of the hands, pointing out that the orthodox conservative treatment of these often gave disappointing results. He described the open reduction of some common fractures and dislocations, saying that repair of the associated damage of the soft tissues was sometimes all that was required to make reduction of fractures stable.

Mr. R. G. PULVERTAFT agreed with Mr. Gissane about the repair of fractures, and went on to speak about the treatment of divided tendons, discussing the indications for primary and secondary repair. Repair of the flexor tendons in the middle and proximal segments of the finger, where grafting was often necessary, was best deferred. At the wrist, and usually also at the distal part of the finger, tendons should be repaired at the primary operation. When function was limited after tendon repairs tenolysis might be useful.

The panel were not in full agreement about the palmar flap for covering skin tips, but Mr. CLARKSON made the point that replacement of lost tissue should be by tissue resembling it as closely as possible; he claimed that the palmar skin was the best from this point of view, and it also gave good sensation. The panel also agreed that if several fingers were completely "degloved" it was probably a mistake to try to save them all, and the less useful might be amputated.

With regard to fracture fixation, Mr. GISSANE said that for the juxta-articular fractures soft-tissue suture was usually adequate. For fractures of the shafts of the long bones of the hand he had found mattress sutures of wire satisfactory.

The panel seemed to agree that ischaemia produced by a pneumatic tourniquet, such as a sphygmomanometer cuff, could be safely maintained for two to three hours. It was suggested, however, that prolonged ischaemia might favour the development of wound infection.

Acute Intestinal Obstruction

Moderator: Mr. A. DICKSON WRIGHT

Public discussion of the most serious subject usually gains from a leavening of humour; but there is always a critical level beyond which a debate cannot stray without lessening its usefulness. Under the direction of a moderator introduced by Prof. WALTERMAN WALTERS, of the Mayo Clinic, as "a well-known surgeon and raconteur," the panel opted squarely for entertainment.

Nevertheless some valuable points emerged. The three collaborators agreed with the modern view that suction with a long intestinal tube is of benefit in the treatment of certain cases, and that fluid and electrolytic balance are all-important. Regarding the treatment of large-bowel obstructions Prof. P. H. T. THORLAKSON (Winnipeg) energetically defended caecostomy in certain cases, though this view was attacked by Mr. J. B. OLDHAM; while Prof. M. JOHN WAUGH (Rochester, Minnesota) considered that in left-sided colonic obstruction due to a growth, colostomy 5-6 in. above the growth was a good operation, allowing the later excision of both growth and colostomy with end-to-end anastomosis.

Cardiovascular Surgery

Chairman: Prof. HENRY W. CAVE

In this symposium experts from both sides of the Atlantic gave short papers covering a wide field. Those accustomed only to the British way of conducting similar meetings may have regretted the absence of general discussion of the papers which a less crowded agenda would have permitted. They were reminded, however, that the sectional meetings of the American college serve as refresher courses for many American surgeons working

in isolation from the great centres of surgical research—a fact that justifies their rather didactic character.

Mr. R. C. BROCK's exposition of modern techniques in intracardiac surgery invested the relief of the various valvular stenoses with a deceptive appearance of simplicity. Simpler it has indeed become with the discovery that the chambers of the heart can be directly entered with instruments, thus rendering superfluous the retrograde introduction of valvulotomes through an artery—the means by which Brock first undertook the relief of an aortic stenosis less than ten years ago. How little cardiac surgeons are inclined to rest on their achievements was shown by Mr. Brock in referring to the method he has used of open operation on the valves and interventricular septum under direct vision. A dry heart is secured by clamping the great vessels. This has been made possible by the introduction of hypothermia. The oxygen requirements of vital organs are thus reduced and the dangers from ischaemia of their tissues minimised. This illuminating glimpse of the intracardiac surgery of the future suggested that an extracorporeal circulation, with its enormously difficult management, may become superfluous.

The treatment of aneurysms of the aorta by resection and replacement by frozen arterial homografts is now a well-established procedure, as was shown by Prof. MICHAEL E. DEBAKEY (Houston), who reviewed some 60 cases in which this operation was done. Until very recently its scope was limited to aneurysms which could be dealt with without interrupting the blood-flow through arteries supplying vital organs, such as the renal arteries and the celiac axis. This limitation has now been practically overcome by operating under hypothermia, and these arteries have been clamped long enough for grafts to be inserted, without impairing renal or hepatic function. Only the spinal cord remains intolerant of the ischaemia resulting from the necessary section of numerous intercostal arteries in certain cases.

The management of arteriovenous aneurysms was discussed in a thoughtful paper by Sir JAMES LEARMONT.

Technical problems relating to the collection, preservation, and insertion of homografts have lately tended to dominate discussion of surgery of the aorta and of the peripheral arteries. It was significant that Prof. C. G. ROB, with experience of over 60 cases, dwelt rather on the clinical indications for reconstruction of the large arteries. He usefully reminded his audience that what is technically possible is not necessarily therapeutically advisable, and that below the level of the iliac arteries the replacement of segmental obstructions in arteriosclerotic patients is very apt to fail, either through local thrombosis or from subsequent crippling angina pectoris or fatal cerebral or coronary thrombosis. In these circumstances he regarded grafting as usually justifiable only in cases with established or threatening gangrene in which a major amputation was the alternative. This might be postponed for a year or more by a reconstructive operation.

The clinical aspect was also emphasised by Prof. MICHAEL BOYD, who indicated the importance of classifying claudicants according to the severity of their functional incapacity. He regarded sympathectomy as the sheet-anchor in treatment, but in his view this was not indicated in the mild cases which almost any conservative treatment would relieve, nor in the severest cases for which tenotomy of the tendo Achillis provided the surest and simplest relief. He regarded long-continued administration of large doses of alpha-tocopherol as a valuable means of prolonging the effects of sympathectomy.

Arterial spasm remains the dark horse of peripheral-arterial disorders. Its rôle in the causation of symptoms, and the efficacy of sympathectomy in combating it, has always been regarded with more reserve in this country than on the continent of Europe. Sir JAMES PATERSON

Ross said that the time had come to review what we know, rather than what we suspect, about the origin of arterial diseases. Sympathectomy, which is of great value in acrocyanosis with spasm of the arterioles, was useless in the treatment of spasm of the larger arteries such as occurred after trauma. He showed graphically by means of a film made by Mr. J. B. Kinmonth how this spasm is abolished by the local application of papaverine-sulphate solution.

Dr. FREDERICK W. COOPER, jun. (Emory, Georgia), also speaking of vascular spasm, wisely hinted that sympathectomy might benefit some patients even if no actual spasm existed, for in certain conditions abolition of normal vascular tone would improve the circulation in a limb.

Those who heard the symposium were left with the sobering impression that, while the seemingly impossible is being achieved again and again, therapeutic judgment remains the most necessary and the most difficult task of the cardiovascular surgeon.

Pancreatitis

In a Moynihan lecture Prof. WALTER C. MACKENZIE (Edmonton, Alberta) observed that with increasing awareness of pancreatitis this disease was being diagnosed ever more frequently, particularly since it had been recognised that the lesion might vary in severity from mild oedema to fulminating necrosis of the gland. There seemed to be no doubt that in acute pancreatitis the essential pathological feature was the escape from the lumen of the gland of activated pancreatic juice; but it was far from clear why this occurred.

Professor MacKenzie described a case of acute pancreatitis following embolism of the celiac artery and reported work showing that pancreatitis could be produced experimentally by intra-arterial injection of fat emulsions after ligation of the pancreatic duct. In some cases of pancreatitis evidence of intravascular fat could be found, and he suggested that this might, under certain circumstances, derive from the liver. Workers in Wangensteen's laboratory had noted the similarity between the microscopic picture of pancreatitis and the Shwartzman phenomenon—both gave rise to venous and capillary thrombosis—and they had produced pancreatitis experimentally by appropriately administered doses of bacterial toxins. Professor MacKenzie suggested that, while there were probably several aetiological agents in pancreatitis, in many cases the essential factor was the development of a vascular lesion while the gland was under a pronounced secretory stimulus.

Of the 97 cases of acute pancreatitis that he had treated, Professor MacKenzie classified 15% as acute oedematous lesions and only 6% as fulminating. In this series over 50% of the women, compared with only 25% of the men, had concomitant biliary disease, and the really severe forms of the disease were commoner in those with no disease of the gall-bladder or bile-ducts. Of the 5 patients who died 3 were in their thirties. In all cases there was a distinct rise in the serum-amylase level, but this was often transient and lasted only twenty-four hours. In a large series of control cases of other acute abdominal conditions a raised serum-amylase level was found only very rarely. The diagnosis of acute pancreatitis depended largely on awareness of the possibility of the condition supported by a raised amylase level.

Professor MacKenzie recommended conservative, non-operative treatment. The blood volume must be restored by the infusion of plasma or blood, and it was probably in this way that albumin was beneficial. A careful check must be kept on the electrolyte balance, and acute disturbances of carbohydrate metabolism detected quickly. Every effort should be made to prevent stimula-

tion of pancreatic secretion; continuous gastric aspiration should be carried out; fluids should be administered intravenously; atropine and 'Probanthine' should be given; and pethidine rather than morphine should be used to control pain. 45 cases had been treated in this manner, with a mortality of 9%.

If gall-stones or other biliary disease was present, this should be treated appropriately as soon as the acute attack of pancreatitis had settled down. Despite this treatment some patients developed recurrent pancreatitis: in 2 such cases sphincterotomy gave relief; but Professor MacKenzie had not found this operation of benefit in patients without gall-stones, and he suggested that in such cases bilateral thoracolumbar sympathectomy might be necessary to relieve pain. In the group of patients with chronic, as opposed to recurrent, pancreatitis Professor MacKenzie had treated 4 presenting with obstructive jaundice. Even at operation it had not always been possible to be certain that the pancreas was not involved by a growth, but all 4 cases had done well following cholecystojejunostomy. A further 12 cases of chronic pancreatitis with coincident gall-stones had done well after cholecystectomy, but in certain selected cases with crippling pain excision of the pancreas might be necessary.

Progressive Exophthalmos

Prof. HOWARD C. NAFFZIGER (San Francisco), in a Hunterian lecture on progressive exophthalmos, described how he first became interested in this subject. Twenty-four years ago a patient was led into his clinic, totally blind with severe exophthalmos and protruding red masses of conjunctiva. This patient had undergone thyroidectomy for Graves's disease six months before; six weeks later he died from intracranial infection, which was the usual outcome of the untreated disease. When, shortly afterwards, Professor Naffziger saw a nurse with a similar condition, rapidly going blind with progressive exophthalmos and choked discs, he did his first orbital decompression. Entering the anterior fossa by the lateral route he unroofed the orbit and removed as much bone as possible from the walls. The annulus of Zinn was cut to release the pressure on the nerve (but this had not subsequently been necessary). The operation had been altered latterly only in that the bony removal had been made more extensive. The ethmoids were not entered because of the risk of infection; but it is possible to encroach on the frontal sinus as Poppen had suggested and thus get more room.

The main feature of the disease was the greatly increased retrobulbar pressure, and for this reason orbitometric measurements—i.e., measuring the tension in the orbit—were of more value than exophthalmometer readings, which measured the amount of protrusion of the eyeball. His most surprising statement was that there was no fat to be seen in these orbits at operation, but that the muscles were enormous, and that when the disease had been present for some time, these might show hyaline degeneration. Almost all the reported necropsy accounts of orbital dissections in exophthalmos had emphasised their increased fat content, and the work of Rundle, Pochin, and others suggested this as a cause of the exophthalmos. When the exophthalmos was progressive, increase of fat was clearly not the exciting factor; and this might possibly be another pointer differentiating ingraevescent exophthalmos from the protrusion usually seen in Graves's disease.

Professor Naffziger had operated on only 40 patients in the years 1930-50 despite the fact that his hospitals were responsible for some 250 thyroidectomies a year. The condition was extremely rare, and the only indications for this operation were a threat to the eye or to vision. 65% of his patients were females and 29 had

required bilateral operations. He had not succeeded in controlling the condition with any form of endocrine therapy or X rays.

As regards investigation of the aetiology of exophthalmos, the most profitable line seemed to be that pursued by Dobyns, of Cleveland, who had isolated from the anterior pituitary an exophthalmos-producing factor distinct from the thyroid-stimulating hormone.

Retrorenal Fibroplasia

The demonstrations included one of experimental work on retrorenal fibroplasia by Dr. Norman Ashton in the department of pathology of the Institute of Ophthalmology.

It was shown that high concentrations of oxygen at atmospheric pressure induce in the growing retinal vessels of the kitten a peculiar type of vasoconstriction which progresses to complete obliteration of the vessels, whereas concentrations below 35% have no such effect. This vascular closure is rendered permanent by thrombosis or adherence of the opposing vascular walls, so on transferring the animal to air severe anoxia develops in the retina and extensive and abnormal proliferation

of vessels occurs, producing a picture which exactly parallels the early stages of retrorenal fibroplasia in the premature baby. The two conditions thus appear identical in origin, and Dr. Ashton described some recent experiments which have further elucidated the problems involved.

It has been found, for instance, that the administration of ethyl bisoumacetate ('Tromexan') prevents intravascular coagulation within the obliterated vessels, which reopen normally in air—abnormal vasoproliferation does not then occur. While it is now clear that oxygen should be administered to the premature baby only when essential, and then only in the smallest quantity consistent with survival, it would appear that anticoagulants, such as heparin, may be the best preventive measure where the risk of exposure to high concentrations of oxygen must be taken.

Dr. Ashton and Mr. C. Cook demonstrated a new technique which permits microscopical examination of the living retinal vessels through a "limbal window"; by this means the visitors saw growing retinal vessels in a kitten's eye gradually constrict and finally obliterate when the animal was subjected to high concentrations of oxygen.

Special Articles

THE PREVENTION OF MENTAL ILLNESS

Some Lessons from Holland

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THE Minister of Health has repeatedly drawn attention to the congestion in our mental hospitals, and lately he has announced that half the £2 million allotted this year to hospital construction will be used to provide more psychiatric beds. The main reasons for this congestion are the rising age of the population, the development of outpatient clinics which detect more cases, the increasing willingness of patients to enter mental hospitals, and the relative unwillingness of the public to have aged relations home afterwards. The cost of maintaining an elderly and perhaps troublesome relation at home compares unfavourably with the freedom from responsibility obtained when the patient is kept in hospital at public expense. Mental hospitals have now become free, comfortable, and respectable.

These conditions will probably continue in the future, and the cost of this side of the health service is therefore likely to rise. Already 42% of all hospital beds and 13% of the cost of hospital services are devoted to psychiatric patients. The annual cost of their care in the United Kingdom is some £30 million.

The four Metropolitan hospital boards, serving the 14 million people of London and the Home Counties, maintain 52,500 mental hospital beds at an annual cost of £11 $\frac{1}{4}$ million and an average cost of £4 per bed per week. There is 1 bed per 276 of the population and nearly all the hospitals are overcrowded. Any attempt to deal with this problem by providing further beds will cost a great deal more money than is likely to be available, and even so it is doubtful whether any such scheme could overtake the growing number of cases that current socio-economic circumstances produce. Other European countries are facing the same problems and the Netherlands have set up a preventive service which repays study.

THE DUTCH BACKGROUND

Holland has a congested urban and industrial civilisation, and its social problems have many points in common with those of this country. But it is broadly true that during the last twenty years the Dutch have developed a preventive mental-health programme

planned to keep people, as far as possible, out of hospital, while the British have succeeded in overfilling their mental hospitals.

The Dutch are realistic in their approach. They are perhaps more conscious of economic competition from other countries, especially from Germany, than we are, and they hold that the expensive social and health services of all highly developed countries must contribute to the efficiency of productive industry, on whose success in the world markets these services ultimately depend. They recognise that many of the problem cases who drift from job to job and from hospital to hospital are a heavy and recurring drain on public funds. Some of these people, as in all societies, also become delinquents.

Under the post-war Dutch legislation, hospital treatment is free to 85% of the people, and is paid for by contributions to a social-security fund. The administrators of this fund, which has only limited resources, have to meet many claims besides those of the hospitals, and they recognise that preventive medicine is often a true economy. They also believe that preventive measures and treatment are often more effective when carried out in home and factory, with family and workmates, than in the artificial surroundings of a clinic or mental hospital.

This concept is analogous to the treatment of psychiatric disorders in the United Nations Forces in Korea. Throughout the recent campaign, these cases were treated near the front line, and 80% were returned to duty within 48 hours. In Korea, hospital care was the last resort, because experience has shown that removal to a hospital produces a new situation in which a patient often escapes from his difficulties. Unfortunately, sources of stress recur, whether in Korea, London, or Amsterdam, and escaping into the shelter of a warm friendly hospital may easily become a socially acceptable habit in any part of the world.

MENTAL HEALTH SERVICE OF AMSTERDAM

Amsterdam is a city of 850,000 people living under congested urban conditions. The mental health service, developed over the last 20 years by Dr. A. Querido, is run by the city authorities from a central building. A 24-hour service is provided by a team of psychiatrists and social workers who may be called in by the family doctor, officials of the ministry of labour, or by the police. Once a patient comes under their care, psycho-social treatment is provided in the home, if necessary for months or years. The Dutch believe that mental illness is often caused by a breakdown of social relationships in the family, or at

work, and they believe that it should be treated in close relation to the family and work situation. In Amsterdam patients are only sent to hospital as a last resort, and this step is regarded as an admission of failure by the mental health service. It is never their first choice as it not infrequently is in Great Britain today.

The mental health service is therefore closely concerned with factory and labour conditions. The service believes that work placement, aided by regular home supervision, is often the best way of retaining these patients as productive members of society. It also runs four sheltered workshops where patients can be reconditioned for work while their problems are under care. Great stress is placed on the home as the basis of the normal family. The Dutch contend that only in the home is it possible to co-operate with the family. If the patient is out when a member of the service calls, the visit is as valuable, because the relatives are helped to gain a better understanding of the patient's difficulties.

An excellent relationship has been built up with the police, who are encouraged to report significant antisocial behaviour to the service. This procedure is often more conducive to a permanent solution than a prosecution in the courts. The service also advises the judiciary in more serious charges.

In Amsterdam the work of the service is carried out in teams. Each district has a full-time psychiatrist who is helped by social workers. During their postgraduate training all psychiatrists are seconded for six months from the university clinic to the preventive mental health service to gain a practical understanding of social and industrial conditions.

Although much of their work is done in the home or factory medical department, the doctors of the service have access to first-class diagnostic facilities for psychological and laboratory tests. For this purpose the patient visits the central clinic. There is also an excellent university psychiatric clinic with 200 beds which is an active teaching and research centre. Close liaison is maintained between the university clinic and the service.

About 40% of all adult psychiatric patients referred to the mental health service are never admitted to hospital, and respond with varying success to handling in the home and factory. Where institutional treatment is essential, arrangements are made for the patients care in a mental hospital. On his discharge the service resumes supervision and resettlement at work. Owing to the excellence of the service, superintendents of mental hospitals are said sometimes to discharge their patients too early, no doubt a fault on the right side.

RESULTS

Comparisons between one country and another are notoriously difficult. Is Amsterdam, which has been developing a first-class mental health service for 20 years, mentally healthier than London where the emphasis has been on the provision of outpatient facilities and hospital beds?

The suicide-rate, which is one recognised index, suggests that the Dutch system is more effective. In Amsterdam suicides in 1951 were 7.3 per 100,000. In Greater London they were 11.7 per 100,000, or 60% higher. Again in 1950 Amsterdam had 330 people per 100,000 in mental institutions, while London and the Home Counties had 412 per 100,000. In Amsterdam 0.1% of the population are admitted to mental hospitals annually against 0.32% in London and the Home Counties. The ratio of hospital admissions for Greater London is thus three times as great as that for Amsterdam.

There are better ways of spending public money than building more mental hospitals, and the Dutch experience deserves careful study and adaptation to the needs of this country. Perhaps once again prevention will prove better, and cheaper, than cure.

GENERAL MEDICAL COUNCIL

In a presidential address at the opening of the council's 188th session on May 25, Sir David Campbell observed that of the 110 practitioners who had qualified in this country and had been fully registered after obtaining the requisite experience in house-officer appointments, under the terms of the Medical Act, 1950, 88 had obtained their certificates of experience on the basis of six months spent in medicine and six months spent in surgery; the others had combined surgery or medicine with midwifery.

Since the beginning of last year it had been necessary for practitioners holding recognised overseas Commonwealth and other diplomas who wished to obtain full registration in this country to furnish the council with evidence that they had had such house-officer experience as was required of applicants from the United Kingdom, or other experience not less extensive. In this period, 721 overseas Commonwealth applicants had been fully registered. 250 of these practitioners qualified in Australia, 213 in South Africa, 101 in India, 59 in New Zealand, 31 in Canada, 26 in Pakistan, 19 in Ceylon, and 22 in other parts of the Commonwealth. A further 2 practitioners holding recognised degrees granted in Burma had been fully registered in the Foreign List. In addition provisional registration had been granted to 74 Commonwealth practitioners, 20 of whom subsequently obtained full registration by service in the hospitals in this country; while temporary registration under section 8 of the Medical Practitioners and Pharmacists Act, 1947, had been granted to 456 practitioners from Commonwealth or foreign countries, not eligible for full or provisional registration, who were thus enabled to take up postgraduate employment in our hospitals. Most of this group qualified in foreign countries, including 144 in Europe, 42 in America, and 23 in Egypt. The great majority of overseas applicants for temporary, provisional or full registration came to these shores to undertake postgraduate study; and these figures illustrated the great part that Britain was playing as a centre of higher medical education.

During the session members of the council would be asked to consider the appointment of a new special committee on legislation to examine afresh the question of consolidating the Medical Acts.

The Executive Committee had resolved that the degrees of the University of Agra should be recognised in respect of the Agra Medical College, of the University of Delhi in respect of the Lady Hardinge Medical College, of the University of the Punjab, in respect of the Amritsar Medical College, and of the University of Gauhati in respect of the Assam Medical College.

The President said that in his address last November he expressed the concern of the Disciplinary Committees at the emergence of certain professional misdemeanours in connection with the National Health Service which had kept recurring during the past few years, and on their advice issued a warning. He had since learned that this warning had been interpreted in some quarters as indicating that these misdemeanours were widespread and as a reflection on the high general ethical standard of the profession in Great Britain. This was neither intended nor implied. The Minister of Health, when asked in the House of Commons on Jan. 21 what steps he had taken since this statement was made, said:

"I have taken no steps since the statement made by the President of the General Medical Council, but it is fair to say that perhaps the right interpretation has not been put on what was said. As I understand, it was a warning that the General Medical Council quite rightly take a grave view of laxity in these matters, and was not an allegation that fraudulent practices or conduct were at all widespread."

That reply, the President concluded, put the matter in its proper perspective.

In England Now

A Running Commentary by Peripatetic Correspondents

I CAN'T understand why some people are so touchy about having their fingerprints taken to get their visas for the United States. To me that seems the least of the host of bureaucratic trespasses upon the sanctity of the individual. I have to produce my international certificate of vaccination as proof of personal epidermal trauma; I have to declare my many private physical disabilities and disclose if I am pregnant; my psyche is ruthlessly ploughed up to seek the seeds of anarchy. My goods and chattels are laid bare for every mocking eye to scorn. The last shreds of my credit are blown away with the currency certificates.

The photograph which leers out from the pages of my passport could provoke an international incident on its own demerits, the graphic note of the fascinating distribution of my birthmarks may excite the clinical curiosity of the medical inspector of aliens, the gypsy blood in my veins may enthrall the foreign serologists, so why spoil any enthusiast's pleasure in my loops and whorls? For all I care, the Ellis Island experts can chart my dwindling dentition, immortalise my electrocardiogram, and record my refractions; but I hope that delicacy will draw a veil over my I.Q. It seems silly to add to our travelling burdens by carrying chips on our shoulders.

* * *

Mrs. McConachie, the pride of the ward, is a typical product of Glasgow, but more articulate than most of our patients, and a shrewd judge of character, particularly of her medical advisers.

She attended Dr. A. at another hospital some time ago. "An awfy man, yon! Telt me to go hame tae ma bed and said Ah'd be deid in a month, but if Ah wisnae deid Ah'd tae come and see him again. Well, here Ah am, and that was two years ago. Another time he treated me wi' quinidine, an' Ah've never felt mair ill in ma life. Ah wis takin' faintin' turns, so Ah telt 'im. He jist said, 'Mrs. McConachie, don't you worry if you have an attack. You might have another in ten minutes, but don't let that worry you. My! a cheery man yon, but a rerr doctor!'"

Then there was Dr. B. "Ye ken, the handsome man at the Infirmary; fair, wavy hair an' an awfy nice voice. He helped me a lot."

The third medical specialist whom she has weighed in her balance is Dr. C., of the same hospital. "The cleverest doctor in the West of Scotland; Oh, an awfy clever man yon. Gied me thiorcil, an' Ah continued it too long an' developed oedema mixed; stupid, wasn't Ah?"

We are just a little apprehensive of Mrs. McConachie's future comments. We like to flatter ourselves that they will be favourable. "Awfy sympathetic men, yon. Ay, an' awfy good doctors too." Still, we are taking extra pains with Mrs. McConachie.

* * *

In the middle of our hospital a tall chimney rises. Out of its summit, day and night, clouds of black smoke pour and pollute the neighbourhood. To eliminate this nuisance would cost, I am told, a great deal of money. It is evidently cheaper to treat those who have been poisoned by it than to remove the cause, even though this does mean stoking the boilers to keep them warm in hospital.

So that all who pass by may learn of this vicious circle it has been proposed that the following inscription be attached to the base of the chimney:

This is the stack,
That belches smoke,
That comes from the fire,
That burns the coke,
That heats the wards,
That house the folk,
That breath'd the smoke,
That caused the choke,
That worried the nurse,
That ordered the hearse,
That took the blook
That lay in the bed the stack filled.

* * *

In my corner of the railway carriage speeding along from Bristol to London I fell to thinking of Isambard Kingdom Brunel, who was only 27 when he was commissioned to survey a route for the proposed London and Bristol railway. This he did, on horseback, in six weeks, and even offered his principals alternative routes north or south of Marlborough Downs. Unable to decide which was the better way he had no hesitation in suggesting a consultation with George Stephenson, when the northerly route was chosen. But though a good many railway travellers have heard of Brunel the civil engineer, I wonder how many doctors have heard of Brunel the hospital architect. Yet his design for portable sectional field hospitals was used at Erenkeni, Dardanelles, during the Crimean War, and the similar type of field hospital often used by the United States army in the late war seems to have been based on his ideas. And he was prepared to act as engineering consultant too. Once by accident a sovereign lodged in one of his bronchi and all attempts to remove it failed. The coin remained inside for about six weeks to his ever-increasing distress. At last he had made a wheel mounted on a stand, and to this wheel he was fastened, Ixion-fashion, and rapidly turned upside down. The manoeuvre was successful, and the coin was immediately coughed out.

* * *

News from School.—"You read the letter of a supposedly reformed boy:

1.40. Left Bischester for Harringay Arena.

3.40. Watched the Queen in shop television set, while others joined short queue.

4.20. Amid much rhubarb-muttering from latter end of queue, took our places by our comrades.

4.40. Had argument with an ice-cream vendor. Self stressed that wares should be on the house.

4.50. Men came up with movie-camera and caught party smoking. We hope film will not be widely distributed.

6.00-6.30. Member of party converted from Society of Friends to Plymouth Brethren.

6.30-7.00. Plymouth Brethren gospel-spreader converted (not very wholeheartedly) to Quakerism.

7.00. Crowd moved forward an inch. Hysterical old lady at my side told queue not to get excited.

7.02. First stretcher leaves queue. Hitherto-faint singing grows into glorious discord. Bischester contingent, in adding "harmony" to *Bread of Heaven*, made object of ill-disguised displeasure. Queue moves forward another inch. Surreptitious locking, bolting, chaining, barring, and wedging of doors.

7.30. Scared-looking man came out and said we could go to stadium and listen to the broadcast. Queue divided, part A going, as directed, to stadium, while part B unsheathed daggers, unfurled umbrellas, and advanced towards the official muttering furiously. We went, complaining gently, in the A party, leaving poor official preparing to meet his doom. Just as we reached the stadium entrance, the choir began to sing National Anthem. Either we had to disrespectfully walk on or bar the way to the 2000-odd people behind us. We were disrespectful. When the anthem and some hymns were over, a man welcomed all the other gatherings which were listening to the broadcast. List included two in Bischester!

8.00. Billy Graham came out, told us how nice it was that we were there, hoped we would not be too cold, and disappeared. Hymns (sung like hit-tunes).

8.05-8.55. Billy Graham told us all what worms we were and how we were acting like the pig in Rowland Hill's story, 'The Beans and the Pig.'

9.00-9.30. Those among us who thought it necessary were saved.

9.30. Left stadium, 87½% of us reformed.

10.30. Arrived at Victonloo and asked an engine-driver if he knew where he was going. We asked because his buffers were against the end of the line. He said he did, but where did we want to go? 'Bischester,' said I; 'do you know the way?' He didn't seem over-certain, but we decided to risk it.

10.40. Ate our school tea in the train, preparing inedible foodstuffs for throwing out.

11.30. Threw out inedible foodstuffs.

12.00. Arrived at Bischester, wished the ticket-collector good-morning, and walked up to the school.

12.45. Effected an entry and went to bed (better boys)."

Letters to the Editor

MAMMARY CANCER TREATED BY BILATERAL ADRENALECTOMY

SIR.—We read with great interest the article last week by Mr. Pyrah and Mr. Smiddy and we congratulate them on their results.

Bilateral adrenalectomy has now been carried out in this hospital on over 30 patients, and our findings are remarkably similar. A paper reporting the first 20 cases will be published shortly. Our operative mortality has also been 1 case. The longest survival in our series is now one year, with very marked regression and no evidence of any further spread. The patient is in excellent health, having gained over one stone in weight.

We would like to make the following points :

(1) We have not found that the histopathology of the primary tumour is of any real value in assessing its suitability or otherwise for operation, but on the whole the better differentiated the growth the more favourable will be the result.

(2) Young patients with multiple metastases who have failed to react to testosterone in small doses have been found to respond unfavourably to adrenalectomy.

(3) We feel strongly that the treatment of metastatic breast cancer by androgens in large doses is not justified, because the alleviation of symptoms is offset by the undesirable effect of virilisation. In our experience small doses are equally effective.

(4) Oestrogens, by depressing the gonadotrophic hormones of the pituitary without any undesirable side-effects, are more suitable in the palliation of late cases.

(5) Adrenalectomy should not preclude the use of high-voltage radiotherapy in the treatment of individual metastases—e.g., a solitary deposit in the lumbar spine. Indeed, it seems likely that the combination of adrenalectomy with irradiation gives considerably better results.

W. P. GREENING
MICHAEL HARMER
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TREATMENT OF DEAFNESS

SIR.—The recent letters on this subject did not, I feel, clarify the principles and difficulties of auditory training in adults.

Information is represented in speech in a multiplicity of ways, and this becomes apparent when the acoustic wave-form of speech sounds is analysed. Several information-bearing elements exist in the wave-form, and may be lost owing to noise, moderate deafness, &c., without appreciable reduction of intelligibility so that communication by speech can be carried out under various adverse conditions. The ear and the brain are adapted to exploit the enormous redundancy of natural speech.¹ It is possible to reduce the highly complex wave-form of speech to a much clipped version and yet the speech remains intelligible. The elimination of a number of information-bearing elements has its limits, and at a certain point only fragmentary elements, insufficient for decoding, remain—as happens in severe deafness.

It is, however, possible to teach a deaf person to attach the same meaning to these fragments as is normally attached to the full acoustic-wave form of speech. This is the basis of auditory training in the deaf child, who learns to attach meaning to a set of acoustic symbols. This process of learning is the same as that of acquiring normal language. Therefore, as emphasised by Dr. Fry and Miss Whetnall, in their article of March 20, it is extremely important to start this training early.

For a very deaf adult, learning such new “language”,² based on fragmentary information-bearing elements of speech, is comparable to learning a foreign language for

¹ Ayers, E. W. The Parameters of Speech. Paper read to acoustic group of the Physical Society, April 12, 1954.

a normal person. It may be a slow process in middle-aged or elderly deaf persons. Success depends on a variety of factors such as intelligence and ability to learn; so claims that a short course of “auditory training” will improve the “hearing” should be judged critically.

What improves as a result of auditory training is not the individual’s hearing but his ability to decode the clipped-down acoustic waves of speech. This, of course, has nothing to do with peripheral hearing. It is a cortical function not dependent solely on the hearing function of the cortex but also on its other functions.

Another serious difficulty exists. Normally we continually receive a mass of incoming signals, and we select those which have certain characteristics, or to which, according to circumstances, we attach the greatest importance. We thus avoid overloading the mechanism which carries out a final analysis of speech.³ In selecting incoming signals, some of the information in the signals that are finally rejected is in fact used in deciding to reject them.

For the very deaf person, all acoustic stimulation carries a potential message: but he is unable to decode all signals and to select or reject automatically from them. He has two alternatives: to pay attention all the time, but thus to overload the mechanism carrying out the final analysis of speech; or to pay no attention at all. His listening ability is thus affected. A person who has been trained to recognise a limited number of signals only still has this difficulty in selection, which can be largely overcome by paying attention to non-auditory clues; in adults these are often more important than auditory clues.

I do not wish to minimise the importance of auditory training but to emphasise its difficulties for the deaf adult. Mr. Robin (March 13) was fully justified in warning the medical public of extravagant claims. We know very well that such claims have been made by some firms in connection with the sale of hearing-aids. The National Institute for the Deaf did a great service to the deaf by preventing their exploitation, and one can happily say that, as a result of the institute’s activities, the standards of most hearing-aid firms have risen. The same policy should be applied to claims of various forms of “treatment” or “re-education” of the deaf.

Harrow, Middlesex.

L. FISCHI.

NURSING BY THE MOTHER

SIR.—We were impressed recently by reading⁴ the advice given to a national conference, called in London in 1906 to consider ways and means of reducing infant mortality, by Mr. John Burns, then President of the Local Government Board (who sacrificed his career to his principles on Aug. 4, 1914). He urged the assembled doctors to “Concentrate on the mother—for as the mother is so will the children be.” What words of wisdom, years ahead of his time, for we have not quite caught up with them yet! We early realised in this hospital that it paid to concentrate on the mother, and that a well-fed, contented, and comfortable mother, with no home worries, tended to produce the same attributes in her infant patient.

Dr. Lowenfeld (April 10) and Dr. MacCarthy (April 24) have visualised many of the prerequisites to successful mother-nursing. As they say in their letters, correct structure is the basis of success. The building should preferably be designed by someone who has to work in it and not by an architect who has never heard of cross-infection or mother-nursing. We have two epigrams which we have found useful to apply to operations and anaesthetic methods and to design: “the simpler it is

² Broadbent, D. E. Attention and Memory in Listening to Speech. Paper read to acoustic group of the Physical Society, April 12, 1954.

³ Quoted by McNeil, C. *Brit. med. J.* March 6, 1954, p. 533.

the better it is" and "aim at function and all else shall be added unto you."

Dr. MacCarthy will be pleased to know that in addition to individual rooms there is provided at this hospital a comfortable sitting-room for the mothers' use in the evenings (for those who can safely leave their charges). A telephone is always available for a mother's use and she invariably keeps or is kept in touch with her home. There are adequate bathroom and lavatory facilities for mothers only and there is a sun-room furnished with brightly coloured cane chairs, also for mothers only (no infants allowed), where they can have morning and afternoon tea. The "gossip shop" one of us calls it. It has become the custom for one of the mothers, in rotation, to act as hostess for the day; she gets the tea-trolley, pours out the tea, hands round the cups, and all the others defer to her as their hostess. It is a very pleasant custom and we wish you, Sir, could drop in some morning about 10.30, when most of the patients are asleep, and see this happy group of mothers, and perhaps be asked by the hostess of the day, "Would you take a cup of tea with us, doctor?" An invitation not to be lightly refused for it would probably be better fare than we would get in the "doctor's room" and much pleasure would be shown if we consented. What is more, much may be learned from the mothers' talk.

From all of this, Sir, you would perhaps sense a somewhat different atmosphere from that usually found in a children's ward.

We would like to tell Dr. Lowenfeld that, in choosing a trained nurse for this kind of hospital, we have found it best to place temperament above professional qualifications and experience. A nurse can be trained easily and quickly (if you catch 'em young enough), but to change a woman's temperament by training may be quite impossible. A nurse who has been trained somewhere where all mothers are considered stupid nuisances, and who might regard the mother as usurping some of the duties she has been trained to do herself, who had a hasty temper, or told mothers off sharply for doing something she considered wrong, would soon wreck the whole scheme. The mothers' hackles would be up, there would be cliques, mutterings, and mutiny, and *all the babies would suffer*. We have been through that experience and have profited thereby. We have also learned the truth of Kipling's couplet: "For the Colonel's Lady an' Judy O'Grady Are sisters under their skins." It even does not seem to matter if the skin is brown or white. There is supposed to be no colour bar in this country, but a little certainly exists, and we were at first doubtful if Maori mothers would "fit in"; but they often do marvellously well. The other mothers are invariably kind and sympathetic to the somewhat nervous Maori woman, they teach her the ropes of the hospital, and tell her what a lovely baby she has—and she has too, for a Maori baby is one of the most attractive things in the world. The Maori mother responds by smartening herself up and behaving like her "sisters." Incidentally, she usually speaks much better English than they do and is very quick in learning from observation.

Neither does the social stratum of the mother seem to make one scrap of difference. On one occasion an upper-class mother who applied for treatment for her infant declined to come too, but said the child's Karitane (Truby King) nurse would accompany it! One of us was for replying that if she did not wish to look after her own first baby she should take it somewhere else, but the other said: "Let the Karitane come, there will be more than one operation necessary with an interval, and we will see what happens." When the patient was sent for next the mother said that she would like to come herself this time! She proved an ideal mother-nurse and "fitted in" well. When she left, her thanks were real and she said it was an experience she would not have missed for anything. But to get this sort of nursing started one has to put one's shoulder to the

wheel—very much so. It is not something which is likely to drop into one's lap like a ripe plum, and when one has the facilities the system has to be learned.

Finally, perhaps we should state that there has been no mortality from any cause for nearly 4 years in this small research hospital, despite the large number of anaesthetics, the small ages of the patients, the difficulties and length of some operations, and the extra risks with Maori infants. Moreover, no parenteral therapy was given and the use of antibiotics was cut to the utmost minimum. This seems so remarkable, even to us, that we mention it with diffidence, and hope that it may continue for another 4 years.

The Bassem Hospital,
near Wellington,
New Zealand.

CECILY M. PICKERILL
H. P. PICKERILL.

SIR.—In your leading article of Feb. 27 you say that to give three good reasons is to win the argument. Nevertheless, I am not quite convinced.

In the first place, you say that the child would tolerate injections, &c., far more cheerfully when sitting on its mother's knee. Our experience is different: we find the children far quieter without their mothers.

Who is going to care for the family when the mother is in hospital with any of her children that needs admission? In Holland it would be very difficult to find someone to replace the mother, and I presume that circumstances in England are no different.

Many mothers tend to exaggerate the importance of the illness to their children. In hospital, without his mother, the child learns that he is no worse off than his fellow patients. We think that the attitude a mother takes toward her child's illnesses may be one of the things that can hamper the child's normal emotional development. I do not doubt that many nurses should be instructed by seeing the mother nurse her child, but the nursing of a child sick enough to need admission to hospital should be in hands qualified for the job.

Pædiatric Department,
St. Elisabeth's Hospital,
Haarlem, Holland.

R. SCHOO
Head nurse.

STAFFING OF HOSPITALS

SIR.—Many will agree with the views expressed in Registrar's letter in your issue of May 15 (p. 1031). The senior-registrar exchange scheme was suspect from its very beginning. Teaching hospitals are very much more generously staffed than regional hospitals, but only 15% of the hospital work of the country is done in the teaching hospitals.

Most consultant and senior registrar posts, in the main specialties in particular, are filled by men who have spent most, if not all, their time in teaching hospitals. Entry to general practice is easier after one or two years in hospital than after a longer stay, and the financial returns are much greater. Is it surprising therefore that there is a critical shortage of junior staff in those very hospitals that carry the main burden of the hospital work of this country?

The recent proposals put forward by the Strachan Committee envisage the creation of what amount to junior and senior hospital medical officer posts in regional hospitals, and the elimination of registrar and senior registrar posts in these hospitals, unless the latter are combined appointments with teaching hospitals. It is thus hoped that security of tenure will tempt men into the regional hospitals. It is said that the path to consultant status will be through these glorified S.H.M.O. posts, most of which, by the very nature of the work of regional hospitals, must be in the main specialties.

Judging by the present and the recent past, the numbers of consultant posts in the main specialties will

be very limited and there will be enough senior registrars in or attached to teaching hospitals to fill them. One cannot foresee any appreciable reduction in the numbers of teaching-hospital senior registrars because of the very nature of the teaching-hospital set-up. The chance of a regional-hospital man ever achieving consultant status will be very poor indeed, no better than at present. The new proposals are as dubious and as specious as those made in the past.

Will these new posts attract the calibre of men needed to carry the main burden of the hospital work of this country? Has the new scheme been conceived with the interests of the population genuinely at heart, or is its main intention to provide some form of staffing of the regional hospitals, which, it is hoped, will pass muster while safeguarding the special interests of a minority?

We have heard much recently about departures from Spens in relation to the increased rates of pay for hospital staff. We have heard much about "consultant and specialist" work being done on the cheap by S.H.M.O.s and of the great discontent amongst these men. We know that the number of "consultants and specialists" in the country is only part way to the intended number, but there has been more than enough work for the full intended number since 1948. Much of this work has been done for the past 6 years by S.H.M.O.s, senior registrars, and registrars.

Now, after all this, we find the profession's representatives going to the Ministry with proposals which will radically alter Spens, and which will greatly increase the number of "dead-end" S.H.M.O. jobs in the country—proposals which cannot solve the problem of junior staffing. There is only one solution and that is the recognition that "consultant and specialist" work must be done by "consultants and specialists" and paid for at that rate—the creation, in fact, of more "consultant and specialist" posts in the main specialties. A little clear and honest thinking about the connotation of the term "consultant and specialist" as envisaged in the Spens report is long overdue. The men for these posts are there, fully trained and waiting. Most have been doing this work for years and are now nearly 40, not 32. Only by giving present senior registrars justice and "clearing the decks" can any start be made with improving junior staffing. The solution of this problem demands the recognition that 85% and not only 15% of those requiring hospital attention need a first-class hospital service. Such a service can only be produced by a system which affords genuine promotion, right to the top, in regional hospitals, with real alternative prospects in general practice all the way up.

ANOTHER REGISTRAR.

THE PLIGHT OF SENIOR REGISTRARS

SIR,—From time to time the British medical press appears to groan under a spate of letters from unhappy registrars "bewailing their outcast state." One must sympathise with many of these men, and particularly those who are older and have families to support; but, at the same time, one wonders whether any of them have any desire to be aware of the opportunities immediately outside their own bailiwick.

Immediately after the war I joined two other men in a good type of general practice. I had high hopes (and even ideals) but realised, after July, 1948, that working under the National Health Service was not to my liking. Accordingly, my wife and I decided to make a complete change, and early in 1950 we moved our family and possessions to Canada, where I had been appointed to a very junior position on the staff of a tuberculosis sanatorium.

After two years' very hard work learning the basic elements of chest diseases and taking the equivalent of medical finals all over again, I was lucky enough to join

the permanent staff of an institution that enjoys the reputation of being one of the best sanatoria in the U.S.A. We work in close association with the local medical school, enjoying all the benefits of such an arrangement. The salary is adequate and, after only two years here, we are starting to buy a house.

There is a fair sprinkling of British medical men in this country, who have taken a big chance and who kick themselves daily for not having taken that chance sooner.

Seattle, Washington,
U.S.A.

M. A. LINELL.

OUR CHANGING MENTAL HOSPITALS

SIR,—With reference to your note last week (p. 1087), I would point out that the increase of accommodation, &c., at Saxondale Hospital, recommended by the reconstruction subcommittee in 1947, was a paper transaction only. The statutory accommodation remains, even in 1954, unchanged.

Saxondale Hospital,
Radcliffe-on-Trent, Nottingham.

JAMES MCGREGOR
Medical superintendent.

CHILDREN'S NUTRITION COUNCIL

SIR,—May I briefly record the fact that the Children's Nutrition Council, the organisation originally established by Miss Eleanor Rathbone, Sir Gowland Hopkins, and others in 1933, has now decided to terminate its existence? Many of your readers may remember that the council (first called the Children's Minimum Council) campaigned for a number of years to promote legislation on the various nutrition services. During the war its members interested themselves in the development of school meals and in the growth of the various milk and vitamin schemes. With the close of the war it became evident that the aims of the council had all been achieved, even if much still remains to be done to improve the administration of the services themselves. Some doubt was felt whether in its existing form the council had any further work it could usefully do; and with the deaths of several of its leading members the time seemed to have come to wind up its affairs. A small balance in hand has by committee resolution been transferred to the National Society of Children's Nurseries on the understanding that it is to be used to assist research and publications on the care and feeding of young children.

London, E.C.1.

F. LE GROS CLARK.

DOSAGE OF MEPHENESIN

SIR,—I would like to give a short note of my own experience in treating those multiple "rheumatic" conditions with which every general practitioner is faced. Earlier correspondents have made special reference to the dangers of phenylbutazone and the spasmolytic efficacy and side-effects of mephenesin.

There is no doubt of the value of phenylbutazone in relieving rheumatic symptoms, but this drug is now generally agreed to be unsuitable for prolonged use, so that the general practitioner, with his flood of rheumatic patients, is left in the same position as before. In all rheumatic conditions the clinical picture is one of muscle spasm occurring per se or in response to underlying inflammatory rheumatic changes. Moreover, pain produces mental tension and a consequent vicious circle of increased sensitivity to pain. It appeared to me, therefore, that a logical approach to the problem was to treat every aspect of the disease by a combination of suitable drugs.

I have therefore prescribed in the past a small dose (0.1-0.2 g.) of mephenesin, for its sedative and muscle-relaxing properties, in combination with salicylates in doses below average. More recently, I have tried 'Arthripax' tablets, which comprise a very small dose of mephenesin plus salicylamide. My experience with this preparation confirms my previous impressions in every

respect, and supports the suggestion of Dr. Cross in his letter of April 17. It achieves relaxation with a dosage of mephenesin that does not cause any gastric reactions. I have not found the drug to be well tolerated in the dosage generally recommended.

During the past twelve months I have successfully treated in this way well over 100 patients suffering from a wide range of rheumatic disorders.

London, N.W.2.

H. H. MARGULIES.

BRONCHIOLITIS TREATED WITH DETERGENT AEROSOLS

SIR.—I was interested to read Dr. Gans's paper (May 15). It is difficult to see what advantage aerosols of detergents have over aerosols of water since it is the increased viscosity of the partially dried mucus film that causes the trouble; in fact, the surface tension itself is substantially the same as water. Perhaps if Dr. Gans had performed a control series, using an aerosol of plain water, the advantage of the detergent, if any, would be demonstrated. A mucus-dissolving enzyme would probably be the best additive to the water aerosol, but in the absence of such a preparation a trial of hyaluronidase would appear to be justified.

Marlow, Buckinghamshire.

BRENNIG JAMES.

PROVOKING AND LOCALISING FACTORS IN POLIOMYELITIS

SIR.—The experimental study by Professor Trueta and Dr. Hodes in your issue of May 15 is most instructive. The findings of these workers are an important contribution to our knowledge of the factors which may influence the severity of poliomyelitis. For a number of years I have doubted the wisdom of carrying out spinal puncture in cases of this disease, and their article prompts me to quote a case in support of their observations:

During a period when frank cases of poliomyelitis were occurring, a boy aged 15, after a prodromal period of about 48 hours, lost the power of his right arm. The diagnosis was not in doubt, but despite this a lumbar puncture was performed, none too smoothly. The boy suffered considerable pain at the site of the puncture—indeed it was the main thing he complained of. There was no further extension of the paralysis until approximately 72 hours after the lumbar puncture, when the legs became flaccid. While it is possible that a late spread of the disease to the lower limbs would have occurred, nevertheless, in view of the findings of Trueta and Hodes, it seems highly probable that the degree of paralysis of the legs would not have been as great had the infective process not been aggravated by local trauma.

Reviewing this case in the light of the recent work of Trueta and Hodes, may I urge that the dangers of spinal puncture in cases of poliomyelitis be made known widely and without delay.

Jedburgh.

L. T. POOLE.

POLIOMYELITIS AND DENTAL EXTRACTIONS

SIR.—There is evidence that indicates an additional risk of poliomyelitis following surgery, especially in children, at the time of the expected seasonal increase in the disease. If there is risk in, say, the removal of tonsils, may there not be a similar risk in the removal of teeth in children? Is there any evidence that the extraction of teeth that are "cold" should wait for a less dangerous time?

The condition of children's teeth, especially in the very young in rural areas, is such that the necessity for multiple extractions is again becoming frequent. When poliomyelitis threatens, should the extraction of teeth be limited to the extraction of those that give trouble? If there is, in fact, any risk it would be, administratively, a serious matter for school dentistry, since there might have to be a fairly prolonged "close season."

Cambridge.

J. R. TOLLER.

TREATMENT OF VARICOSE ULCERS

SIR.—Following Mr. Maurice Lee's letter (April 3) about ulceration of the leg and deep thrombophlebitis, I would like to point out that as a rule ulceration does not develop until the thrombosed deep veins have recanalised, usually after 12–18 months. If deep veins remained thrombosed there would be less trouble from ulcerated legs.

The pre-ulcerous indurated areas above the malleoli are due to necrosis of the fat, which, together with its overlying skin, gradually dies as a result of the high pressure in the veins draining the affected area which hampers the usual capillary circulation. Mr. Lee refers to the retention of metabolites in this part, but actually, after the oedema, fat necrosis occurs, and on incising these areas in order to ligate inefficient perforating veins above the ankle, a creamy material like pus often escapes which is part of this process of fat necrosis.

The division of inefficient communicating veins above the ankles, described by Cockett and Elgan Jones,¹ is an excellent remedy to prevent ulceration after deep thrombophlebitis and to keep an ulcer from recurring. It is an exacting procedure, and skin healing after it is prone to be tardy, but it is well worth while. In this respect Mr. Lee's practice differs from mine.

In my experience, after doing many lumbar sympathectomies for ulcerated legs, I find that they are seldom worth doing. The opinion has crystallised that skilful pressure bandaging (continued for long periods but frequently changed), daily exercise, and ligation of defective saphenous and communicating veins are the best remedy. I am now sceptical of deep-vein ligation. Physiotherapy to the lower limbs and mobilisation of the feet and ankle joints is also helpful, but in patients over 50 it must be given carefully or the scar tissue will break down. Protection of the cicatrised area for life by stout elastic stockings is also necessary to buffer the part and to prevent recurrence; indeed, it requires as much care to keep an ulcer scar healed as to heal it!

London, W.1

HAROLD DODD.

GRADUATE WIVES

SIR.—The statement by Dr. Annis Gillie last week of the view taken by the Medical Women's Federation of the employment of married women doctors in the public-health service is helpful and timely.

The great need of the public-health service is for full-time men and women, especially young doctors with the D.P.H., who wish to remain in it and to cover a wider field than maternity and child welfare alone. The extreme difficulty of obtaining them at the present salary rates should be causing much more concern than it is, and undercutting by the acceptance of low rates for sessional work would be against the true interests of the public and the local-authority service, as well as of the profession.

Indeed, there is a case for raising the sessional rate, which has remained the same while the salaries of assistant medical officers have slightly increased during the last few years.

There is a proper place for the sessional and part-time employment of some married women in maternity and child-welfare centres, provided that they give to this educative and preventive medical work the continuity needed to build up the personal relationships with mothers and children upon which success depends.

Dr. Lennox (May 8) partly answers her own complaint that it is difficult to obtain sessional work "in between bringing up a family" when she says that husband and family must come first. Of course they must, but this is no inducement to prospective employers, who well know how the appetites, ailments, and education of young

1. Cockett, F. B., Elgan Jones, D. *Lancet*, 1953, i, 17

children can play havoc with the most carefully arranged sessional programme.

We must admire those women doctors who manage to be loyal both to family and work, but we must not encourage the belief that the medical staffing problems of the public-health service can be solved by the part-time or sessional employment of married women.

Trowbridge, Wiltshire.

C. D. L. LYCETT.

PORPHYRIA TREATED WITH NEOSTIGMINE

SIR.—In view of the report by Dr. Gillhespy and Mr. Smith in your issue of May 1, describing the successful treatment of porphyrinuric polyneuritis with neostigmine, I would like to report a similar case at present under treatment, which has failed to respond in any degree to repeated exhibition of the drug.

The patient is a 67-year-old woman who was admitted on April 16, 1954, with a progressive polyneuritis of 7 days' duration and affecting all four limbs. This began shortly after a colporrhaphy, when she received small doses of barbiturates. The cerebrospinal fluid was normal; blood-urea level 140 mg. per 100 ml.; the urine showed a few granular casts and contained porphyrins. Porphyrinuria was also detected in one of her daughters, who is in good health.

The condition progressed rapidly, affecting the diaphragm and intercostals, and requiring the intermittent use of a respirator. Neostigmine (1 mg. subcutaneously t.d.s. increasing to q.d.s.) was given for a week. The drug was then discontinued and recommenced after a further week. No beneficial response was noted.

North Staffordshire Royal Infirmary, Stoke-on-Trent.
J. A. C. WILSON.

CANADIAN APPOINTMENTS

SIR.—The letter from M.D. in your issue of May 1 is very timely. Not only are the prospective conditions described in terms of monetary living standards entirely misleading, but the conditions and type of appointment are at complete variance with English experience and types of appointment.

The appointment in question (by a government authority) provides a regrettably misleading description. Further, it may well be that this type of appointment is *non persona grata* with the Canadian Radiological Society. Notwithstanding that in the current *Canadian Medical Association Journal* two or three fully qualified radiologists with knowledge of Canadian conditions and this type of appointment are advertising for practice appointments, they are hardly likely to apply for this appointment. It is for these reasons that advertisements appear in the British journals where there is thought to be an abundance of unemployed specialists suitably qualified and experienced!

Canada.

VERITAS.

PREVENTION OF AIRBORNE INFECTION

SIR.—I am interested in the letters you have lately published about the prevention of airborne infection and the value of aerosols.

In July, 1951, I contributed an article in the *Medical Officer*, entitled *The Nursery Nose*, on the subject of nasal infection in a 20-place residential nursery for children up to the age of 3. This, I feel, showed the value of aerosols in the prevention of cross-infection.

For some 12 months, children admitted to the nursery had developed nasal catarrh about four days after admission, which persisted in spite of all attempts at local treatment. Swabs revealed mixed organisms only, with, as far as the bacteriologist was able to ascertain, no pathogens.

A suitable rota was worked out for each room and by using a 'Phantomiser' containing 'Aeryl 4' (propylene glycol) we were able to clear the infection in 15 of the 18 infants in just over three weeks, in spite of a breakdown in the apparatus which lasted three days. The remaining 3 cases finally cleared up with further local treatment.

These cases of cross-infection were, I am convinced, primarily due to inadequate ventilation in an adapted

building, and since the infants have been re-housed in more suitable premises there has been no recurrence of this type of infection.

Rotherham.

Jos. A. GILLET
Medical Officer of Health.

MORE SELF-HELP

SIR.—In your annotation last week you referred to my address to the Institute of Almoners on Clients and Patients, and you said that there are some 5–12% of families in any area who have precious little self-confidence and self-respect to keep them going.

I think I should explain that in this part of my talk I was speculating on the future, under the subtitle "Who Needs Help?" My exact words were "the proportion of problem families must vary from area to area, and with the prosperity of the times, but it seems clear that a small number of people, varying perhaps from 5 to 12%, will continue to need intensive care."

Department of Human Ecology,
University of Cambridge.

LESLIE BANKS.

SEX AND SOCIETY

SIR.—Those of us who hoped for a lead from the *Practitioner* in its symposium¹ on Sex and its Problems must have been sadly disappointed. Nowhere is a radically new approach to sex suggested. If our criminal law on male homosexuality were to be civilised, as in France, Scandinavia, Switzerland, and most socially advanced European countries, many of these problems would simply fade away. Fifty years ago the most frantic rubbish was uttered about the deadly evils of masturbation. In another fifty years posterity will likewise marvel that we could make such a mountain out of the molehill of homosexuality. Let us hope that a kindly and earthy sexual common sense will then prevail, which would minimise homosexuality and other sexual disabilities more than anything else. Meanwhile, let us all do what we can to urge overdue reforms in law and opinion.

London, W.8.

GEOFFREY G. SHERRIFF.

"THE DANGER OF MACHINES"

SIR.—My attention has been drawn to an article in the *Daily Express* of May 19 which purports to report remarks made on the previous morning by Mr. Dickson Wright to a meeting of the American College of Surgeons. The article imputes a deplorably low standard of behaviour to anaesthetists in general. Its final paragraph, which mentions my own name as president of the Association of Anaesthetists, might have given the impression that I was present at the time and that Mr. Wright's remarks had my tacit approval, neither of which is true. It would not be necessary for me to refute these remarks if they had reached only those of us who are familiar with Mr. Wright's form of jocularity and who would give them the weight they deserve, but the American visitors may not be so familiar. It will be a pity if they have been left with a wrong impression of the standard of anaesthesia in this country, which is generally considered to be as high as anywhere in the world.

The effect of the article is to undermine the confidence of patients about to undergo surgical operations and can only be deplored—it is, as always, too late to undo the harm. I feel some sympathy with Mr. Wright that his light-hearted comments have received wider publicity than he intended. For the future, I feel that we should all remember that exaggeration as a humorous device is not wisely used in what is meant to be serious discussion and probably never when it involves the denigration of colleagues.

GEOFFREY ORGANE
President,
Association of Anaesthetists
of Great Britain and Ireland.

¹ Practitioner, April, 1954; see Lancet, April 3, 1954, p. 737.

SHUNTING IN THE HUMAN KIDNEY

SIR.—In my letter of Jan. 9 I said that Prof. J. T. Louw, during caesarean section in a case of concealed accidental haemorrhage, had seen the renal artery in unmistakable spasm. In this my recollection was at fault: what Professor Louw actually told me was that he had *felt* the renal artery in a state of spasm. I offer my apologies both to Professor Louw and to your readers for misreporting his observation.

London, W.1.
JOHN SOPHIAN.

ISOLATION OF CASTLE'S INTRINSIC FACTOR

SIR.—The letter from Dr. Glass in your last issue prompts us to write further on this subject.

The material we described in our communication of March 6 has been further purified in that the small amount of impurity has been removed in a preparative ultracentrifuge. We have also reported,¹ along with appropriate data, that the material is homogeneous after electrophoresis at different pH levels and at differing ionic strengths, as well as in the ultracentrifuge. Its clinical activity has been satisfactorily demonstrated in two patients with pernicious anaemia previously untreated. Details of full clinical trials will be published as soon as possible.

There are a number of different mucoproteins in gastric juice. From data already published, the clinical activity of "soluble glandular mucoprotein" would appear to be very little greater than freeze-dried gastric juice. We therefore feel that we cannot regard at all seriously any evidence derived from it in relation to the chemical nature of Castle's intrinsic factor. It is only a fortunate coincidence that the latter has turned out to be a mucoprotein. Our own material possesses clinical activity some hundred times greater than "soluble glandular mucoprotein."

More detailed publications will appear during the next few months. There are some points, however, that we feel we should make. We do not regard as very significant the elementary analysis of a protein but we do regard as significant a difference of more than 1% in the nitrogen content when the total nitrogen is of the order of only 10%.

We are now using a different technique for hexosamine estimation. This will no doubt have been responsible for some confusion, for which we must apologise.

Department of Pathology, King's College, University of Durham, Newcastle upon Tyne.	A. L. LATNER R. J. MERRILLS LAUREEN C. D. P. RAINES.
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THE BOMBS

SIR.—It is impossible not to feel impressed with Dr. Comfort's reasoned analysis of the Cold War, and the group feelings from which its springs of action derive. To confuse this analysis, and what is implied by it, by a call to identify with the attitude of one side, in this case the West, as Dr. Stafford-Clark recommends, seems to me a mistake. The possibility that a "deliberate mistake" by one of those in a central position of authority may lead to the military use of the hydrogen bomb, as Dr. Comfort suggests, underlines the urgency of some fresh action to find a way out of the frustrating arguments by either side which we daily read about, and which are merely the rationalisations of separate hostile states of mind.

Some support for Dr. Comfort's views may, I think, be discerned in the incentives offered by either side to those in opposition. The Eastern bloc, repugnant as its structure is to the liberal Western mind, offers a very real promise of future change in the form of society. This implied change must have a profound appeal to the under-privileged, who are usually of necessity also the

¹ Latner, A. L., Merrills, R. J., Raine, L. C. D. P. Proc. biochem. Soc., Edinb. May, 1954. (Abstract in press.)

under-educated and hence poorly developed in critical judgment. That the price of this change is the loss of personal freedom and a break with the traditions and culture of the past and, in fact, all that has gone before is clearly of little import to the poor, hungry and ill-educated individual, who feels frustrated by his present politico-economic system. The strength of this appeal appears to have been underestimated by the present political leaders in the U.S.A., who, to oppose it, offer little alternative to those dissatisfied with their present society, except appeals to the tradition and past achievements of Western civilisation. This is essentially a defensive position, it seems, from which sudden aggressive action using the bomb in a deluded attempt to regain the initiative may well occur.

The Easterners, whose philosophy teaches anyway the ultimate disintegration of the West and its replacement by their system, must feel successful as they observe the spread of their ideas after the late war. They would seem to have far less motivation for any sudden aggressive intervention in a change they regard as inevitable. Of course, they seek to accelerate by every less dangerous method this assumed process in the political and economic fields.

There is in this country a growing opposition to the idea, put forward by some politicians, that the bomb represents the sole hope of checking the East. As doctors, surely our duty is to support those whose policy is to abandon the use of the bomb. If, as some of your correspondents suggest, there is some risk in this policy, then it may be better to risk suffering a hideous crime than to commit one.

East Croydon,
Surrey.

F. B. CHARATAN.

SIR.—Future generations, were they to rely solely on this correspondence as far as it has gone, would easily be misled into thinking that Dr. Stafford-Clark's opinions were those of an unpopular minority in the medical profession.

In fact the opposite is the case and one can only presume that the great majority of your readers feel that his views are so clearly expressed that nothing need be added in print to complete what most of us take for granted in our minds.

London, W.1.

T. M. L. PRICE.

SIR.—Despite their disagreement with me—and mine with them—I have some sympathy with each of the four contributors to this correspondence whose letters you published last week. This will be my last contribution to it. I entered it, not to discount the moral challenge of the hydrogen bomb—still less to champion indiscriminate destruction, whether by bombs, rockets, or submarines—but because I believe that moral issues in general must rest upon a surer foundation than expediency if they are to prevail.

Arguments about the bombs which tend to dismiss as irrelevant other and even more fundamental considerations, such as the value accorded to the liberty, spiritual worth, dignity, and responsibility of man in society, cut the ground from under their own feet and are therefore ultimately unrealistic and inevitably misleading.

Guy's Hospital,
London, S.E.1.

D. STAFFORD-CLARK.

A LEAFLET WITHDRAWN

Messrs. Lusterlite Products write:

We recently put out a leaflet entitled "Angled Prosthetic Femoral Heads," on the inside cover of which we included a few notes on the past history of acrylic prostheses. One paragraph mentioned the research carried out by Dr. J. T. Scales, of the Plastic Unit of the Institute of Orthopaedics at the Royal National Orthopaedic Hospital, Stanmore, and Dr. J. M. Zarek, of King's College, London. As this paragraph has been thought capable of misconstruction, we should like to make it clear that neither Dr. Scales nor Dr. Zarek is in any way associated with this company. They have never received from us any financial assistance in their research and they have not authorised us to mention their names or work. Recipients of the leaflet have been asked to destroy it.

Parliament

Homosexual Crime

In the House of Lords on May 19, Earl WINTERTON called attention to homosexual crime in Britain. He thought it might aid the committee which had been appointed by the Government to inquire into this subject if discussion took place in Parliament, the press, and elsewhere. Between 1938 and 1952 unnatural offences known to the police rose from 134 to 670, attempts to commit unnatural offences (including indecent assaults) rose from 822 to 3087, and cases of gross indecency rose from 320 to 1686, but there was little public or parliamentary interest in the subject until last year. Since then there had been considerable propaganda to change the law so as to legalise homosexuality between adults. He did not question the sincerity of the advocates of this viewpoint. It was for the committee to adjudicate upon it, but the effect of this propaganda might be to give the impression that the main issue was whether the law should be changed in favour of homosexuals. That question was most important, but it was not more important than investigation into the cause of the rise in criminal vice, and above all the moral issue of how a further rise could be prevented.

A change in the law was not going to be so easy as its supporters suggested. He admitted the strength of the contention that sending homosexuals to ordinary prisons spread homosexuality, but the obvious answer was that in future homosexual prisoners who attacked juveniles should be given special treatment in special prisons. The theory that, because of heredity, environment, physical condition, or mental outlook, some men could not help being homosexual was really based upon Freudian ideas which had done some good but had also done immense harm to the modern world.

Earl JOWITT said it was twenty-five years ago that he became Attorney-General and was oppressed to discover that there was a larger quantity of blackmail than he had ever realised, and at least 95% of the blackmail cases which came to his knowledge arose out of homosexuality. They should never make the mistake of thinking that they should attempt to make the area covered by the criminal law co-extensive with the area covered by the moral law.

He hoped that the committee appointed by the Government would contain among its members someone who knew something about the treatment of criminals. They might usefully look at what was being done in Scandinavian countries, where this problem was by no means as prevalent as it was here. It might be possible to institute a system whereby the person sentenced was allowed to go out in the day-time to earn his living in the normal way, and had to come back to his hall of detention during the night-time and for weekends.

Lord LLOYD, under-secretary to the Home Office, said that the number of indictable homosexual offences known to the police was between four and five times as great as it was before the war. That was a most serious state of affairs. It was the view of the Government that a thorough investigation by a well-qualified body would make a valuable contribution to the problem of dealing with this difficult and controversial matter.

The Bishop of SOUTHWELL declared that judgment must not be clouded by passion. Further medical and psychological knowledge might lead to a more enlightened, or at any rate to a different, approach to the whole question; and to yield to a clamour for vindictive action, or for even harsher punitive measures, might easily defeat the ends. This was a state some people were in through no fault of their own and there was nothing reprehensible about being in that position. Society through all its agencies should be co-operating and trying to help people so frustrated and conditioned—whether men or women—to live happy and socially useful lives. Without condoning these offences, they had to ask themselves seriously whether making this particular kind of wrong-doing a crime might not be only aggravating the total problem. In the present state of public opinion they were here on very dangerous ground because one of the results of the immense volume of social legislation

in recent years was that the popular mind tended to equate right and wrong with legal and illegal. If the law was going to take cognisance of these offences among consenting parties, what was the ground for differentiation between male and female perverts?

Lord RITCHIE OF DUNDEE said it now seemed clear that considerable sections of Church opinion favoured some re-examination of the law, and he was assured that many members of the Judicature were of like opinion. He believed that the majority of the public, especially the younger generation, would welcome the Government's decision to set up a committee of inquiry.

Medical Treatment and Aftercare of Prisoners

In the House of Commons on May 20 Mr. VICTOR YATES expressed concern about the medical treatment of prisoners and welfare arrangements on their discharge. He appreciated that there was a shortage of medical officers; but from his personal observation while visiting Parkhurst he believed that the arrangements, particularly for prisoners with tuberculosis, were totally inadequate. There was also need for closer examination by the Home Office, the National Assistance Board, and the aftercare associations of the arrangements for helping these people, and more especially the homeless prisoners.

Sir HUGH LUCAS-TOOTH, under-secretary of State for the Home Department, said that every prison had a medical officer, and some had more than one; some of the smaller ones had only a part-time officer. At the end of 1953 there were 9 principal medical officers in the service and 33 full-time medical officers. Taking the part-time officers into account there was 1 medical officer to just under 500 prisoners in jail at any time. At the end of 1953 there were 11 vacancies; but since then the number had slightly increased, and the Prison Commissioners were trying to bring the number up to establishment and meet the shortage. Every prison had a separate hospital, or, in the case of smaller prisons, separate sick-rooms. There had been a substantial increase in the mass-radiography examinations from 2900 in 1952 to 5700 in 1953.

Every prisoner was medically examined on reception, transfer, and discharge. On reporting sick a prisoner was examined by the medical officer on his rounds. In cases of sudden illness or accident in the day-time, the prisoner was taken to hospital immediately; and at night-time if a sick prisoner rang his bell the night duty officer had complete discretion as to what action he should take. A prisoner who was dissatisfied might ask to see the director of medical services. He might also petition the Secretary of State, and might thereafter write to a member of Parliament—a right which was pretty freely exercised. He had no wish to be complacent; he knew that there was a deficiency of medical officers, and the present overcrowding in prisons was a very grave menace. But last year there were no serious outbreaks of infectious disease, and prisoners generally were in better health on leaving prison than when they came.

Pharmacy Bill

In the House of Lords on May 19 the Earl of BUCKINGHAMSHIRE, on behalf of the Lord Chancellor, introduced a Bill to consolidate certain enactments relating to pharmacy with corrections and improvements made under the Consolidation of Enactments (Procedure) Act, 1949. The Bill was read a first time.

Animals (Anæsthetics) Bill

In the House of Commons on May 21 the Protection of Animals (Anæsthetics) Bill was read the third time and passed. An amendment was accepted which reduced to three months the age-limit for castration of dogs without anaesthetics.

QUESTION TIME

Agene in Flour

In the House of Lords Lord HANKEY asked whether a suitable substitute for agene in flour for human or animal consumption had yet been found, and whether an approximate date could now be named when it could be abandoned, in accordance with the Government's assurance last June.—Lord CARRINGTON, joint parliamentary secretary to the

Ministry of Agriculture and Fisheries, replied that a sub-committee of the Interdepartmental Standing Committee on Medical and Nutritional Problems was at present considering the results of recent tests by the Medical Research Council on methods of flour improvement. "The Government have every intention of abandoning the use of agents when a suitable substitute has been found," but the most careful inquiries were necessary before any substitute was accepted.

Silicosis and Pneumoconiosis Death Certificates

In the House of Commons, replying to Mr. H. J. FINCH, Mr. R. H. TURTON, parliamentary secretary to the Ministry of Pensions and National Insurance, said that in 1953, the Silicosis Medical Board dealt with 537 applications for death certificates for the purposes of schemes made under the Workmen's Compensation Acts; in 397 cases the board certified that death had been caused by the disease. Under the Pneumoconiosis and Byssinosis Benefit Scheme of 1952, 394 awards of death benefit were made in 1953 for deaths from pneumoconiosis, and 159 applications were rejected because the Silicosis Medical Board certified that death was not due to the disease.

Mr. FINCH: In view of the disparity between the figures of applications to medical boards in respect of death from pneumoconiosis and the number of certificates granted and the large number of cases in which there has been a refusal to grant certificates, and the differing views of medical men at inquests as to the cause of death, will the Minister cause an investigation to be made into this aspect of pneumoconiosis? —Mr. TURTON: If the hon. member will study the figures I have given I think he will find that there is not a great difference between the numbers. I am aware that dissatisfaction has been felt on the question of coroner's inquests and medical boards. The Minister is at present discussing this matter with the Home Secretary, and the Minister of Fuel and Power has also undertaken to raise the matter with the Home Secretary. I think it had better be left there.

Old People in Mental Hospitals

Replying to Mrs. JEAN MANN, Commander T. D. GALBRAITH, joint parliamentary under-secretary of State for Scotland, said that he was not aware that it was the practice, when there was a shortage of beds in general hospitals, for old persons to be given accommodation in mental hospitals. Some forms of senile mental illness could be cared for properly only in a mental hospital; and where admission as a voluntary patient was not accepted, certification might be the only way of securing that the patient got the care and treatment which he needed. The conditions to be met before a person could be certified were laid down by statute, as also were the terms in which the relative certificates must be given. There was no power to permit any deviation from the terms and conditions laid down by statute. A white-paper dealing with this matter was probably to be expected within a reasonable time.

Group-practice Loans in Scotland

Replying to Miss MARGARET HERBISON, Commander GALBRAITH said that applications had been received for an interest-free loan to establish group practices from eighteen groups of doctors in Edinburgh, Glasgow, Ayrshire, Fife, Lanarkshire, the Lothians, and Stirlingshire.

Capital Expenditure on Mental Institutions

In answer to a question by Mr. J. K. VAUGHAN-MORGAN, Mr. IAIN MACLEOD, Minister of Health, gave the following estimates of capital expenditure on mental health and mental-deficiency services, based on the capital programmes of hospital boards:

	£	Percentage of total estimated capital expenditure
1950-51:		
Mental health ..	982,728	.. 12
Mental deficiency ..	508,309	.. 7
1953-54:		
Mental health ..	923,993	.. 11
Mental deficiency ..	770,448	.. 10
1954-55:		
Mental health ..	1,777,703	.. 17
Mental deficiency ..	1,314,437	.. 13

Education of Handicapped Children

Replying to Mr. IREMONGER, Miss FLORENCE HORSBRUGH, Minister of Education, said that in December, 1953, local education authorities in England and Wales were providing special educational treatment for 53,118 pupils accommodated in special schools (other than hospital schools), boarding-

homes, or independent schools, and were seeking special school places for a further 19,861. They were also educating 2077 handicapped pupils at home, some of whom were awaiting places in special schools, and about 8000 in hospital. The number of special-school places was being increased as rapidly as resources permitted. Nearly 15,000 additional special-school places had been brought into use since the war, and the provision of a further 9000 was either in progress or would shortly be put in hand.

Replying to Mr. R. W. SORENSEN, Miss HORSBRUGH, said that for educationally subnormal children there were 92 boarding special schools providing about 6600 places, and 140 day special schools providing some 15,000 places. Returns from local education authorities showed that in December, 1953, there were 12,794 educationally subnormal children awaiting vacancies in special schools.

Public Health

Vitamin Standards for Margarine

On the advice of the Food Standards Committee,¹ the Minister of Food has made the Food Standards (Margarine) Order, which requires that vitamins A and D shall continue to be added to all margarine sold by retail. The order, which came into force on May 16, prescribes that margarine shall contain between 760 and 940 international units of vitamin A per ounce and between 80 and 100 international units of vitamin D per ounce. This vitamin-A content, which is greater than that formerly required, is roughly equivalent to that of butter. The required vitamin-D content remains the same (apart from a tolerance of 10%) as it did when margarine was controlled. Hitherto manufacturers have been required, under the terms of their licence, to add specified amounts of vitamin A and D to all domestic margarine. The amount of vitamin A required was 450-550 international units per ounce and that of vitamin D 90 international units per ounce. The new order applies to all home-produced and imported margarine sold by retail, including margarine sold as such by a caterer, but not to margarine used by him in made-up foods or in cooking. It does not apply to sales of margarine to a caterer.

1. See *Lancet*, Feb. 27, 1954, p. 469.

Appointments

HARDING, H. E., F.R.C.S.: hon. orthopaedic surgeon, Hospital of St. John and St. Elizabeth, London, N.W.8.
JAMIESON, J. G., B.M. Oxf., D.C.H.: chief asst. school M.O., Leeds.
LYON, J. B., M.B. Camb., M.R.C.P.: consultant dermatologist, Ipswich hospitals group.
MENZIES, ALEXANDER, M.D. Edin., D.P.H.: medical superintendent, Inverness group of hospitals.
RUSK, MAEVE, M.B. Glasg., D.O.M.S.: part-time consultant ophthalmologist, Northern Regional Hospital Board.
WILLIAMSON, T. B., M.D. Lond.: asst. pathologist (s.h.m.o.), Royal Cancer Hospital, London.

Colonial Medical Service:

BAKER, A. M., M.R.C.S.: M.O., Uganda.
BAKER, C. H. J., M.R.C.S., D.P.H.: health officer, Federation of Malaya.
CLIFFORD, P. P., M.B. N.U.I., D.L.O.: M.O., Kenya.
GALLAGHER, J. A., M.B. N.U.I.: M.O., Tanganyika.
MELVILLE, R. M., M.B. Edin.: M.O., Federation of Malaya.
PERKS, B. K., M.B.: M.O., Leeward Islands.
PERKS, R. H. G., B.M. Oxf.: M.O., Leeward Islands.
ST. JOHN, W. A., M.R.C.S.: M.O., Barbados.
SIMON, A.: district M.O., Dominica.
TAVARIA, DINSHAW, M.B. Witwatersrand, D.P.H.: M.O., Seychelles.
TAYLOR, THOMAS, M.B. Lond.: M.O., Hong-Kong.
VAN DEN BRUL, P. J., M.B. Lond.: M.O., British Honduras.
WHEATE, H. W., M.B. Lond., D.T.M. & H.: M.O., Tanganyika.
WILSON, J. M. M., M.B. Edin.: M.O., Somaliland Protectorate.

South-Western Regional Hospital Board:

CATTON, M. J., M.B. Lond.: registrar in pathology, Southmead Hospital, Bristol.
FOX, J. H., M.B. Sheff., D.P.H.: registrar in diseases of the chest, Bristol clinical area.
MORGAN, RHONA E., M.B. Wales, D.O.B.S.T., D.C.H.: medical registrar, Cheltenham General Hospital.

Appointed Factory Doctors:

CAILE, RONALD, M.B. Durh.: Southport, Lancs.
DONALDSON, D. B., L.R.C.P.E.: Taynuilt, Argyll.
MCINNES, A. A., M.B. Camb.: Raunds, Northants.
PATTERSON, A. L., M.R.C.S.: Amersham (nos. 2 and 3), Bucks.

Notes and News

RECONSTRUCTION IN LINCOLN'S INN FIELDS

The completed great hall of the Royal College of Surgeons of England was first used on April 22, for the delivery of a Hunterian lecture. This chamber is not only dignified and well proportioned but light and cheerful, as those found who attended the college's monthly dinner on May 19. These monthly dinners are deliberately informal, and the speeches were limited to a few friendly words from Sir Cecil Wakeley, the president, and Sir Bernard Dawson. Thereafter Mr. Geoffrey Keynes, the curator of the college's art collection, described his charge, which includes works by Holbein, Hogarth, Lawrence, Romney, Reynolds, and Zoffany. Many of these are now being restored, but the curator of such a collection has a heavy task in deciding where to draw the line. Reynolds's study of John Hunter in old age, for instance, though "a sombre ghost of what it was," could be restored only at the price of changing its character. This is no new trouble. Reynolds was an experimentalist who was given to the use of fugitive pigments; and Horace Walpole suggested that his works should be paid for by annuities so long as they lasted.

On May 20 the new council room was brought into use.

THE CAMBRIDGE MEDICAL SCHOOL

REPORTING on the work of the Cambridge medical school in 1952-53, Sir Lionel Whitby, the regius professor of physic, explains that "organized facilities for undergraduates to complete the full clinical course in Cambridge are not yet available, and this is ordinarily taken in London or at some large provincial teaching hospital." Nevertheless a limited number of undergraduates can get instruction as medical clerks, surgical dressers, or obstetrical clerks, and residential courses in midwifery are offered to undergraduates and postgraduates. During the year some 55 students registered with the medical school for attendance at outpatient sessions, ward rounds, clinics, and the like, of whom 33 were postgraduates (including practitioners from Australia, Ceylon, France, West Germany, and the United States) and 22 were undergraduates. Among the other teaching activities of the school is a monthly clinicopathological conference, which gives local practitioners and others an opportunity to meet the staff of the hospitals and of the various departments of the medical school. In addition, one-day symposia on subjects of particular interest to general practitioners are held once a month, on Saturdays; and last year the attendances at these numbered 290.

The departments comprising the school of postgraduate teaching and clinical research are those of medicine (Sir Lionel Whitby), experimental medicine (Prof. R. A. McCance, F.R.S.), radiotherapeutics (Prof. J. S. Mitchell, F.R.S.), and human ecology (Prof. A. L. Banks); and the pathological and biochemical services of the United Cambridge Hospitals are provided by university teaching officers under the direction of the professors of pathology and biochemistry (Prof. H. R. Dean and Prof. F. G. Young, F.R.S.). A year ago the department of medicine and the administrative staff of the medical school completed their transfer to new temporary premises, in the grounds of Addenbrooke's Hospital, which include haematological and chemical laboratories, consulting and examination rooms, and accommodation for the regius professor, the lecturer in medicine, the research chemist, and research students. To have these new premises within the hospital precincts will, it is hoped, help to bring the medical staff of the university departments into closer contact with the medical staff of the hospitals.

TEACHING-BEDS AT A REGIONAL HOSPITAL

AGREEMENT has been reached between King's College Hospital Medical School, the South East Metropolitan Regional Hospital Board, and the Camberwell Hospital Management Committee for the use by the medical school of eight wards in Dulwich Hospital for undergraduate teaching. This scheme of association for the use of beds in a regional-board hospital is the result of long negotiations by successive deans of the medical school, and the Minister of Health has agreed to a special grant of £30,000 to the South East Metropolitan Regional Hospital Board for 1954-55, earmarked for the purpose. Three medical, two surgical, and three obstetric wards have been put at the disposal of the medical school, and, in addition,

some of the gynaecology beds will be available for teaching purposes.

The teaching will be done by the consultants from King's College Hospital and by some of the consultants already on the staff of Dulwich Hospital. The Camberwell Hospital Management Committee is to recruit more nurses to cover the extra demands of teaching-beds, and efforts will be made to increase the number of maternity cases (900 last year) to 1200. Medical students will spend a period in residence at Dulwich Hospital as part of their midwifery training. Probably some of them will also live-in for a short time at St. Giles' Hospital, Camberwell, and at St. Alfege's.

Though the scheme of association came into force on May 1, some months will elapse before it is in full operation. Meanwhile, additional registrars and resident medical officers are being appointed to Dulwich Hospital.

B.C.G.

THE use of B.C.G. vaccination is not yet so widespread as to be familiar to the public, or indeed to all members of the profession. To provide reliable information, the National Association for the Prevention of Tuberculosis has reissued, in revised form, its previous leaflets (nos. 30, 36, and 59), and has added a new one.¹ This points out that B.C.G. vaccination schemes are organised by the medical officer of health, though the vaccination may actually be done at the chest clinic. The association suggests that B.C.G. vaccination (which is free) should be considered seriously for people in the following categories: those in contact, or living, with a patient with pulmonary tuberculosis; nurses, medical students, and hospital workers; young babies of tuberculous mothers; and 13-year-old school-children. Attention is drawn to the fact that children cannot be vaccinated without the written consent of a parent.

The importance of protecting the adolescent has recently been emphasised in our correspondence columns.² More and more children now reach adolescence or adult life without being exposed to tuberculous infection sufficient to give them a positive tuberculin reaction: thus one of our correspondents says that of 418 boys entering a public school since January, 1952, only 140 gave a positive response; and of 180 of the negative reactors who have been retested annually, only 3 have changed to a positive response. Not having acquired a primary infection or developed natural immunity, these adolescents, before mixing in the wider world, should have any protection that B.C.G. can give them. If fully informed, many parents would certainly wish to have their tuberculin-negative children immunised before they reach adolescence; and children who receive B.C.G. vaccine at an early age may need further doses later to maintain whatever immunity it confers.

ENDOMYOCARDIAL FIBROSIS IN AFRICA

At a meeting of the Royal Society of Tropical Medicine and Hygiene on May 20, Dr. J. D. Ball, of the Makerere College Medical School, Kampala, Uganda, described work on Endomyocardial Fibrosis, in collaboration with Prof. A. W. Williams and Prof. J. N. P. Davies. The changes in this condition are striking.³ The endocardium is grossly thickened; and the fibrosis often involves the mitral and tricuspid valves, binding the posterior cusps to the endocardium so that the valves become incompetent. The result is heart-failure, usually with oedema and ascites. Dilatation of the heart, with a loud systolic murmur at the apex, is usual. The patient may be of any age and of either sex. This disorder, whose aetiology is obscure, is one of the three common causes of heart-failure in Uganda.

Dr. Evan Bedford referred to some 40 cases seen by him in West African troops, and noted that there was rapid onset of right-side heart-failure and the aorta itself was often small. This smallness of the aorta added to the embarrassment of the heart, or in conditions of stress might even cause such embarrassment. It might reflect malnourishment during the period of growth in childhood; and in this way there might be a nutritional factor, which was obviously not present in the well-fed and selected troops. This was evidently only

- No. 60. *Look Ahead I—Reasons for Vaccination.* Pp. 41, 6s. per 100 copies. From the N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.
- Lancet*, April 24, 1954, p. 880; *Ibid*, May 1, 1954, p. 933; *Ibid*, May 15, 1954, p. 1033.
- Ball, J. D., Williams, A. W., Davies, J. N. P. *Ibid*, May 22, 1954, p. 1049.

part of the story, though possibly the fibrosis was the result, rather than the cause, of the progressive cardiac dilatation.

Dr. E. A. Beet commented on the cardiac conditions he had found in Northern Nigeria, some of which, he thought, were cases of endomyocardial fibrosis. The formation of keloid of the skin was a well-known feature in Africans, and the formation of fibrous tissue in the heart might be related to this tendency—a point which Dr. Ball took up in his reply, saying that this was being investigated in relation to the plasma-proteins.

WORLD HEALTH ORGANISATION

In a plenary session of the seventh World Health Assembly at Geneva on May 15, the Federation of Rhodesia and Nyasaland was admitted by unanimous vote to associate membership of W.H.O. A resolution that the next assembly should consider methods of assessing only active members for the regular budget was adopted, and those States which have not been taking an active part in the work of W.H.O. were invited to resume participation as soon as possible. Mexico City was chosen as the site of next year's assembly.

On May 19, the committee on programme and budget decided that W.H.O. should henceforth prepare two completely separate programmes, the first to be financed from the regular budget and the second from Technical Assistance funds. The joint programmes with the United Nations International Children's Emergency Fund (UNICEF) were considered to have been among the most important activities of W.H.O.; the committee felt that this co-operation should be continued and recommended to the assembly various measures to this end. Out of the regular budget of \$9 $\frac{1}{2}$ million already voted, the committee recommended that \$8 million be devoted to the operating programme of W.H.O. More than \$1 $\frac{1}{2}$ million of this will be used for the central technical services, mainly operated from W.H.O. headquarters at Geneva (epidemiology and quarantine, health statistics, drug standardisation, technical publications), and nearly \$5 million will go to W.H.O. advisory services to governments (disease control, sanitation, public-health services, and technical training); the remainder will go to regional offices and to expert committees and conferences. The reduction of \$800,000 decided upon by the assembly is to be made in the budget of advisory services by reducing or deferring new projects planned for 1955.

NUTRITION RESEARCH AT COONOR

The nutrition laboratories maintained by the Indian Council of Medical Research at Coonoor continue to do good work, as is shown by their report for 1952-53.

Protein studies are an important part of the programme. Previous observations had shown that people on vegetarian diets excrete smaller amounts of nitrogen in the urine and that the proportion of urea-nitrogen to the total is smaller than on diets containing animal protein. In the further investigation two subjects were kept on three different diets, in which the total quantity of protein was the same but its origin differed. The urinary nitrogen, and the proportion of it present as urea, increased with increase in animal protein in the diet. Clearly this is leading to a new appraisal both of the protein requirements of man and of the mechanisms of utilisation. Some hint of these may come from the studies of the effect of varying dietary protein on the enzyme content of rats' liver. Low protein intake is associated with falls in levels of transaminase, *d*-amino acid oxidase, and succinic acid oxidase, but with a rise in alkaline phosphatase. Acid phosphatase content seems to be unchanged. A detailed study of the chemical processes involved in necrosis of the liver following carbon tetrachloride poisoning has also been made. Dietary supplements of methionine, cystine, and glutathione were all able to mitigate the effects of the poison. Considerable reduction in liver glutathione was noted within six hours after injection of carbon tetrachloride. Presumably the protective action depends upon the readily available —SH groups.

Important observations have been made on the changes in body composition in famine oedema. In all cases there was a great increase in extracellular fluid, which ranged from 35 to 59% of body-weight, but there also seemed to be an increase in intracellular fluid. This was deduced from the results of determinations of total body-water using the urea-dilution method. As the general applicability and reliability of this method is unproven, especially where water metabolism is disturbed, this conclusion requires confirmation. Measurements of basal metabolism before and after rehabilitation showed that though the absolute value for the B.M.R. rose, and

also the value per sq. metre, the oxygen consumption per kg. of cell solids remained unchanged. The renal response to variations in sodium and chloride intake was apparently not impaired in nutritional oedema. A failure to excrete salt cannot be a primary cause of the water retention. Experiments on rats indicated that starvation reduces the capacity of the liver to destroy antidiuretic hormone. This may be a possible basic cause of the oedema.

Other interesting work includes the production of the classical ocular signs of vitamin-A deficiency in monkeys. This should help to clear up many present difficulties. The biosynthesis of riboflavin in the rat, the histological changes in rachitic cartilage following vitamin-D administration, the trypsin inhibitor in duck egg-white, the alleged toxicity of Indian pulses, and the iso-oleic acids in cow and buffalo butter fat have all been examined.

Coonoor must be one of the largest and best-equipped nutrition laboratories in the world. A possible criticism of the direction of their activities is that the staff do not appear to have turned their attention very seriously to the educational and anthropological problems that underlie nutritional disorders in so many parts of the world.¹ The field work that is being done is all fundamentally chemical, and the answers are given in chemical terms. No doubt the reply to this comment would be that the staff are a group of biochemists, pathologists, and clinicians, and that there are enough problems in these fields to occupy all their energies. This is true. But these disciplines do not encompass the whole of nutrition.

To end this brief summary of an admirable report on a critical note would be wrong. The problems chosen for study have clearly been tackled with skill and imagination. One of the achievements of Coonoor is that it continues to set a high standard for basic laboratory research in Asia.

REABLEMENT OF RAILWAY WORKERS

PERIODS of absence through injury or illness tend to be longer in heavy than in light industry, partly because the normal work is more arduous and partly because special light work is scarce. The Western Region of British Railways have taken an important step in establishing at Swindon a reablement workshop for those constructing or repairing engines or rolling-stock. In this workshop, which was officially opened on May 10, the aim is to provide productive employment for convalescent patients by means of machinery adapted for graduated work; an endeavour is made to provide several kinds of occupation in a working period, to prevent boredom and fatigue. Normally the stay in the workshop is limited to eight weeks, and during this time the men are paid at the basic rate applying to their normal work. At present ten men are employed in the workshop, but eventually up to fifty may be taken. The great majority are recovering from fractures or orthopaedic disorders, but it is hoped to accept also those recovering after operation or long illness. British Railways acknowledge help in initiating this enterprise from Vauxhall Motors, of Luton, which has its own reablement workshop.

BORSTAL GIRLS

Dr. Phyllis Epps, who made a previous study² of 300 borstal girls, has now reported³ on the further career of 100 of these, comprising 90 recalled for additional training and 10 who served prison sentences for offences committed before the end of their borstal sentence. She compares the original 300 (group A) with the present series of 100 back-sliders (group B), and includes an assessment of the change in the attitude and behaviour of the latter after their original training period.

In both groups the average age on reception was 18.8, and larceny (about 45%) was the commonest offence for which they were sentenced. The proportion with parents separated or divorced was 25% in group A and 35% in group B, and the proportion brought up in institutions 9% in group A and 13% in group B. In both groups 10% were illegitimate. There was not much difference in respect of school records or of intelligence, but group B contained rather more girls of dull mentality (51% against 46%). Emotional instability also seemed commoner in group B (37% against 28%). The proportion sufficiently promiscuous to be

1. *Lancet*, Feb. 13, 1954, p. 350.

2. Epps, P. *Brit. J. Delinquency*, January, 1951, p. 187; see *Lancet*, 1951, i, 518.

3. Epps, P. *Brit. J. Delinquency*, 1954, 4, 265.

classified as prostitutes rose from 34% in group A to 39% in group B.

Dr. Epps says that trainees who form the hard core of later recidivism should be picked out early in their delinquent careers, in remand homes or approved schools, and given more intensive treatment. They need more individual handling and should be treated in smaller establishments where the usual régime could be supplemented by group and individual psychotherapy. Careful classification is also needed to prevent sexually promiscuous girls from contaminating the less experienced. Those who fall into the "larval" group of prostitutes described by Glover⁴ might suitably be treated in a smaller group.

The girls who fail with borstal training need careful scrutiny to decide what treatable factors in their delinquency may have been overlooked. They are said to be conscious of failure but apathetic about the future.⁵ Those returning to unsatisfactory homes required much help from social workers, especially when they had an illegitimate baby.

HOSPITALS

Two new journals concerning the technical side of hospitals have begun publication under almost identical titles: *Tecnica Ospedaliera*, published from Via Fra Mauro 12, Lido di Venezia, Italy, every two months, and *Técnica Hospitalaria* from Apartado Postal 1063, Caracas, Venezuela, quarterly. The first issue of the South American journal (dated March, 1954) deals with the organisation of Swedish hospitals, recovery wards, pharmacy in hospitals, fluoroscopy and protection against X rays, and preventive medicine in hospitals. Its lay-out is good but not so ambitious as that of the Italian journal, whose combined fourth and fifth issues (dated December, 1953) deal with actual and proposed construction of Italian hospitals, the modern clinical-research laboratory of the Ospedale al Mare on the Lido of Venice, the architecture of the new hospitals in Stockholm and Bergen, and technical apparatus.

THE MAMMAL SOCIETY

At a conference held at the University of Birmingham last month the Mammal Society of the British Isles was brought into being. In welcoming those present, Prof. S. Zuckerman, M.D., F.R.S., emphasised the reciprocity between field and laboratory studies and suggested that the new society would be of value to physiologists and other experimental scientists. In his opening paper on the Study of Mammals, Prof. Alastair N. Worden, M.R.C.V.S., indicated the relationships between mammalogists and those engaged in agriculture, forestry, conservation, pest control, veterinary science, and human medicine.

The following officers were elected: president, the Earl of Cranbrook; chairman, Professor Worden; secretary of the scientific advisory committee, Mr. H. N. Southern; hon. treasurer, Mr. H. G. Hurrell; and hon. secretary, Mr. T. J. Pickvance, Department of Extra Mural Studies, University of Birmingham, Edmund Street, Birmingham, 3. Doctors will be welcomed as members of the new society, further details of which may be had from the hon. secretary.

University of Cambridge

On May 15 the following degrees were conferred:

M.D.—D. V. Bates, R. J. R. Cureton, P. A. Emerson, A. P. Waterson.

M.Chir.—J. S. W. Whitehead.

M.B.—D. G. Dingle.

University of London

On April 6 the degree of M.D. was conferred on S. G. Browne and E. C. Turton.

The following have passed the final examination for the degree of M.B., B.S.:

Honours.—June M. Cheetham (c), Roy. Free; R. D. Clements (b), St. Bart's; H. P. Cook (b), Westminster; I. C. Cree (c), U.C.H.; D. A. M. Ellis (e), Westminster; Marlon C. Handscombe (d), London; P. R. Holt (a), London; D. E. Hyams (c, e), London; Barbara M. Isles (e), St. Thomas's; Wendy L. Jefferson (c), St. Mary's; J. J. Lewis (c), Westminster; J. C. A. Madgwick (d), London; Margaret S. Meyer (b, d, and university medal), Roy. Free; Oswald Morton (a), Guy's; Celia M. Oakley (b, e), Roy. Free; P. J. Scheuer (e), Roy. Free; A. K. Thould (b), St. Bart's.
(a) Distinguished in pathology; (b) distinguished in medicine; (c) distinguished in applied pharmacology and therapeutics; (d) distinguished in surgery; (e) distinguished in obstetrics and gynaecology.

4. Glover, E. *Psychopathology of Prostitution*. London, 1945.
5. Report of Commissioners of Prisons. H.M. Stationery Office, 1951, p. 77.

Pass.—P. T. Abear, R. M. Adam, M. J. T. Adams, Richard Agius, H. E. Aldridge, Patricia M. Alexander, Barbara A. M. Allen, L. N. Allen, Sheila Allison, J. B. Anderson, J. K. Anderson, Margaret G. Anderson, J. W. H. Andrews, R. H. D. Andrews, H. H. Annamanthodo, T. D. Annear, Per Apall-Olsen, B. M. Archer, A. P. Ardouin, Christine M. Armstrong, Keith Ashcroft, P. J. Ashton, W. L. Ashton, Diana Austin, Margaret G. Bailey, C. R. W. Bain, A. S. Baker, P. L. R. Baker, Jacqueline E. Banbury, V. C. J. Barker, Laurence Barsey, V. H. Bartley, M. W. Beaver, D. G. Bennett, Abraham Berry, G. P. Billingham, E. D. Bird, John Blagdon, A. S. Blake, Anthea Blofeld, W. W. Blue, A. P. Bolt, Gwyneth J. D. Botherway, W. N. F. Boughey, Harold Bourne, J. J. Bowen, Andrew Bradley, Evelyn L. F. Brazchnor, R. A. Briggs, Elizabeth Britain, Angela I. Brooks, M. W. Brown, T. L. M. Brown, J. A. A. Bullard, D. M. Burgess, J. C. Burt, P. F. Cameron, N. MacD. Campbell, Mary R. Capon, Jean Carrberry, G. W. Carp, Patricia M. Carpenter, P. J. Carrduis, K. C. Carstairs, Mary E. Carter, G. V. P. Chamberlain, C. C. D. Chandler, Brenda A. P. Clark, R. M. Clark, B. M. G. Clarke, C. D. Collins, Leonard Collins, J. P. Colmer, R. C. R. Connor, T. P. Connor, Ronald Conroy, P. J. Constable, David Constad, Wendy A. Cook, J. F. Copplestone, Olive M. Cory-Wright, W. R. Costain, A. G. Cox, V. E. Crapnell, Jean E. Cree, B. W. Cromie, M. R. Crompton, S. C. Cross, James Curley, K. J. Daigleish, J. H. Darrell, J. L. Davies, J. R. E. Davies, M. K. Davis, R. N. Davis, R. E. Davis, W. A. Dawkins, Brian Dawson, M. H. Day, Diana M. Dean, A. N. J. de Soysa, J. H. Dines, P. R. Donaldson, L. N. Dowie, Jean E. Drake, J. E. O. Dunwoody, R. J. Eagger, Evelyn J. Edgcumbe, R. W. Edmonds, Lise L. Elinen, K. B. Ellington, Rosalind A. Elliott, R. A. Ellis, Carice Ellison, R. W. Emmerson, D. A. Evans, Gwilym Evans, P. A. S. Evans, N. O. Eve, Rosemary B. Felton, Paul Field, M. E. Fielding, K. J. I. Finlayson, Eva L. Fisch, P. J. Fitzpatrick, A. F. Floyd, R. D. Foord, P. I. Forbes, R. E. Forgie, Helen P. S. Foulds, A. S. E. Fowle, B. N. Foy, D. L. French, G. E. Fulford, A. T. R. Fuller, Peter Garmon-Jones, E. B. Garner, R. A. Gawn, D. J. Gee, Grace M. Gee, E. R. Gibbons, A. W. Gilks, J. F. Gill, L. H. Glaser, Norman Gold, Harry Gordon, D. J. Gorham, A. C. Graham, A. I. Graham, R. A. Grande, Rosemary A. Grange, Michael Grant, A. V. Grasset, B. P. Gregory, Eirwen Griffith, W. F. Griffith, E. A. Griffiths, H. C. Crockett, W. P. Hadlow, M. A. Hargreaves, F. A. S. Harris, Jean G. Harrison, Kathleen M. Harrison, Pamela M. Harrison, L. M. Hart, R. D'A. Harvey-Kelly, Elizabeth H. G. Haslam, M. J. Hawken, Peter Hays, S. F. Hazelton, G. E. Hicks, J. P. Hicks, David Hide, J. D. Hill, K. A. Hillard, Peter Hinds, J. T. Hobbs, J. F. Hogben, F. A. Holden, G. M. R. Holliday, J. G. Holt, D. P. Honey, P. E. Hoogewerf, D. J. Hudson, T. C. Hughes, J. G. P. Hunt, John Ifland, Joan R. Inwald, A. D. Isaacs, D. C. Jackson, Marjorie D. Jackson, C. V. James, E. M. James, P. D. C. Jarman, J. G. Jeffreys, Peter Jenkins, Bridget M. Johnson, F. C. Johnson, R. D. Johnston, R. D. Johnston, D. McK. Jones, F. W. Jones, H. D. Jones, I. H. Jones, Tecwyn Jones, J. A. Kay, G. B. Kelly, J. H. Kerridge, I. A. Key, D. W. S. Klee, J. M. Kneebone, P. F. Knight, P. O. Knight, K. K. Korsah, R. G. Lacey, Joan E. M. Lambert, C. E. Langham, N. A. G. Leadbeater, R. H. Lethbridge, Julia M. Levi, J. V. V. Lewis, R. J. R. Lewis, Patricia J. Lindop, P. F. Lippold, A. F. M. Little, Antonia Loftus-Pierson, David Longbourne, G. A. Low-Bee, R. J. Luck, W. S. Lund, P. R. Lyon, Irene M. McAndrew, H. R. B. McCauley, John McIntosh, Angus Mackay, J. H. K. Mackie, I. E. D. McLean, J. A. McMillan, E. L. McNeil, A. G. Malleson, Pauline A. Manfield, H. R. Marker, P. A. T. Martin, Bernard Martin-Smith, Sheilagh Mathias, A. H. Maynard, J. D. Maynard, W. M. Mee, S. C. Melnick, Helen D. Meredith, H. C. Meredith, H. O. Middleton, Audrey Millar, M. G. Miller, K. F. Moles, A. A. D. Moore, K. A. M. Moore, W. G. Moore, B. R. Morgan, Janet E. Morgan, L. J. G. Morgan, Ruth Morlock, A. O. N. Morris, D. C. F. Muir, Sheila M. Mullally, A. W. Munro, D. D. Munro, J. S. Murrell, K. D. Neame, Grace E. Nicholls, Elizabeth M. Nicholson, T. W. Nicholson, Wendy E. Noble, Joan H. Nuttall, Janet F. Nye, Bernard O'Connor, Margaret M. R. O'Garra, H. W. L. Oliver, A. T. Otaki, J. G. Owen, L. W. Padgett, Mary G. Paine, Patricia Painter, E. G. Palmer, D. C. Panday, Raymond Parkes, J. L. Pead, Arnold Pearce, J. F. Pearce, K. I. Pearce, A. J. Pearson, J. S. Peet, E. J. K. Penikett, Valerie J. Perkins, Margaret E. Pickering-Pick, D. H. Pickett, Diana J. Pipett, J. M. Pirrie, R. E. Plested, Henry Poirier, B. J. Pollard, Mary D. Pollock, P. A. P. Pompa, C. W. Pook, B. J. Poole, A. M. W. Porter, M. W. Potts, J. K. Price, J. J. Prior, D. G. S. Randall, J. R. Rawstron, Dorothy S. Read, J. L. Read, A. L. A. Reid, Derrick Roberts, Anne E. Robinson, A. T. Robinson, J. F. Robinson, J. R. Robinson, Philip Rodin, E. J. Roebuck, K. L. Rogers, W. F. Ross, Jill P. Rosser, H. E. Rowley, C. P. Royall, D. H. Rubens, Margaret Russell, Pamela D. Rustin, Joan M. Sadler, A. L. Sanderson, J. G. Sanderson, J. R. Scarf, D. G. Scott, Jane M. Scott-Brown, O. H. Shaheen, J. L. H. Sharp, Lawrence Sharpe, Helen L. Shaw, A. M. R. Shirazi, J. C. Sibley, M. J. Smart, D. L. Smith, Enid P. Smith, Gillian M. W. Smith, J. C. Smith, R. H. Smith, R. W. Smith, D. L. Smithson, I. I. Snobar, Froma Somerville, J. G. Spink, Dorothy G. Stanley-Roose, Derek Stansfield, F. L. D. Steel, Anthony Stenhouse, G. M. Stern, Manfred Stern, J. A. Stevens, J. H. Stevens, Leo Stimmer, John Stubbs, M. M. L. Sulcliffe, R. A. Sutherland, K. H. Sutton, Jane Sewatman, G. W. Tamlyn, T. H. Taylor, T. J. Taylor, H. A. J. Thomas, Eileen N. Thompson, Deryck Thorpe, E. E. D. Tomlin, K. H. Trigg, E. A. M. Tuck, Margaret J. Turpin, Annie M. N. Tustin, V. R. Twyman, G. H. A. Ullmann, J. F. Urquhart, H. L. D. Utidjian, Margaret M. Voysey, A. F. Wade, J. G. Wall, Alison S. Wallace, Betty Walmsley, D. A. Walmsley, F. W. Ward, A. A. Watson, R. W. Watson, D. A. D. Weir, J. A. Whitehead, H. W. Whitting, Dorothea M. Wigfield, Marian A. Wilkinson, D. H. Williams, A. J. P. Willis, J. H. P. Willis, A. H. Wilson, Harry Wilson, A. J. Winterton, F. W. Winton, A. R. Wisdom, D. F. P. Wooding, Joan M. Woodley, David Woodroffe, Celia B. M. Wooley, Enid M. Wozencroft, S. H. Wydell, B. A. Young, Sheila J. Young, C. F. A. Younger, C. L. Zoob.

University of Leeds

On May 19 the court of the university conferred the degree of doctor of laws honoris causa on Prof. F. W. Rankin, president of the American College of Surgeons.

University of Sheffield

Mr. R. P. Jepson has been appointed to the full-time chair of surgery in succession to Prof. R. St. Leger Brockman, who is retiring at the end of this session.

Mr. Jepson was educated at Queen Mary's Grammar School, Clitheroe, and the University of Manchester. He graduated B.Sc. (anatomy and physiology) in 1938 and M.B. in 1941. After a year as house-surgeon to Sir Geoffrey Jefferson, Mr. Jepson entered the Army, in which he served as a surgical specialist. He returned to Manchester in 1947, and has been successively resident clinical tutor, assistant lecturer, lecturer, and reader in surgery. He became fellow of the Royal College of Surgeons in 1947, and in 1951 was awarded a Commonwealth Fund fellowship, which he held as a research fellow at the Western Reserve University, Ohio. In 1949 he was awarded the Walter Dixon scholarship for work on segmental pain reference, and in 1951 a Hunterian professorship on the problems of the Raynaud phenomenon. Mr. Jepson's published work deals mainly with neurovascular disease.

A separate department of genetics is to be established within the faculties of pure science and of medicine. Mr. J. M. Thoday, Ph.D., at present lecturer in cytogenetics in the departments of botany and zoology, has been appointed head of the new department, with the status of senior lecturer, as from Oct. 1 this year.

Royal College of Physicians

Dr. J. L. Livingstone will deliver the Mitchell lecture on Tuesday, June 15, at 5 p.m., at the college. He has chosen as his subject Observations on the Treatment of Pulmonary Tuberculosis at the Present Time.

Royal College of Surgeons of England

At a meeting of the council on May 20, with Sir Cecil Wakeley, the president, in the chair, Prof. Arthur Steindler (Iowa City, U.S.A.) and Dr. G. Gavin Miller (Montreal) were admitted to honorary fellowship. The following were admitted as elected fellows: Mr. J. W. H. Grice (Tunbridge Wells), Professor G. Hadfield (London), Prof. J. Trueta (Oxford), and Mr. W. A. Jackman (Bristol).

Mr. R. S. Handley (Middlesex) was elected and Mr. G. Qvist (Royal Free) re-elected members of the court of examiners for a period of three years.

The following awards were made:

Morinhan lectureships.—Prof. L. Deloyers (Brussels), Prof. Niels Dungal (Iceland).

Joseph Henry lectureship.—Dr. R. A. M. Case.

Imperial Cancer Research Fund lectureships.—Dr. J. Bamforth, Dr. E. F. Scowen.

Begley prize.—Maurice A. Cowan.

Licences to practise were conferred on the candidates named in the report of a comitia of the Royal College of Physicians (*Lancet*, May 8, 1954, p. 990) and on V. E. R. Spence, who have passed the final examination of the conjoint board. Diplomas in tropical medicine and hygiene and in anaesthetics were awarded to the candidates named in the same report.

The following diplomas were also granted:

F.F.A..—P. C. Calvert, J. R. Bennett, K. L. Owen, A. F. Forbat, A. J. Heber, D. W. Clark, Bridget A. Evans, M. W. J. Grummitt, Walter Norris, J. V. McDermott, B. W. Peckett, Satyananda Pramanik, Stephanie Saville, Josephine J. Candy, Deryck Duncalf.

F.D.S..—J. J. Williamson.

D.C.H..—Susanne M. Salvisberg, Elizabeth C. G. Miller.

Royal College of Obstetricians and Gynaecologists

At a meeting of the council held on May 22, with Mr. Arthur Gemmell, the president, in the chair, the following were elected to the council:

As representatives of the fellows.—H. H. Evers, Newcastle upon Tyne; C. H. G. Macafee, Belfast; T. N. MacGregor, Edinburgh; W. C. W. Nixon, London.

As representatives of the members.—I. McG. Jackson, London; Robin Murdoch, Glasgow; James Walker, Aberdeen.

The following were admitted to the fellowship:

Herbert Agar, A. F. Anderson, A. J. S. L. Boyd, J. C. McC. Browne, J. A. Chalmers, Mary P. John, William Kearney, Oswald Lloyd, D. J. Malan, Patricia J. H. Massey, G. P. Milne, R. B. K. Rickford, C. Scott Russell, J. M. Scott, Ruby G. Sharp, A. M. Sutherland.

The following were admitted to the membership:

G. T. D. Barr, E. R. Broadberry, Vivienne A. Croxford, H. F. Daghestany, P. J. Dwyer, A. L. T. Easton, J. R. Elliott, D. W. S. Gordon, T. P. Grant, John Greenwell, Kenneth Greig, R. W. Hughes, G. A. Humphreys, P. D. C. Jackson, K. B. Layton, C. V. Love, A. C. McInnis, Peter Manolis, Mrinmoyee Mukerji, F. A. Murray, R. F. O'Donoghue, G. D. Pinker, D. E. Savage, Satwant Ganda Singh; H. J. Tighe, J. R. D. Tomlinson, A. C. Turnbull, Rama Vaish, P. S. Watson, V. T. White.

Scottish Society of Anaesthetists

The following officers have been elected for 1954-55:

President, Dr. I. M. Campbell Dewar; vice-president, Dr. F. G. Gibbs; hon. secretary, Dr. A. G. Miller; other members of the executive council, Dr. W. M. Shearer, Dr. R. G. Grieve, Dr. M. C. Macqueen, Dr. R. M. P. Milne, Dr. M. Shaw, Dr. D. W. Shannon, and Dr. R. Lawrie.

The prize which the society awards annually for the best paper submitted by an anaesthetist of, or below, the grade of senior registrar has been awarded this year to Dr. J. B. Stirling.

Society of Anaesthetists of South Wales

The following officers have been elected for 1954-55:

President, Dr. D. S. Jones; vice-president, Mr. F. Y. Pearson; treasurer, Dr. D. K. W. Picken; secretary, Dr. H. G. Middleton.

A clinical meeting will be held at the Plastic Surgery Centre, St. Lawrence Hospital, Chepstow, on Saturday, July 3, at 9.30 a.m.

Royal College of Medicine, Bagdad

Dr. R. Wheeler Haines, who is at present senior lecturer in anatomy in the University of Sheffield, has been appointed to the chair of anatomy in this college.

Royal Medical Benevolent Fund

The 118th annual general meeting of the Fund will be held at 11, Chandos Street, London, W.1, on Friday, June 4, at 5 p.m.

Whipps Cross Hospital Medical Society

Dr. W. Burridge, formerly professor of physiology at King George's Medical College, Lucknow, will address this society at the hospital on Friday, June 4, at 8.30 p.m. He will speak on Excitation and Inhibition.

North-Western Tuberculosis Society

The summer meeting of this society will be held at the Baguley Hospital, Wythenshawe, Manchester, on Thursday, June 17, at 3 p.m.

International Congress for Individual Psychology

The International Association for Individual Psychology and the Swiss Association for Individual Psychology are organising a congress to be held in Zürich on July 26-29. Dr. Alexandra Adler will preside. Further details may be had from Frau Dr. E. Schmid, 14, Krönleinstrasse, Zürich, Switzerland.

British Council for the Welfare of Spastics

This council is to hold a conference on the Treatment of Cerebral Palsy on Sept. 28-30 in the hall of the British Medical Association, Tavistock Square, London, W.C.1. Applications for tickets should be addressed to the council, 13, Suffolk Street, Haymarket, London, S.W.1.

Fourth Commonwealth Health and Tuberculosis Conference

This conference will be held at the Royal Festival Hall, London, from June 21 to 25, 1955. Further information may be had from the secretary-general, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1.

Modern Aspects of Thyroid Disease

The Postgraduate Medical School of London is holding a course on this subject for consultants from Sept. 20 to 24. Further particulars may be had from the dean of the school, Ducane Road, London, W.12.

Oxford Graduates' Medical Club

The summer dinner will be held on Friday, July 2, at 7 p.m. in Oriel College, Oxford, with Mr. Ogier Ward in the chair. Guests may be invited. Tickets, at 32s. 6d., may be had from Mr. Selwyn Taylor, 3, Roedean Crescent, Roehampton, London, S.W.15, before June 26. The club was founded in 1884 to maintain associations with the university and promote good fellowship among members. Membership has now been opened to women graduates. The life subscription is one guinea.

Congress on Welfare of Cripples

The International Society for the Welfare of Cripples are holding their sixth world congress at the Hague and Scheveningen, Netherlands, from Sept. 13 to 17. The address of the British committee is 34, Eccleston Square, London, S.W.1.

Emergency Bed Service

On June 1 the telephone number of this service will be changed from Monarch 3000 to Hop 7181, on the removal of the offices to 28, London Bridge Street, S.E.1. On June 8 the branch offices at Leytonstone, Woolwich, and Ealing will be permanently closed, and thereafter all calls should be made to Hop 7181.

Central Council for Health Education

The council is to hold its summer school this year at Reichel Hall, Bangor, in August. The lecturers will include Dr. Grantly Dick Read, Prof. F. A. E. Crew, F.R.S., Dr. A. R. Harrison, and Dr. A. J. Dalzell Ward. Further particulars may be had from the council, Tavistock House North, London, W.C.1.

Society for the Study of Fertility

This society is holding a conference on July 22 and 23 at the house of the Zoological Society of London, Regent's Park, N.W.1. Further particulars can be had from the secretary, Mr. H. H. Fouracre Barns, 31, Weymouth Street, W.1.

Sheffield Medical School Old Students Association

This has recently been formed and the inaugural dinner is to be held on Oct. 2, in Sheffield. All old graduates are being circularised, but anyone who has not received a letter is asked to get in touch with the secretary of the pathology department, The University, Sheffield, 10.

Western Provident Association

This association is a mutual non-profit organisation providing its subscribers with cover against the cost of private medical care at hospital or nursing-home, including consultations. At the annual general meeting on April 30 it was announced that since the introduction of improved benefits at the beginning of 1953 membership had risen steeply. Income (including interest) increased by £10,153, or 41%, over 1952 compared with a percentage increase of 16% in 1952 over 1951. Notwithstanding the higher benefits paid, the revenue reserves and provisions for outstanding claims and unexpired risks increased by £5936 to £40,916 by Dec. 31, 1953. There was a surplus on the year's working of £3481.

Doctors are welcomed as full members of the association, but there is also a special scheme for members of the medical profession who do not feel that they need full cover. Further particulars may be had from the secretary of the Western Provident Association for Hospital and Nursing Home Services Ltd., Royal London House, Queen Charlotte Street, Bristol, 1.

56 (London) Armoured Division

The medical officers of the 56 (London) Armoured Division, T.A., held their first annual dinner on May 18. The A.D.M.S., Colonel J. A. Dudgeon, was in the chair, and Brigadier A. L. Crockford, honorary colonel, was also present. Among the principal guests were Major-General D. Dawney, the divisional commander, Major-General B. C. H. Kimmins, Director of the Territorial Army, Major-General A. Sachs, D.D.M.S., Eastern Command, Colonel Walter Mourand, jun., U.S. Army Medical Services, and Dr. H. Seaward Morley, master of the Society of Apothecaries.

CORRIGENDUM : Our Changing Mental Hospitals.—Dr. L. C. Cook's address to the Royal Medico-Psychological Association, to which we referred last week (p. 1087), was prepared jointly with Dr. Matthew Radzan, who read the paper.

Prof. L. J. Witts has been elected to honorary membership of the Association of American Physicians and of the Danish Society of Internal Medicine.

Sir Geoffrey Jefferson, F.R.S., is visiting Italy until June 6, to lecture for the British Council.

Diary of the Week

MAY 30 TO JUNE 5

Monday, 31st

- POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. O. G. Edholm : Effects of Environment in Man.
INSTITUTE OF CARDIOLOGY, National Heart Hospital, Westmoreland Street, W.1
9.30 A.M. Sir John Parkinson : Palpitation.
INSTITUTE OF OBSTETRICS AND GYNECOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Prof. J. Louw (Cape Town) : Eclampsia.
UNIVERSITY OF EDINBURGH
5 P.M. (60, George Square). Prof. Bruce Mayes (Sydney) : Experiences in Management of Pregnancy Toxæmia in Sydney. (Macarthur postgraduate lecture.)

Tuesday, 1st

- WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Prof. H. B. Maitland : Histamine-sensitising Property of *H. pertussis*.
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. P. D. Samman : Reticuloses.
UNIVERSITY OF EDINBURGH
5 P.M. (University New Buildings, Teviot Place.) Dr. John W. Clegg : Surgical Pathology of Pulmonary Tuberculosis. (Macarthur postgraduate lecture.)

Wednesday, 2nd

- ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.15 P.M. Section of History of Medicine. Lord Webb-Johnson Memorabilia. (Presidential address.)
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. H. Haber : Necrobioses and Erythema Elevatum Diutinum.
INSTITUTE OF OBSTETRICS AND GYNECOLOGY
NOON. (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Professor Louw : Rupture of Uterus.
MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (18, Nicolson Street.) Mr. Ian Lawson Dick : Backache.
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Prof. David Sloane : Physiological Studies on the Nasal Circulation. (Arris and Gale lecture.)

Thursday, 3rd

- POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. Brian Ackner : Emotions and the Circulatory System.
ROYAL SOCIETY OF MEDICINE
5 P.M. Section of United Services. Surgeon Commander M. A. Rugg-Gunn : Glandular Fever.
INSTITUTE OF OBSTETRICS AND GYNECOLOGY
3 P.M. (Chelsea Hospital for Women, Dovhouse Street, S.W.3.) Professor Louw : Urethral Pathology as it Affects the Gynaecologist.
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. F. S. Fiddes : Alcohol and Road Safety—Role of the Doctor in Examining Suspected Car Drivers.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Medical School, Small's Wynd, Dundee.) Prof. U. S. von Euler (Stockholm) : Functional Relationship Between Suprarenal Medulla and Adrenergic System.

Friday, 4th

- POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr. E. F. Chin : Surgery of Acquired and Congenital Defects of Diaphragm.
ROYAL SOCIETY OF MEDICINE
5 P.M. Section of Paediatrics. Dr. A. White Franklin, Hon. Mrs. Geoffrey Edwards, Mrs. Pudney : Adoption.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. G. B. Dowling : Scleroderma.

Births, Marriages, and Deaths

BIRTHS

- EASTCOTT.—On May 16, at Iver, Bucks, to Bobby, wife of Mr. H. H. G. Eastcott, F.R.C.S.—a daughter.
HELLER.—On May 18, at Robroyston Hospital, Glasgow, to Betty, wife of Lieut. M. D. A. Heller, R.A.M.C.—a son.
O'SULLIVAN.—On May 13, at DorisCourt Nursing Home, Manchester, 16, to Una, wife of Dr. J. G. O'Sullivan—a son (Timothy Francis).

MARRIAGES

- HILL—MANDELBAUM.—Last week, in Kensington, Dr. Roy Hill, medical registrar of the Bristol Royal Infirmary, to Dr. Lisa Mandelbaum, senior registrar for chest diseases, Frenchay Hospital, Bristol.

DEATHS

- LOGAN.—On May 10, at Southend Hospital, Anne Mary, much loved wife of J. Stevenson Logan, Medical Officer of Health, Southend-on-Sea.

BACKACHE AND THE DISC *

G. K. ROSE

M.B. Birm., F.R.C.S.

CONSULTING ORTHOPAEDIC SURGEON TO THE ROBERT JONES
AND AGNES HUNT ORTHOPAEDIC HOSPITAL AND THE ROYAL
SALOP INFIRMARY

In the terminology of Hollywood it is now some twenty years since Mixer and Barr "discovered" the intervertebral disc. Since that time its popularity has grown, at first slowly but with gathering impetus, until it is now probably at the pinnacle of its fame and therefore qualifies to be included in the limited group of subjects considered suitable material for music-hall jokes. Psychologists, of course, have long pointed a warning finger at the hidden significance of jokes, but all that an orthopaedic surgeon can deduce probably from this phenomenon is that the term "the disc" has now reached a stage of universal misunderstanding. In view of the immense number of facts known about this subject, and, more important, the tremendous volume of hypothesis and heresy which has grown around the hard core of facts, it is wise that we should review the current theories from time to time in as critical light as possible.

Study of backache in its widest aspect has been hampered by the distortion of the objective-subjective relationship which one has been taught to regard as a necessity from the start of one's medical training. Too often, despite the complaint of bitter pain, objective findings are very few, even when ancillary diagnostic aids are used. When such objective findings exist, it is difficult, even in the light of modern knowledge, to formulate an accurate and convincing hypothesis which will explain them. From the practical standpoint, however, it is important to realise that in many patients the condition is not self-limiting: its acute phase may pass without treatment, but may leave residual symptoms—often classed in the past as rheumatism and regarded as incurable both by the patients and the doctor, although of late the tendency has been to classify them frequently as psychoneurotic. It is hard to believe that pure psychoneurotic pain exists, but it is easy to understand that the patient's response to pain varies widely and deteriorates the longer the pain persists and treatment fails to give relief. It may be epitomised in the phrase "chronic pain corrupts." This also carries the implication that in dealing with such a patient, if the original nature of the condition can be discovered and remedied, the result may be more rewarding, both to the patient and the practitioner, than possibly the remedy of a more serious organic lesion in a more robust type of person, if one assesses success in terms of restoration to fullest activity of the patient as a whole.

Investigation of these cases is often difficult and may be disappointing; for, as Laurens Van der Post has reminded us, "there are people and nations who create, with submerged deliberation, a sense of suffering and of grievance, which enables them to avoid those aspects of reality that do not minister to their self-importance, personal pride, or convenience. These imagined ills enable them to avoid the proper burden that life lays on all of us." But one cannot avoid trying, when one has seen so many patients labelled as hopeless neurotics become changed people under adequate treatment. Further, the more rational and decisive one's treatment becomes, the greater will be one's incidental opportunities in the field of preventive psychology.

There is also another, perhaps less well appreciated, aspect of the relation of a patient's temperament to his disease. In these days of rush and anxiety many patients are temperamentally unable to accept the limitations of

treatment, particularly when the treatment may involve a change in their way of life which is prolonged or permanent. In effect the proposition that they put to their doctor is that they wish to be cured, but in no circumstances will they undertake any treatment inconvenient to themselves. They are in consequence attracted by the reputation of any practitioner, orthodox or unorthodox, who will promise a quick, if not instantaneous, cure, and it is only if the doctor has a definite and rational plan of treatment worked out that he can avoid the pressure to undertake a series of often empirical treatments in no very definite order in the hope of achieving some spectacular result. On the other hand, the doctor must realise that the disease is not fatal, and therefore he must at all times take care not to institute treatment which is worse than the present state of the disease. This necessitates an accurate assessment of the disability caused by the condition initially, the patient's normal way of life and responsibilities, experience with the methods of treatment used, and an attention to detail in those methods.

Anatomico-physiological and Mechanical Considerations

In the human body the spinal cord and the spinal nerve-roots happen to be intimately related to the central skeletal system, and this relationship is most vociferous at the point where, in the skeletal system, pathological changes of one kind or another are most likely to occur. Where the great nerves of the cervical and lumbar plexuses flow out from the spinal cord, pressure upon or irritation of these nerves and neighbouring ligaments will cause widespread pain. In the thoracic region, as the nerves are small and supply small areas of tissue, the pain is less widespread but gives a typical picture.

Cervical Spine

The cervical spine is vulnerable because of the anatomical instability of the intervertebral joints, the high degree of mobility, and the liability to repeated minor injuries, particularly in the first two decades of life, and because, as in the lumbar region, the arrangement of muscles to brace the cervical spine—a legacy from our four-footed ancestors—is a poor one.

Lumbar Spine

In the lumbar spine the prime function is that of carrying weight and withstanding the strain imposed to the long leverage of the thoracic trunk and arms, particularly in the fully flexed position. In view of the proximity of the hip-joint, mobility is a secondary feature. However, there is some mobility in the lumbar spine, and the point of maximal wear is the site of junction between the spine and the pelvis—i.e., the lumbosacral region, which is probably the most used and most abused joint in the spine. Furthermore, in the erect position there is a shearing strain as lumbar vertebra 5 tends to ride forward on sacral vertebra 1. Here too one finds a relatively high incidence of congenital lesions, some of which may be minor but are I believe significant in the consideration of backache. As in the cervical spine, the bracing of the lumbar spine by muscles is relatively inefficient. Here the anterior bracing is a function of the abdominal wall, which too often loses its tone early in life, either from pregnancies or disuse.

Thoracic Spine

The thoracic spine, on the other hand, is well supported by the bony cage of the chest and bears relatively less weight than the lumbar region, and its limited mobility is mainly in a rotational plane.

Intervertebral Disc

The anatomy of the disc is now too well known to necessitate any reiteration of the main points. Beadle (1931) described it as a hydrodynamic ball-bearing, the

* Paper read before the Midland Surgical Travelling Club.

function of which is to control the continual and infinitely various cross-currents, tension, torsion, pressure, and mechanical shock, which interplay with one another as injurious agencies during every moment of life. He pointed out that, whereas each of the three main structures of the disc is highly important in itself, it depends also on the others:

If the cartilaginous plate is perforated, even with pinpoint holes, its function as a semipermeable membrane is destroyed, and the water content of the nucleus pulposus, on which its efficiency depends, is diminished. On the other hand, if relatively large holes appear in the cartilaginous plate, as they do almost without exception in the fifth and later decades of life, the nuclear material may flow in the adjacent vertebral bodies and no longer maintain its hydrodynamic action.

A similar situation occurs in a rupture of the annulus fibrosus. Further, it must be appreciated that the nuclear material is almost entirely non-compressible and non-elastic, and the dynamic action of a disc is entirely a property of the spiral arrangement of fibres within the annulus. Where the annulus has been torn, significant permanent changes must take place in this mechanism.

The work of Coventry et al. (1945) shows clearly that we must be careful to take account of the degenerative changes which continue decade by decade. They point out that the disc progresses in its development until about the age of 18, when retrogression starts, and it is in the third decade that the annulus fibrosus begins to show, almost in all cases, degenerative changes. Unfortunately the nucleus is rather behind the annulus in its retrogression, and at this point is at its maximal function, with a uniform soft buffer action. Though it is now at the peak of its hydrodynamic efficiency, if the annulus ruptures, the mechanism set up is basically similar to a hydraulic ram working in reverse, and the expansive force pushing its way through the annulus is many times reduced compared with that in the nucleus (fig. 1). It can, however, travel a considerable distance (compared with the diminution in disc space) if this principle obtains. But the analogy must not be carried too far, for the piston lies on (not in) the wall of the cylinder, and this wall (the annulus) is only partly compressible at the time of the prolapse, although with the passage of years it may undergo almost complete degeneration. Hence, when the compression has reached its limit, the important factor in squeezing the nuclear material posteriorly will be that of flexion, particularly when this is combined with a rotatory angular movement which brings the maximal force laterally against the portion of the annulus least well supported by the posterior longitudinal ligament.

The more one considers this problem, the more one feels that the rate of prolapse—which is in turn an integration of the maximal causal pressure with the effective resistance of the annulus at the point of prolapse—is the important factor in determining the degree and type of prolapse. To use a further crude analogy, it is the boil which needs forceful squeezing which is eventually shot out most vigorously. Only, therefore, during a relatively short period when the annulus has not yet degenerated far but is slightly less efficient than the hydrodynamic state of the nucleus, can acute prolapse take place. Bulging of the whole disc posteriorly, and even its sequestration into the spinal canal, can occur later in life, particularly in the cervical region, but the acute nuclear prolapse never.

In the fourth decade the annulus, although it continues to degenerate, is in less danger, owing to the opening of safety valves. The cartilaginous plate begins to give way, at first microscopically, with interference in the semipermeable properties, and later macroscopically, allowing vertical prolapse of the nuclear material. The material of the nucleus is starting to lose water and becomes more fibrous, and its properties change from those of a fluid to those of a soft solid. The hydraulic-ram principle ceases to act, and, even if a lesion develops

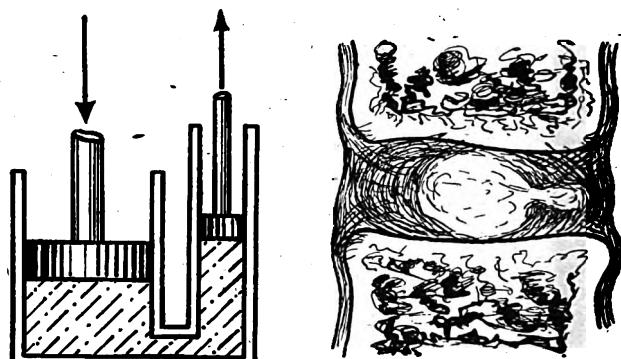


Fig. 1.—The reverse hydraulic press principle indicates that the pressures which cause protrusion of the disc are probably less than was previously thought, at any rate initially, but the pressure is prolonged even though the disc material is reaching the posterior longitudinal ligament.

in the annulus, the outward pressure tends to be equal around its whole surface. Hence it tends to bulge symmetrically rather than to split.

In the fifth decade the hydrodynamic principles seem even further away. There is degeneration of the cartilaginous plate now with many defects. The annulus continues to degenerate, but the components of the nucleus become less distinguishable, and a gradual fibrous replacement is going on. The nucleus is now almost completely fibrocartilaginous and blends more and more with the annulus, which, although it shows a high proportion of tears posteriorly, very seldom shows protrusion of the disc substance.

It is reasonable to suppose that, where a frank posterior prolapse of the intervertebral disc has taken place, the breakdown of the hydraulic mechanism is likely to be enormously accelerated, and one must conclude that any conception of the prolapsed intervertebral disc as a lesion which can result from an almost infinite repetition of similar events—analogous to a lesion due to repeated dislocation and reduction of the semilunar meniscus—is entirely erroneous. Radiography at the time of a posterior prolapse of the intervertebral disc rarely shows any change, even where a massive central prolapse has occurred; but, if these cases are followed up, almost inevitably after five or six years a typical thin disc space can be seen. It is likely that, where at the initial prolapse only part of the nuclear material has been protruding, a secondary protrusion of the remaining material consequent on further annular degeneration may take place within the next one or two years, but I have never seen a definite prolapse after a much longer interval than this; and certainly a classical and common history of sciatica in the third decade, followed by an attack of sciatica some twenty years later, is never due to a recurrent prolapse, because one never sees these cases in their later attack with root pressure.

We should remember, however, that the whole disc can degenerate quietly without any posterior prolapse—as a result of some mild trauma or of prolapse through the cartilaginous plate.

Causation of Symptoms

So that the treatment in all cases of backache should have a rational basis, an effort must be made to analyse the phenomena presented by patients with backache, sciatica, and brachial neuritis. In doing this, allowance must be made for several barriers which exist between the understanding of a patient and the surgeon.

The simplest one, of course, is the ordinary meaning of words or association of words, and this means that the surgeon must devise a series of unambiguous questions and insist on answers to them. On visiting clinics throughout the whole country, one is struck by the unconscious but almost fiendishly ingenious way in which patients

avoid these answers. Every medical school insists that its students should learn the technique of the elicitation of physical signs accurately, and the technique of interrogation is just as important here. Too often one hears :

- Q. Does rest help the pain ?
- A. I never rest.
- Q. Do you never go to bed ?
- A. But I feel worse when I get out of bed.
- Q. I mean, are you better in bed ?
- A. Not until I have got into a comfortable position, &c.

Another barrier between the understanding of the surgeon and the symptom picture is psychological, and here it is the surgeon's psychological attitude that is important. One is apt to be irritated by the patient who tells his story in too great detail, suspecting, often correctly, that he is introspective and allows his symptoms to weigh too heavily; but nevertheless it is often in the words of these chatteringers that one can find the key to their problems.

Provided allowances are made for these two factors, it becomes apparent that the pain of which a patient complains in backache is a compound phenomenon consisting in various sensations which belong to one or more of the groups described below. I do not believe that these groups are entirely well-defined specific entities, but they appear to represent important functional units, at any rate from the point of view of treatment and probably from that of aetiology.

PAIN OF MUSCLE SPASM

This pain is often severe and is accompanied by a characteristic "seizing up" of the affected muscles, which are tender. It is characteristically phasic, and may be induced or aggravated severely by a slight movement. It is often sudden in onset, and its relief may be equally sudden, following some manipulative procedure either given deliberately or sustained accidentally by the patient in slipping. The pain is always relatively local—e.g., in a lumbar-spine lesion the typical pain of lumbago—and the spasm is a reflex action, one almost might say overaction, to attempt to immobilise the intrinsic lesion. In this respect it is analogous to the muscle spasm which accompanies the fracture of a long bone and this, as we know, diminishes and disappears when one takes over its function by the application of splintage to the fracture; and it is those cases which have the very acute spasm which often respond most satisfactorily and quickly to immobilisation. It is fairly rare in the cases of backache seen in consulting practice but is common enough in general practice. It has not been possible to determine precisely the site of the afferent nerve-endings, but one suspects that these are in the annulus or in the posterior longitudinal ligament. However, some cases of muscle spasm do not respond to immobilisation satisfactorily, and in these cases the pain is, I believe, analogous to that of a dislocated major joint, where immobilisation without reduction does not give relief. This analogy seems so important that it leads one to think that most often, where manipulation has a dramatic effect with complete relief of pain, one is dealing with a lesion of the intervertebral articulation, possibly a simple nipping of the synovial fringe or even a displacement of a loose body between the surfaces of the intervertebral articulation; for, as Macnab (1952) of Toronto has shown, loose bodies in these articulations are not uncommon, particularly in the middle-aged.

NERVE-ROOT PAIN

It is strongly disputed whether pressure on a nerve-root causes pain. Murray Falconer et al. (1948) and Inman and Saunders (1944) deny that it does, and have pointed out that pressure on a peripheral nerve, which one can test easily for oneself, does not produce pain, but moderate loss of power and paraesthesia are followed by

numbness, the actual sequence of events depending on the speed at which the pressure is applied. However, there are many who hold the opposite view, and many surgeons who have explored the nerve-root under local anaesthesia have been equally emphatic that manipulation of a nerve-root—particularly angulation—will produce severe pain; but none have indicated, so far as I know, the area of radiation of this pain. The difference in behaviour of a nerve-root on compression from that of a peripheral nerve can be explained only by the intimate dural covering which accompanies the nerve-root right to the intervertebral foramen: Stöhr has indicated that there are sensory nerves and innumerable autonomic and vasomotor nerves in the dura, and he has further suggested that the endings of these nerves are probably receptors for conveying information about changes of pressure in the cerebrospinal fluid.

Two important phenomena in regard to root pressure need to be fitted in with any hypothesis about the causation of the pain. The straight-leg-raising test has been demonstrated convincingly, at any rate between 30° and 70°, as a method of increasing pre-existing root pressure. Besides being a test for root pressure it is an important indicator of the effects of root pressure, and it seems to be significant that, when the test is made, patients complain of pain not in the distribution of the sciatic nerve but in the buttock. This indicates that the effects of root pressure are at least twofold—one on the nerve-root, which is essentially similar to a peripheral nerve, and the other on the covering of the nerve-root. We know that the covering is richly endowed with nerve-fibres, and probably it is an efferent receptor station for the sclerotogenous type of pain (see below); and it is equally important to realise that this pain is not related to the distribution of the nerve which the dura covers.

It is less easy to explain the other phenomenon, which occurs less often than a positive result of the straight-leg-raising test but nevertheless is very characteristic when present—i.e., the sciatic radiation of pain on coughing or sneezing. In interrogation of the patient one must clearly differentiate this from the local backache which is so common on coughing and is due to an increase of tension in the spastic muscles of the back and to jarring of the intrinsic lesion. It has been said that the increased tension of cerebrospinal fluid within the theca on coughing presses the nerve-root against the prolapsed disc, but there seems to be no doubt that the effects are very different from the mechanical extrinsic pressure which occurs with the straight-leg-raising test. We know that the dural sac and the free portion around the nerve-root are distended on coughing normally, and that this does not cause pain. Presumably, where there is pressure on the nerve-root, congestion and oedema due to the pressure render the nerve-root sensitive to this distension—cf., the tension pains arising in the air sinuses of the skull. However, it is still difficult to explain why this pain should have sciatic radiation, and my general purpose in introducing it here is to draw attention to the fact that careful observation and interpretation of symptoms are very necessary, because with different types of stimulation, and probably with stimulation of afferent receptor endings less than a millimetre apart, the effects may be very different.

SCLEROTOGENOUS PAIN

This term was coined by Inman and Saunders of the University of California, who describe a pain which is slow, deep, aching, and accompanied occasionally by constitutional disturbances, giving more or less subjective uselessness to the affected part, and having a rather ill-defined distribution in relation to the dermatomes. Furthermore it is accompanied by local tender spots situated at the insertions of tendons into bones and by aching in the muscles (Inman and Saunders 1944).

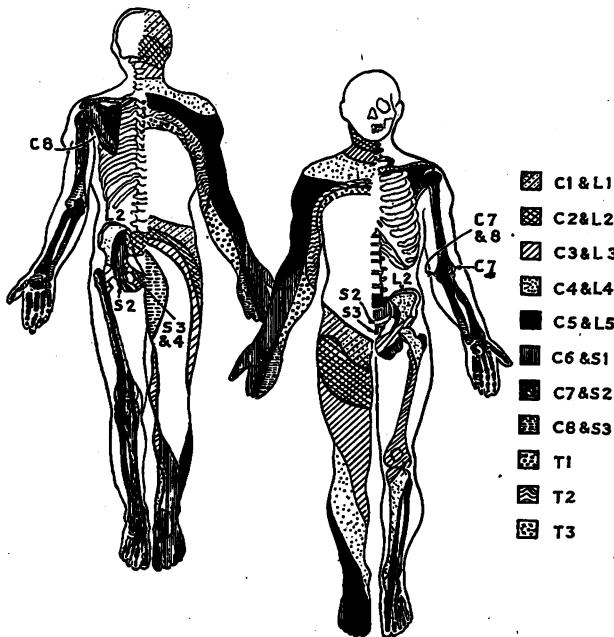


Fig. 2—Dermatomal and sclerotomal innervation of the extremities in man (after Inman and Saunders).

Kellgren did much original work on this type of pain, inducing it experimentally by the injection of saline solution into an afferent area, and his method has been used in mapping out the various sclerotomes. Kellgren (1939) pointed out that sclerotogenous pain induced by stimulation of any part of the afferent side of the arc will be identical, and has shown, for example, that angina-like pain can be produced by the injection of saline solution into the region of the interspinous ligament between dorsal vertebrae 2 and 3. He performed this experiment on a group of doctors who were well aware of the true nature of angina inasmuch as they were sufferers from this condition, and they confirmed that the pain was identical with that which they had during a genuine anginal attack. This experiment incidentally points a warning ; for, as so often happens in the absence of objective signs, once one begins to recognise the various sclerotomes it is easier to believe that they all arise in the more central area, as I am sure the great majority do, and to ignore other possibilities. The pain in a patient's arm may be the classical pain of a cervical nerve-root irritation ; but to treat it without careful examination of the axilla is to do so at one's peril. On the other hand, if the axilla is examined routinely, the tender area in the sclerotome of C8, shown by Inman and Saunders (fig. 2) immediately below the glenoid fossa, will be detected remarkably often. The richest distributions of afferent areas are those in the posterior longitudinal ligament of the spinal cord, the annuli, the dura, and probably the capsules of the intervertebral articulations.

Clinically the phenomenon of sclerotogenous pain is demonstrable by tender spots which accompany it, and classical examples of these tender areas are found around the posterior superior spine, most often just lateral to it on the wing of the ilium, over the tip of the transverse processes of lumbar vertebra 3, and over the external epicondyle of the humerus, where they may be mistaken for tennis-elbow. We also know that many patients with coccygodynia have in fact this area of referred tenderness via the 2nd sacral sclerotome. The tender area in relation to the posterior superior spine is particularly interesting because it has given rise in the past to what Schmitter (1937) called the sacro-iliac cult. When these areas are examined closely they are often far from the sacro-iliac joint and lie on the lateral wall of the ilium,

and they are always at a point where a tendon is attached to the bone. Schmitter was equally caustic over the fatty-nodule cults : there is no part of the body where fatty nodules are more easily felt, both in health and disease, than in this region, but on careful examination the nodules can always be pushed aside to enable the deeper lying tender area to be palpated.

Patients and some surgeons—though they have no difficulty in accepting the subjective phenomena in amputation stumps—find it hard to accept this principle of referred tenderness. Nevertheless I have seen many cases which showed it clearly.

One patient, for example, had a highly mobile spondylolisthesis in the region of lumbar 4-5. In the past he had gained some relief by having the tender areas in his buttock injected with procaine, but these areas disappeared completely when the affected area of the spine was grafted. When the graft fractured they reappeared, but they disappeared finally when, after a further period of immobilisation, it became completely consolidated. In all this time no local treatment to the tender areas was given.

One can often find that certain postures induce the appearance of these tender areas, and I have seen patients who, when lying prone, had no tender area whatsoever, become tender below the posterior superior spine when they were in the lateral position.

It is important at this point to consider in more detail coccygodynia, which Schmitter (1937) postulated to be an adjunct to sciatica, like lumbago. Dittrich (1951) regards it as a referred pain from a primary source overlying the second sacral vertebra. Recently Richards of the Robert Jones and Agnes Hunt Orthopaedic Hospital, has postulated that it is due to a central prolapse of the lumbosacral intervertebral disc pressing on the 2nd sacral nerve (Richards 1953). The chief basis for this hypothesis is the fact that the condition is much commoner in women than in men—in his opinion because the lumbosacral angle differs in the sexes. Whatever the mechanism may be, the pain is obviously sclerotogenous in type ; but, as has been pointed out, this is not excluded by the root-pressure theory. I personally think that a posterior central prolapse is an unlikely cause, for coccygodynia develops often before, or, less commonly after, a lateral posterior prolapse, and it seems unlikely that both central and lateral prolapse, sufficient to cause nerve-root pressure, ever occur at one disc space. Further, it is sometimes associated with complete sequestration of the lumbosacral intervertebral disc, obviously of long standing. I have seen cases of sixteen years' duration, and I do not believe that root pressure can last so long. However, the excellent results of efficient immobilisation of the lumbosacral area in this otherwise intractable condition give a clue to the essential pathology.

JOINT PAINS

Pain undoubtedly arises from the intervertebral joints, which are deranged by diminution of the intervertebral disc space. Loose bodies occur, and osteo-arthritis changes may develop.

Probably, apart from local aching in the joint, most of the pains which arise from the intervertebral joints are either sclerotogenous or due to muscle spasm, but reduction of a loose body here can have a dramatic effect and be called reduction of a prolapsed intervertebral disc. All osteo-arthritis joints later in life are subject to sudden tense effusions after minor trauma, and locking of the back with muscle spasm in older people may be called a prolapsed intervertebral disc.

Further, the relation of the joint to the nerve-root is important, and capsular changes in the joint may involve the nerve-root either by pressure, adhesions, or round-cell infiltration. In the cervical region the relationship of the nerve-root and the articular periphery is much more intimate than in the lumbar region, and osteophytic

changes here therefore are more likely to press directly on the nerve.

SPECIAL AREAS

Certain areas of the spine have a special function, and any interference in the mechanics of the spine will disturb this function. The upper cervical muscles and spine are concerned normally in balance and determination of the position of the head and the body in space. Skeletal derangement in this area will give symptoms of vertigo and even secondary nausea, the posterior cervical syndrome of Barré.

Relation of Symptoms to Pathology

Sooner or later it becomes necessary to outline the progressive pathology of a disc lesion in relation to symptoms. With much unproved, this is a hazardous proceeding. Evidently there are two basically inter-related problems—skeletal derangement, and nerve-root pressure. This, I believe, remains true whether we are dealing with disc lesions or any other of the many causes of backache (except perhaps neoplasm), and the distribution, type, and timing of the pain can be an important guide to differential diagnosis.

In a classical case of posterior prolapse of the intervertebral disc in the second or the third decade the nuclear material forces its way through the annulus, and it is during this stage that the first twinges of sclerotogenous pain are felt. There is evidence from the post-mortem studies of Coventry et al. (1945) that the condition can be arrested at this stage, possibly owing to the toughness of the peripheral portion of the annulus. This may happen spontaneously or through limitation of forward flexion, which increases the pressure against the posterior portion of the annulus. This limitation may be by muscle spasm or by external fixation. When, however, nuclear material continues to break through the annulus it eventually comes to lie underneath the posterior longitudinal ligament, carrying with it some outer fibres of annulus, and it is likely that pressure on this ligament, with its subsequent elevation, represents the climax of sclerotogenous pain. As the collection of nuclear material increases it may press on the nerve-root, most commonly with the posterior longitudinal ligament intact, but in about 1 in 10 cases after the posterior longitudinal ligament has been ruptured, this rupture being the resultant presumably of the rate of prolapse and the degree of ligamentous degeneration. The degree of pressure exerted will also depend on the mobility of the nerve-root and on its immediate relations, a very small prolapse laterally being much more effective as regards root pressure than a central one, where almost always, before the root-pressure symptoms develop, the prolapse needs to be massive.

Changes also take place in the nerve-root—local oedema has been described often—and in this way the effects of extrinsic pressure may be enhanced; and, even when the pressure has been relieved, permanent changes may remain in the nerve-root, usually to a minor degree and noticed by the patient as increased sensitivity to pressure of the sciatic nerve peripherally and notably at the buttock and knee.

I have described what I believe may be the effects of pressure on the nerve-root and advanced the hypothesis that these may be both sclerotogenous from pressure on the dura and due to peripheral nerve pressure, but I believe that the sclerotogenous element from this source is slight compared to that from ligamentous sources. The pain picture which is seen without root pressure indicates this. Also, where the posterior longitudinal ligament has ruptured, low back symptoms tend to be the less important part of the pain picture.

Reduction of Prolapse

When one has seen a fresh specimen of the intervertebral disc and has had experience of the prolapsed

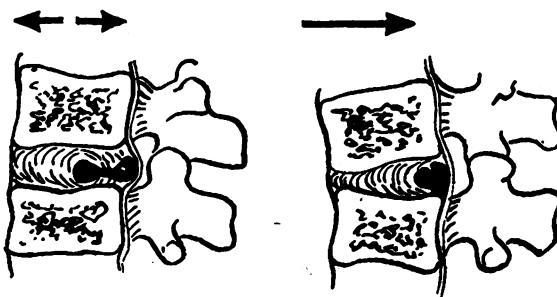


Fig. 3.—Whilst the size of the prolapse is reduced by forward flexion tension is increased.

intervertebral disc at operation, it seems impossible to believe that a prolapsed nucleus pulposus can be permanently reduced. Though it is agreed that flexion of the spine will reduce the size of the prolapse visible at operation, this is due only to tightening of the posterior longitudinal ligament. One can deduce from mechanical considerations that tension of the prolapsed intervertebral disc against the posterior longitudinal ligament is in this situation increased both because the ligament has tightened and because of the rolling of the nucleus pulposus posteriorly (fig. 3). This is suggested too by the fact that, in low back pain of disc origin without root pressure, local extension of the spine will decrease sclerotogenous pain, and flexion increase it. Hence any decrease in the size of the intervertebral disc on flexion really bears no relation to reduction and would in any case disappear when the patient stood erect. Even if one could be persuaded that the nuclear material could flow back into the "pillbox" of the annulus, one cannot believe that reduction of nuclear material ever takes place as a dramatic specific event.

A different case might be made out for the annulus ruptured later in the life-history of the disc. If the rupture occurs early in life, the same mechanical principles apply as for the nucleus; but later in life the disc is becoming relatively homogeneous, and, if a segment of annulus were broken off and flapped open posteriorly—taking with it, as it must, a segment of the posterior longitudinal ligament—we can imagine this being reduced into the space it previously occupied and remaining there even when the patient assumed the erect position. The difficulty here is that, these conditions having been postulated and the disc being assumed to act as a completely solid object with most of the weight taken by the remaining annulus and fibrous nucleus, which, owing to the loss of its fluid properties, would not be exerting any localised posterior pressure, it is difficult to see what mechanism could achieve reduction. Here the situation compares most closely to the torn meniscus of the knee, and it is well understood that, when the elasticity of the meniscus has gone, reduction often becomes impossible because return of the meniscus to its former position depends on this elasticity. Further, the manipulation described by practitioners who claim to reduce this type of disc is usually of the extension type. The possibility cannot be discounted, but one can only suppose it to be extremely rare. If then reduction of a prolapsed intervertebral disc is quite exceptional, one is left with the other possibility that pressure on the nerve-root may be relieved by changes in the nerve.

Murray Falconer (1948) has shown that, where a prolapsed intervertebral disc was demonstrable by myelography in an acute phase, after conservative treatment with complete clinical recovery the disc had apparently not changed in any way, as judged from a further myelogram. In one such case an operation was performed and the nerve-root was found to be lying loosely over a large prolapse. My experience is that, though most of these cases can be cured by conservative treatment, where this

has failed one is most likely to find a lateral prolapse of the intervertebral disc. It is in these circumstances, where the nerve-root is confined to a bony passage and where its dural covering is tough and anchored, that the root is least likely to avoid contact with the prolapse.

In his experimental work on the cat, Murray Falconer (1948) produced artificial prolapse of the intervertebral disc by inserting small wooden pegs under the nerve-root. The nerve-root was held under considerable tension, and the cat on recovering from anaesthesia limped badly. However, after a few days the normal gait returned, and, when the area was re-explored, the nerve-root was found lying freely above the wooden peg with no tension whatsoever. All these facts suggest that the root pressure is usually relieved when the nerve-root tension is diminished by the straightening out of the intrathecal portion of the root from its normally slightly tortuous course. To obtain complete relief from pressure in these circumstances, only very slight lengthening of the nerve-root is necessary. It has been said that sciatic scoliosis is adopted unconsciously by the patient to allow the nerve-root to lie to one side of the prolapse, and that this explains alternating scoliosis, because the direction of the scoliosis is immaterial, provided the desired result is obtained at the nerve-root. I think that this is undoubtedly so in many cases; but some cases of sciatic scoliosis do not have root pressure, and in these cases relief of tension on the posterior longitudinal ligament may be the mechanism of the posture. Fixation of the patient in forward flexion suggests that the posterior longitudinal ligament is being tightened to pull the protrusion from just touching the nerve-root.

However, this is not the whole story, obviously. Lindblom and Hultqvist (1950) have shown that the prolapsed disc is absorbed by granulation tissue, which digests the disc tissue at the level of the posterior border of the vertebral body and also digests some of the fibres of the annulus. This must be a slow process—part of the healing of the lesion but clearly not part of the early relief of symptoms.

Traction will apparently enhance this lengthening of the nerve-root, but lengthening will also occur spontaneously, and fixation in a plaster-of-paris corset or spica may well reduce the sclerotogenous element of the pain while it is taking place. Such treatment is also beneficial in preventing the pumping of further material into the prolapse by flexion and extension. Occasionally by manipulation one can get the nerve-root to pass to one side of the prolapse and so help to relieve the symptoms. Continuous traction, which will also reduce the size of the prolapse by tightening the longitudinal ligaments, and immobilisation therefore seem rational forms of treatment for root pressure. Manipulation (certainly under anaesthesia) seems dangerous, and more than a gentle manipulation without anaesthesia irrational. When conservative treatment fails, operation is necessary; but where it is successful, as it is in the great majority of cases if applied systematically, it blends almost imperceptibly into the treatment of the skeletal derangement.

Treatment of Skeletal Derangement

This largely depends on the site. If it is the lumbar region, where the prime function is that of transmission of strong forces, one must make every endeavour both to relieve the symptoms and to treat the intrinsic lesion.

This is a distinction very rarely appreciated by the patient and sometimes poorly understood by the person responsible for treatment. The primary line of treatment must therefore be that of support, and it is obviously ideal that the patient's own muscles should do this. Too often, however, the muscles are past the stage of re-educational exercises and are inhibited by pain. Immobilisation therefore seems to be a rational form of treatment here, particularly when it can be combined

with muscle exercises. Because one's aim is healing of the intrinsic lesion, the immobilisation initially must be efficient and prolonged, until diminution of symptoms enables one gradually to reduce the efficiency of the support to allow the patient's own muscles to take over this function. Initially it may be necessary to use a plaster spica, but in a thin person a plaster corset may suffice and will be much less trouble to the patient. This can be followed by a strong canvas belt, incorporating a leather back-plate (something of the Goldthwait type), and it may be necessary that this should be worn day and night in the early stages. After a time it can be given up during the night, and after six months or so a very light lumbosacral belt can be assumed in its place. With many patients this can be eventually discarded in a further six to twelve months, and one can feel happy that not only is the patient relieved of symptoms but that the intrinsic lesion is healed. Some patients, because of physical or psychological inadequacy, will wear such belts for the rest of their lives, but the great majority eventually give them up.

Review of my own cases seen at the orthopaedic clinics of the Royal Salop Infirmary in the last three years has shown that the best results of treating degenerative lesions have been obtained in those of osteo-arthritis of the knee-joint. This is because a rigid routine form of treatment is used which consists in immobilisation of the knee, where necessary, during the acute and inhibitory phase of the condition, combined with consistent and persistent exercises for the quadriceps muscle. For degenerative lesions of the low back surely the same principles apply, and the high proportion of success with this type of case has encouraged us to believe that we are not wrong in this hypothesis. One must emphasise the principles of the treatment, for if they are not understood and accepted by the patient they may degenerate into the wearing of an inefficient support, giving only minor relief for the rest of the patient's life—a state so rightly decried by many practitioners.

In the cervical region, however, the problem is very different. The chief function of the cervical region is mobility to make the sensory organs resident in the head most efficient. To most patients, the wearing of any support here is an intolerable burden, and manipulation, traction, short-wave diathermy, and increasing mobility give a much better final result than does an immobilising process, although there are ultimately those cases to which the same general principles must apply as in the lumbar region, particularly where degeneration is advanced or root-pressure considerable.

Often patients who have had efficient immobilisation of their lumbosacral region return within a few months with trouble in the cervical spine because the immobilisation of the lumbar spine throws a greater strain on the cervical spine, which may itself be the site of degenerative changes. Spines which show degenerative change at one place are likely to have other lesions elsewhere. It is worth while therefore, if one treats the lumbar spine by immobilisation, to initiate preventive treatment, by means of exercises, in those patients who have a coexisting reduction in mobility of the cervical spine. In the cervical spine skeletal derangement is far the commonest cause of symptoms and posterior prolapse of the disc is very rare at any age. Root-pressure signs occur most commonly late in life and are due to involvement of the root in pathological joint changes. Though posterior bulging of the whole disc occurs at this age, it is not a nuclear prolapse, and the symptoms are usually those of cord compression.

I have said little about lesions of the thoracic spine because they are even less understood than those of the cervical and lumbar spine. The pains arising here are almost all sclerotogenous, but central prolapse with paraplegia can occur.

Extrinsic Causes of Backache

Backache cannot be assumed to have a central origin until all peripheral causes have been eliminated as far as possible.

Whenever muscle tone is reduced a greater strain falls on the joints and ligaments of the back. The commonest acute causes of this are the common cold and influenza. The symptoms are likely to be more pronounced where a mild, possibly subclinical, skeletal derangement already exists, and in these circumstances they may become an inconvenient and apparently permanent lesion from the patient's point of view. A less obvious cause is the gradual loss of muscle tone in people who take little or no physical exercise : there is a lot to be said for the "daily dozen" in some form or other. Persistent pain also may lessen muscle tone generally ; and, since a common type of this is backache, a gradual "running down" may take place with reduced tone, further backache, consequent general fatigue, and further reduction in tone.

As gynaecologists are not agreed about gynaecological causes of backache, it would be dangerous for an orthopaedic surgeon to venture a firm opinion, but it seems likely that pelvic congestion from any cause will increase low back pain, no matter what the intrinsic lesion. There seems to be no doubt that about half of all patients attending gynaecological departments with cervical erosions have their backache cured when this lesion is cured, and it has been claimed that a cervical erosion is an afferent receptor station for sclerotogenous pain in the 1st lumbar sclerotome. It is therefore imperative that the orthopaedic surgeon should include the leading symptom of cervical erosion—i.e., intermenstrual discharge—in his interrogation, particularly of married women ; but it is equally important that the gynaecologist should not seek to remedy backache by a succession of gynaecological operations in the face of a definite spinal derangement. Even in the hands of enlightened gynaecologists there are occasional dangers where a patient presents with backache and also with gynaecological signs and symptoms which demand dilatation and curettage. In these circumstances, particularly where considerable degeneration of the lumbosacral disc exists, the lithotomy position, with the lumbar region forced into flexion by the sharp pull of an enthusiastic house-man, may turn a mild backache into considerable pain, with some loss of confidence on the part of the patient, if nothing worse.

Summary

Some of the problems posed by the ever-increasing number of patients with backache are briefly reviewed, with particular reference to the prolapsed intervertebral disc.

An attempt has been made to analyse the types of pain and to assess them in terms of essential pathology, and by this means to get a clearer picture of the needs of treatment and of prognosis.

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ISONIAZID AND STREPTOMYCIN IN TUBERCULOUS MENINGITIS *

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WHEN isoniazid became available in April, 1952, nothing was known about its use in tuberculous meningitis. We decided to investigate its possible advantages, and for this reason we first reviewed the results of our treatment relating to the twenty months preceding its advent. The analysis showed that, with combined streptomycin and *p*-aminosalicylic acid as a routine treatment and with intrathecal purified protein derivative (P.P.D.) as a selective adjuvant, 25 of 27 consecutive children who were conscious on admission recovered, but of 11 children who were unconscious only 3 survived. The period of observation of these 28 sur-

TABLE I—RESULTS OF TREATMENT OF 38 CASES OF TUBERCULOUS MENINGITIS
(August, 1950-March, 1952)

Conditions on admission	No. of cases	Survivors
Conscious	27	25 (92.6%)
Unconscious	11	3
Total	38	28 (73.7%)

Period of observation 2-3½ years.

vivors is now between two and three and a half years (table I) (Lorber 1954).

In view of these observations it was decided to give isoniazid to all patients who were unconscious on admission and to allocate the conscious patients by random sampling to one of two treatment groups in a controlled therapeutic trial.

Present Investigation

PLAN OF TREATMENT

All the children were given intramuscular streptomycin and oral *p*-aminosalicylic acid (P.A.S.) for at least six months, and all received at least one course of forty-five intrathecal streptomycin injections exactly as in our previous series (Lorber 1954). Isoniazid was given by mouth for at least six months to half the children who were conscious on admission (the controlled trial) and to all those who were unconscious—i.e., who were not included in the trial. The dose of isoniazid was 5 mg.

TABLE II—PLAN OF TREATMENT

Drug	Controls	Isoniazid group
<i>Streptomycin :</i> Intramuscular ..	6 months or longer	6 months or longer
Intrathecal ..	45 injections or more	45 injections or more
P.A.S. (oral) ..	6 months or longer	6 months or longer
P.P.D. (intrathecal)	Optional	Optional
Isoniazid (oral) ..		5-20 mg. per kg. daily 6 months or longer

per kg. body-weight daily ; but, when no toxic effects were observed, this dose was later increased to 20 mg. per kg. daily (table II). If a "control" case was not making progress after an adequate period of treatment it could be transferred to the isoniazid group. Intrathecal tuberculin was used in selected cases in both groups, in accordance with our previous criteria.

The planning of this investigation was such that we could not expect any significant difference in the survival rates of the two groups unless for some reason the

* This paper was delivered at the 25th annual meeting of the British Paediatric Association on April 29, 1954.

TABLE III—ISONIAZID TRIAL IN TUBERCULOUS MENINGITIS
(April, 1952–August, 1953)

Condition on admission	Controls	Isoniazid cases	Total
Conscious ..	10	12	22
Unconscious ..	—	5	5
Other* ..	—	1	1
Total ..	10	18	28

*Treated elsewhere for five weeks before admission.

children in either group fared less well than those in our previous series. If, however, isoniazid were of benefit, this might be reflected in a more rapid recovery with less intrathecal treatment. It would have been more courageous to omit intrathecal treatment in the isoniazid group. Since we had obtained a very high recovery-rate with intrathecal treatment we felt that we could not accept such a risk. Further, such a step would have introduced two new factors instead of one, and this would have led to great difficulties in interpreting the results.

MATERIAL

Between April, 1952, and August, 1953, we admitted 28 patients; 23 were conscious, and of these 10 became controls and 12 were treated with isoniazid. The 23rd child had already had five weeks of treatment in another hospital with streptomycin and isoniazid, and was not included in the controlled investigation (table III). The composition of the two series was similar as regards age, stage of tuberculous meningitis on admission, and incidence of miliary tuberculosis (table IV). There were 5 children aged less than 3 years, and the youngest, aged 5 months, was in the control group. In only 1 case (a control) were no tubercle bacilli found in the cerebro-

TABLE IV—COMPOSITION OF TWO SERIES

Group	No. of cases	Age (yr.)		Miliary tuberculosis	Stage on admission	
		Range	Average		Early	Intermediate
Control ..	10	1/12–14	6 1/2	4	1	9
Isoniazid ..	12	1 1/2–14	6 1/4	6	1	11
Total ..	22	1/12–14	6 1/12	10	2	20

spinal fluid (C.S.F.); it was in a tuberculin-positive boy, aged 13 months, who was known to have had primary tuberculosis. Tubercle bacilli were cultured from his gastric washings. His C.S.F. was repeatedly examined because he had symptoms of early meningitis, and it gradually assumed the characteristic features of tuberculous meningitis.

Results

TREATMENT GIVEN

There was no significant difference in the duration of intramuscular treatment in the two groups. 6 of 8 survivors in the controls and 8 of 11 survivors in the isoniazid group were treated for the minimum period of six months, and all the others completed their treatment in nine months. The 3 children who died were treated for three months or less.

1 child in each group relapsed after completing one six-month course. The child in the control group completed one more six-month course and was perfectly well, but relapsed for a second time, and in her third course isoniazid was added to her treatment. Another child in the control group was given isoniazid after three months' steady deterioration on streptomycin and P.A.S.; he then made a good recovery. The C.S.F. data of this child were only used for comparison with the isoniazid group up to the time of his transfer to that group.

Patients in the isoniazid group required much less intrathecal treatment. 2 of 8 survivors in the controls and 6 of 11 survivors in the isoniazid group required only a single course of forty-five intrathecal injections. The average number of intrathecal injections was ninety in the controls and sixty-five in the isoniazid group (table V). This figure excludes the last course in the 2 children (1 in each group), who relapsed. It is of great interest, however, that 5 children in the isoniazid group and 1 other outside the controlled investigation required a second intrathecal course because the C.S.F. showed a significant and persistent deterioration after intrathecal treatment had been discontinued and while the children

TABLE V—INTRATHECAL TREATMENT IN TWO CONTROLLED SERIES (SURVIVORS ONLY)

—	No. of streptomycin injections				Course of P.P.D.
	45	90	135	Average	
Controls ..	2	5	1	90	1
Isoniazid group ..	6	5	—	65	3

were still being treated with all three drugs, including isoniazid. In 1 child tubercle bacilli reappeared in the C.S.F. in spite of 20 mg. of isoniazid per kg. body-weight given daily at the time. With the resumption of intrathecal streptomycin treatment all these children recovered.

1 of the control children was treated with intrathecal tuberculin and he died. 3 of those in the isoniazid group had intrathecal tuberculin, and 2 of them survived. The occasional need for tuberculin therapy was not eliminated by isoniazid.

CHANGES IN CEREBROSPINAL FLUID

The C.S.F. showed a much more rapid improvement in the isoniazid group, especially as regards the cell-count. In the isoniazid group the C.S.F. was almost normal at the end of six months, but in the controls it was still far from normal (table VI). The C.S.F. findings in the controls were in keeping with our previous experience. A temporary spinal block developed in 1 child in each group, including the control who was later transferred to the isoniazid group. The data from these 2 children were not used for calculating the averages in table VI. No figures are given for the first three months of treatment, because during that period the effect of the intrathecal injections on the C.S.F. are inseparable from the pathological changes. The C.S.F.-sugar level in the two groups was not strictly comparable, because isoniazid is a strong reducing agent. Nevertheless, when this factor had been allowed for, the sugar content appeared to be much higher in the isoniazid group at comparable periods.

SURVIVAL-RATES

The following are the results in April, 1954:

Control series : 8 survivors out of 10.

Isoniazid series : 11 survivors out of 12.

Other isoniazid-treated patients : 3 survivors out of 6 (including 1 intermediate case).

Total : 22 (78.5%) survivors out of 28.

TABLE VI—C.S.F. IN SURVIVORS (AVERAGES)

—	At end of mos.					
	3	4	5	6	7	8
<i>Cell-count per c.mm. :</i>						
Controls ..	111	63	47	35	50	40
Isoniazid group ..	56	28	21	11	8	8
<i>Protein (mg. per 100 ml.):</i>						
Controls ..	131	87	99	61	72	58
Isoniazid group ..	96	102	65	51	48	40

TABLE VII—RESULTS

	Total	Survived	Average period of observation (mos.)
Controls .. .	10	8 } (86.5%)	17
Isoniazid group .. .	12	11	14
Others .. .	6	3	14
Total .. .	28	22 (78.5%)	—

Of the 23 children who were conscious on admission 20 (87%) are alive. These survival figures are not necessarily final, because the period of observation is not quite long enough, although with combined streptomycin and P.A.S. treatment we have not had any late deaths so far (Lorber 1954) in 66 cases.

In the control group the period of observation in the survivors was between eight and twenty-two months (average seventeen months) and in 7 it was more than a year. In the isoniazid series it was between eight and twenty-four months (average fourteen months), and in 5 it was more than a year. In the 3 other children it was eight, nine, and twenty-one months (table VII).

None of the survivors of the two groups have serious sequelæ, and none are deaf, but 1 of the isoniazid-treated patients has a residual facial weakness. Of the 3 survivors outside the controlled investigation the child who was conscious on admission is free from sequelæ. Of the 2 others 1 is recovering from hemiplegia and 1 is a decerebrate idiot. A full assessment of the condition of the survivors will have to wait until the period of observation has been longer.

Discussion

In our experience the addition of isoniazid to streptomycin and P.A.S. in the treatment of tuberculous meningitis has not led to any significant increase in the survival-rate. This may be partly explained by the high survival-rate in our patients treated without isoniazid. One would require much larger numbers to demonstrate small improvements in this respect. The same survival-rate was, however, achieved with fewer intrathecal injections. It may be possible to reduce the number and frequency of intrathecal injections further without impairing the results. This would have obvious advantages, and the problem is under investigation at present.

The outstanding problem is whether intrathecal treatment is necessary at all. It is amply apparent from the work of others that many patients with tuberculous meningitis may recover without any intrathecal treatment. Our object, however, must be to cure the highest possible number of patients, and it has not been shown that this can be done without intrathecal treatment. In a survey of over forty papers on the treatment of tuberculous meningitis with isoniazid we have not found a single controlled investigation in which an attempt has been made to compare two concurrent series of similar cases, one of which was treated with, and the other without, intrathecal treatment, and using systemic isoniazid and streptomycin in both groups. We have not treated any patients without intrathecal streptomycin, but certain of our observations may throw light on this problem. Of 50 consecutive children admitted to us between August, 1950, and August, 1953, who were conscious on admission 45 (90%) are alive. Of all the 66 patients whom we treated during the same period, whether conscious on admission or not, 50 (75.7%) are alive. It would be justifiable to abandon intrathecal treatment only if similar or better results could be achieved without it. The facts that the C.S.F. may often show significant deterioration while the patients are receiving isoniazid, and that such deterioration can be reversed with intrathecal streptomycin, suggest that intrathecal treatment

may still have to be used in all cases because it is impossible to foretell which patient is going to need it.

This investigation was concluded when it became evident that isoniazid was of considerable value in the treatment of tuberculous meningitis.

Summary

This is a report on a controlled trial of isoniazid in the treatment of tuberculous meningitis.

22 patients who were conscious on admission were allocated by random sampling to two treatment groups, 10 being controls and 12 being given isoniazid. The treatment was otherwise identical in the two groups. Intrathecal streptomycin treatment was given in both groups in all cases.

8 of the 10 controls and 11 of the 12 isoniazid-treated patients survived. The average period of observation was seventeen months in the controls and fourteen months in the isoniazid group. None of the patients have serious sequelæ, and none are deaf.

Patients in the isoniazid group required fewer intrathecal injections of streptomycin (average 65) compared with the controls (average 90).

The C.S.F. in the isoniazid group approached normal more rapidly but showed significant deterioration in 6 children after one course of intrathecal treatment had been concluded, and so necessitated further intrathecal streptomycin treatment.

In 1 child tubercle bacilli reappeared in the C.S.F. during isoniazid treatment.

It is concluded that isoniazid is a valuable addition to other drugs in the treatment of tuberculous meningitis, but it has not eliminated the need for intrathecal streptomycin treatment.

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RAYNAUD'S PHENOMENON DUE TO VIBRATING TOOLS NEUROLOGICAL OBSERVATIONS

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Raynaud's phenomenon in workers using vibrating tools is of interest not only as a problem in industrial medicine but also because of the light it may throw on the aetiology of the condition.

Raynaud's phenomenon has been defined by Hunt (1936) as "intermittent pallor or cyanosis of the extremities, precipitated by exposure to cold, without clinical evidence of blockage of the large peripheral vessels and with nutritional lesions, if present at all, limited to the skin." Since Raynaud (1888) first described this group of signs and symptoms there have been two schools of thought about its causation. The one, represented mainly by Lewis and Pickering (1934), believed the condition to be due to a local fault in the walls



Fig. 1.—Pneumatic hammer.

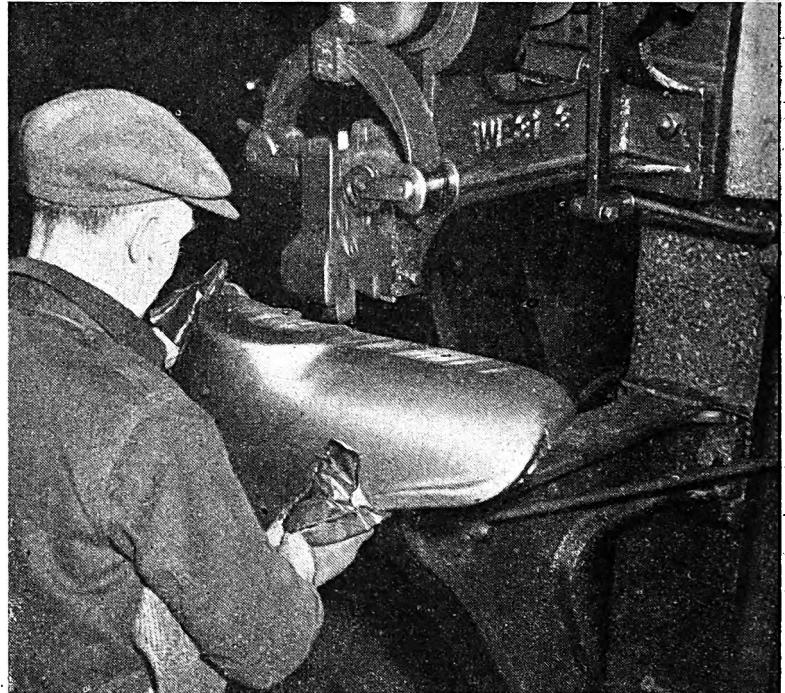


Fig. 2.—Trip-hammer.

of the digital arteries, which became unduly sensitive to cold. The other, supported by Telford (1934), considered overactivity of the vasomotor nerves to be the proximate cause.

Raynaud's phenomenon caused by vibrating tools has been studied by subscribers to both schools (Lewis and Pickering 1934, Telford et al. 1945, Agate et al. 1946, Agate 1949), but all reported little if any neurological abnormality between attacks. Indeed Telford et al. wrote : "Although it is not easy in the toughened skin of these workers to elicit the finer alterations in sensation, our examination has shown no change in the function of the digital nerves even in the older and more severe cases." Jepson (1951), however, reported numbness and clumsiness of the fingers even between attacks, and this he attributed to damage to the digital nerves.

Impressed by the occurrence of persistent neurological defects in workers with traumatic Raynaud's phenomenon we reviewed a group of such cases and report here some of our clinical and experimental observations.

Material

The cases in this series fell into two groups according to the tool with which they worked.

(1) The first group used a pneumatic hammer (fig. 1) weighing $11\frac{1}{4}$ lb. and delivering 2300 blows a minute. The tool consisted basically of a barrel containing a reciprocating piston driven by compressed air led in from a rubber hose. At one end of the barrel was a pistol grip held in the right hand, and at the other a socket into which was inserted the stem of the hammer tool-head gripped by the left hand. The job was to turn an edge of a sheet of steel, 0.036 inch thick, over at an angle of either 90°, when the operation was called "flanging," or 180°, when the operation was called "clinching." The steel sheet was clamped upon a jig during this process. In both flanging and clinching the left hand was exposed to greater vibration than the right. Of the 36 men employed thus, 31 were examined.

(2) The second group used a trip-hammer, and all 9 men employed on this machine were examined. This tool (fig. 2) consisted of a small anvil mounted on a stand at waist level, and a hammer head which pounded upon the anvil and was driven by a spring-loaded eccentric wheel. The men had to

grip a large sheet-steel pressing, 0.036 inch thick, with both hands and to run this between the hammer and the anvil of the trip-hammer, thus ironing out unwanted waves in the steel sheet by causing them to flow along the sheet to a site where their existence was of no importance to the finished form of the pressed steel part. On this work the two hands were more equally subjected to vibration.

Methods

The men were seen in a warm room at a temperature of 70°F. An occupational history and a full account of the condition were obtained, special attention being paid to certain features (see below). The motor and sensory functions of the hand were next tested. The sense of light touch was assessed with graded nylon threads mounted on holders, the strength of the thread being expressed as t , which was the weight in grammes required to bend the thread divided by its radius in millimetres. Sensory assessment on work-hardened hands was satisfactorily achieved by testing the dorsum of the fingers, and by using fingers not involved by the Raynaud's phenomenon as controls to obtain a threshold. The response to pinprick was similarly tested with a standard needle variously weighted. The ability to detect passive movement at the terminal interphalangeal joint was also measured.

Response to Ischaemia

The resistance of the arm nerves to ischaemia was next tested. Sphygmomanometer cuffs 12 cm. wide were placed round the arms, with their lower borders 3 cm. above the medial epicondyle. The arms were next raised for 15 seconds to empty the veins, the cuffs rapidly inflated to 200 mm. Hg, and the arms then lowered to rest on a table. The time of onset and the distribution of paraesthesiae and of subjective numbness, and any changes in motor or sensory functions, were noted in each hand. Ischaemia was usually discontinued after 10 minutes, or sooner in men with poor tolerance, because the length of time that each man was available for testing was limited. 4 men were also examined with a nerve clamp which rendered a segment of a nerve in the upper arm ischaemic.

Clinical Observations

The clinical features of the attacks were broadly the same as those observed by previous workers, but there were some special points worthy of emphasis.

History

The typical story was of attacks of numbness, whiteness, and coldness which began in the tips of the affected fingers and spread proximally for about 5 minutes. The attacks lasted a variable time, depending mostly on how soon the hand could be warmed. The attacks usually passed off when the man started work; otherwise, when the weather was cold, the attack could last all the morning. The end of an attack was marked by flushing of the hand, which was sometimes preceded by cyanosis. The flush spread distally down the fingers and was associated with a feeling of warmth and often of pins-and-needles.

Incidence

The incidence of the condition among men using the pneumatic hammer for flanging or clinching was high, 29 of the 31 men examined having symptoms of various

degrees of severity. Similarly, among those using trip-hammers, 8 of the 9 at risk had the phenomenon. It should be emphasised that this incidence was not that of men reporting sick spontaneously but was found only on survey. The men knew of the condition, but, since it was neither compensatable nor immediately and strikingly disabling, they accepted it as part of the job; it was uncommon, except among those worst affected, for them to complain.

Distribution

The distribution of the attacks appeared to be related to the type of job. Men using the pneumatic hammer began with trouble in the left hand, usually in the terminal phalanx of the little finger. The trouble next spread proximally in that digit and subsequently involved the ring and middle fingers in like manner. The index was occasionally affected, the thumb rarely. In 15 of the 29 workers with the pneumatic hammer the condition was entirely unilateral, and in 4 predominantly so. In the remaining 10, though the left hand had been first involved alone, the other hand was also affected at the time of examination.

TABLE I—ANALYSIS OF CASES OF RAYNAUD'S PHENOMENON

Case no.	Duration of work (yr.)	Duration of symptoms (yr.)	Distribution of Raynaud's phenomenon (digit)				Distribution of sensory loss (digit)				Time to numbness with ischaemia (min.)	
			II	III	IV	V	II	III	IV	V	Left	Right
<i>Pneumatic hammerers (unilateral) :</i>												
1	20	10	+++	+++	+++	+++	-	++	++	++	1·5	> 9
2	20	15	-	+	++	+++	-	-	-	-	> 10	> 10
3	13	6	-	+++	+++	-	-	-	-	-	4	> 8
4	11	5	-	(+)	(+)	(+)	-	-	-	-	2·5	> 10
5	9	6	-	++	++	++	-	-	-	-	5	> 12
6	7	6 ¹ / ₄	-	(+)	(+)	(+)	-	-	-	-	2	> 10
7	7	6 ¹ / ₂	-	+	++	++	-	-	-	-	2	8
8	5	3	-	++	++	++	-	-	-	-	> 10	> 10
9	4	3 ¹ / ₂	-	(+)	(+)	(+)	+++	+++	+++	+++	4	4
10	4	?	-	(+)	(+)	(+)	+++	+++	+++	+++	2·5	4
11	1 ³ / ₄	1 ¹ / ₂	++	++	++	++	-	-	-	-	1·5	> 9
12	1 ¹ / ₂	1 ¹ / ₄	-	++	++	++	-	-	-	-	1	> 10
13	3 ¹ / ₂	2	-	-	++	++	-	-	-	-	7	> 8
14	4 ¹ / ₂	3 ¹ / ₂	-	++	++	++	-	-	-	-	> 10	> 10
15	5	4 ¹ / ₂	-	-	++	++	-	-	-	-	> 10	> 10
<i>Pneumatic hammerers (predominantly unilateral) :</i>												
16	6	5	-	++	++	++	-	-	-	-	> 8	> 8
17	4	3 ¹ / ₂	-	++	++	++	-	-	-	-	2·5	2·5
18	3	2 ¹ / ₂	++	++	++	++	++	++	++	++	> 9	> 9
19	2 ¹ / ₂	1 ¹ / ₂	-	(+)	-	-	-	-	-	-	-	-
<i>Pneumatic hammerers (bilateral) :</i>												
20	3	2 ¹ / ₂	R -	-	-	(+)	-	-	-	-	6	6
			L -	(+)	(+)	(+)	-	-	-	-	-	-
21	10	?	R (+)	(+)	(+)	(+)	-	-	-	-	3·5	9
22	20	19	R +	+	+	+	-	-	-	-	> 5	> 5
23	2 ¹ / ₂	2	L ⁺⁺	++	++	++	-	++	++	++	2·5	> 9
24	1	?	R (+)	-	++	++	-	-	-	-	6·5	7
25	9	8	R -	(+)	(+)	(+)	-	++	++	++	> 8	1
26	3	2	R ⁺⁺	++	++	++	-	++	++	++	3·5	3·5
27	3	2 ¹ / ₂	L (+)	(+)	(+)	(+)	-	++	++	++	9	9
28	1 ¹ / ₄	1 ¹ / ₄	R -	++	++	++	-	++	++	++	> 9	> 9
29	5	4	R -	++	++	-	-	++	++	++	1	11
			L ++	++	++	++	-	++	++	++	-	-
<i>Trip-hammerers :</i>												
30	7	6	R +++	+++	+++	+++	-	++	-	-	9	9
31	5	4	L +++	+++	+++	+++	-	++	-	-	5	5
32	2	1 ¹¹ / ₁₂	R -	-	-	-	++	++	++	++	> 10	> 10
33	25	21	L ⁺⁺	++	++	++	++	++	++	++	> 9	> 9
34	17	10	R (+)	(+)	(+)	(+)	-	-	-	-	> 9	> 9
35	2	1	R (+)	(+)	(+)	(+)	-	-	-	-	4·5	4·5
36	3 ³ / ₄	3	L (+)	(+)	(+)	(+)	-	-	-	-	7	7
37	5	4 ¹ / ₂	R ++	++	++	++	++	++	++	++	5	5
			L ++	++	++	++	-	++	++	++	-	-

+ Raynaud's phenomenon or sensory loss up to distal interphalangeal joint.
 ++ Raynaud's phenomenon or sensory loss up to proximal interphalangeal joint.
 +++ Raynaud's phenomenon or sensory loss up to metacarpophalangeal joint.
 (+) Raynaud's phenomenon of uncertain extent.
 In cases 1-19 the right hand was unaffected and without sensory loss.

There appeared to be 1 exception to the rule that the left hand was first involved: 1 man was certain that the attacks had begun simultaneously in both hands, which were equally affected. It was subsequently discovered, however, that he was ambidextrous and held the hammer with either grip indiscriminately.

In the second group, the trip-hammerers, both hands were usually involved simultaneously and equally. The index and middle fingers were affected first and more severely in contrast to the pneumatic hammerers.

Length of Time at Work before Symptoms Developed

The time a man had been doing the job before he first noticed symptoms varied greatly (table 1). One man (case 1), who had been hammering continually for twenty years, had no trouble for the first 10 years, whereas another (case 32) developed his first attack within a month of starting the job. The commonest time, however, was from 3 months to 2 years after starting work. Since all the men appeared to have been exposed to the same amount of trauma, there must have been a wide variation in individual susceptibility.

Progress

The progress of the condition once it had appeared was very variable. Some men seemed to get steadily worse, in that attacks appeared to involve a greater area of the hand or came on more readily and more often. Others seemed to be static, or their deterioration was almost imperceptible. Ceasing to use vibrating tools was also of variable benefit. Some continued to get worse, others had their downward progress arrested, and one or two showed slight improvement. In no case did the attacks entirely cease.

Disablement

The disablement at work was slight so long as the men remained at the same job; but if an attack developed on the way to work it might impair the speed of handling the hammer until, as the man warmed up, the attack passed off. The condition interfered, however, to some extent with their recreation. Many came from a country area and pursued such pastimes as ferreting, shooting, fishing, and gardening. The attacks of numbness of the hands in cold weather had caused many of them either to restrict or to abandon these activities.

Precipitating Factors

It is usually stated that the attacks only come on in the cold, and when asked what caused the attacks the men invariably replied that it was the cold. More careful inquiry not infrequently revealed that attacks came on when both the hands and the whole body were warm. Thus, of the 37 men with attacks, 13 had them when they were warm as well as when they were cold; 1 had attacks when reading in front of the fire, and several when playing cricket on a hot summer's day; 1 observed that washing his hands in either hot or cold water might precipitate an attack. The use of the pneumatic hammer was not a precipitating factor, for, as has been mentioned, attacks passed off when the man started work.

Nocturnal Attacks

Attacks in bed at night were also a noteworthy feature. 13 men had typical attacks of Raynaud's phenomenon which disturbed their sleep. They awakened sometimes during the numb phase, and at other times during the flushed phase. 8 others had attacks of pain in the arm or forearm; 1 had episodes of pins-and-needles but could not say if they were associated with attacks of numbness as in his diurnal attacks. Though many of the men attributed these nocturnal disturbances simply to sleeping on their arm, it was striking that, when the Raynaud's phenomenon was unilateral, the nocturnal attacks always occurred in the affected arm.

Parästhesiae in Attacks

In 5 cases the onset of the attacks was associated with pins-and-needles in the affected fingers. One of these men, a specially good observer, was certain that the parästhesiae heralded the first appearance of whiteness in the fingers and disappeared before it was fully developed.

Parästhesiae when the attack was passing off were much more common, occurring in 22 cases. In 8 of these though parästhesiae occurred in the normal fingers of the affected hand they were absent or only faintly perceived in the fingers involved by the Raynaud's phenomenon. This was noted in the presence of a good reactive hyperemia in the fingers in question.

Sensation

The results of the sensory testing were striking: 26 of the 37 men had impaired sensibility to light touch. This was usually closely restricted to the fingers involved in the attacks but occasionally was more or less extensive. Sensibility to pinprick was slightly less affected, being impaired in 22 of the cases. 8 patients showed impaired sense of passive movement in the terminal interphalangeal joint. Thus 1 man could only detect movements of 45° in the affected finger, whereas he could recognise movements of 5° at the corresponding joint of the unaffected hand.

Motor Power

13 of the 37 men had some weakness of the affected hand. The abductor digiti minimi was most commonly impaired, being involved in 10 cases. There was loss of power in the first dorsal interosseous muscle in 4 cases and in the long flexors of the fingers in 4 cases.

Experimental Observations

Cuff Test

The use of the cuff test as a measure of impaired function of nerves has been studied by Gilliatt and Wilson (1953), who showed that, when an arm was rendered ischaemic, the time to the onset of subjective numbness in the fingers was greatly accelerated in the presence of nerve lesions, compared with normal controls, in whom subjective numbness developed only after at least 10 minutes' occlusion.

The test was applied to the men in this series to see if there was any evidence of nerve involvement; the results are presented in table 1. In cases 1-15 in the table the Raynaud's phenomenon was entirely unilateral; hence it was possible to compare the time to subjective numbness in the affected arm with the non-affected. The application of Fisher's *t* test to this group shows a significant difference at the 1% level between the two arms.

In the remainder of the series there was slight or severe involvement of both arms. The table shows, however, that the time of onset of the subjective numbness in one or both arms was in many cases much less than the 10 minutes found by Gilliatt and Wilson (1953) to be the normal minimum.

In addition to the premature onset of the subjective numbness during ischaemia, there was in many cases premature impairment of motor and sensory function shown by objective testing. Whereas in normal people impairment of power does not develop until after 20 minutes' ischaemia, many of the men with Raynaud's phenomenon showed weakness in the first dorsal interosseous muscle and abductor digiti minimi after only 4-7 minutes. The power of the normal hand was unimpaired when the test was discontinued after 10 minutes.

The deterioration in the results of objective sensory tests was also premature and considerable in many cases. The sense of light touch in normal people is not diminished until after 15 minutes or more of ischaemia. The sensory

TABLE II—NUMBER OF TOUCHES FELT PER 5 STIMULI DURING ISCHÆMIA IN CASE 9

Duration of ischæmia (min.)	Strength of touch stimulus		
	3t	17t	37t
0	2, 3	2	..
6	0, 0	0	..
8	0	0	3

findings in case 9 (table II) show that measurable sensory loss had developed within 6 minutes of the onset of ischæmia and was severe by 8 minutes.

Nerve Clamp

In 4 men a nerve clamp was also used to study the duration of ischæmia required to produce subjective numbness in the fingers. This clamp (Lewis et al. 1931, Marshall 1953) rendered a 12-cm. segment of the ulnar nerve in the upper arm ischæmic, without impeding either the arterial supply to, or the venous return from, the periphery of the limb. The results of these observations are shown in table III, which shows that rendering a segment of the ulnar nerve in the upper arm ischæmic caused premature development of subjective numbness in the little finger, in 3 cases unilaterally and in 1 case, in which both arms were affected, bilaterally. The

TABLE III—TIMES TO SUBJECTIVE NUMBNESS WITH CUFF AND SECONDLY WITH CLAMP TO ULNAR NERVE ABOVE ELBOW

Case no.	Side affected	Time to numbness with clamp (min.)		Time to numbness with cuff (min.)	
		Left	Right	Left	Right
4	Left	2	> 10	2.5	> 10
6	Left	2.5	> 10	2	> 10
21	Bilat. (L > R)	3	> 10	3.5	9
29	Bilat. (L > R)	2.5	3.5	1	11

duration of ischæmia required to produce subjective numbness in normal people is about 12 minutes.

Discussion

The observations made in these studies raise interesting speculations about the aetiology of Raynaud's phenomenon due to the use of vibrating tools. Though this condition can occur spontaneously, the very high incidence in this survey (37 of 40 men examined) made it clear that it was attributable to the work. There seemed to be nothing to suggest that in any of these men it was spontaneously determined, because there was no history of previous vascular disturbance.

Though the incidence of the condition was high, its severity varied greatly from case to case, even among those who appeared to have had the same degree of exposure to the trauma. One individually variable factor, however, was the tightness of the man's grip on the tool, and this may well be an important factor in determining the severity of the affection. There was some evidence to suggest that those who controlled the hammer with a loose grip did not develop the most severe symptoms. Individual susceptibility, unrelated to any tendency to spontaneous Raynaud's phenomenon, presumably also plays an important part, but evidence on this score was hard to assess.

The distribution of the attacks was remarkable in that they could be confined to one hand, remaining so for many years in some cases. The march of events was very similar in all these cases though differing with the two types of tool. The rate of progress might vary, and many cases seemed stationary far short of the expected full picture for that type of work. These distinct sequences and patterns of affection suggested that, since the whole of both arms and hands was subjected to the

same vibration, it was probably the exact mode of application of vibration to certain sites that determined the distribution of the Raynaud's phenomenon. The fact that so much of the limb, though exposed to the same vibrations, could be spared suggested that it might not be impossible for some slight modification of either the working technique or the tools to reduce this selective trauma and to allow the whole limb to escape.

An important feature of the march of events in this condition was that the symptoms were not cured by removing the man from hammering; usually they became no worse, but sometimes the affection progressed for a time. The lack of regression with cessation of hammering, and the absence of progression beyond a certain stage with continued work, encouraged men to remain at the job and to accept their disability. What their ultimate fate will be is not obvious, for, although some older men have continued over ten years with symptoms without additional complications, it was noteworthy that they did not have the early and severe lesions with which the younger men now presented.

The number who developed attacks when they were warm was surprisingly contrary to general belief. This discrepancy was probably due to our questioning specifically about this point. The men invariably regarded it as a cold-weather complaint, and not one volunteered information about attacks at other times. It was only on direct questioning that they described attacks coming on when both they and their hands were warm. The nocturnal attacks were also interesting in this respect because many of them came on when the hands were warmly under the covers. It was therefore clear that though cold was the commonest precipitating factor it was not a sine qua non for the development of an attack.

From our examination of the cases there was no doubt that traumatic Raynaud's phenomenon could be associated with a permanent neurological defect which, in persons dependent on skilled fine finger movements for their livelihood, would have produced considerable disability. Sensory and motor testing showed clearly involvement of the peripheral nerves at some level, and this was amply confirmed from the cuff tests, which showed subjective numbness developing prematurely during ischæmia in many cases. That the lesion lay in the nerve-fibres and not in the sensory end-organs was shown by the nerve-clamp experiments, in which the ischæmia was confined to the segment of the ulnar nerve in the upper arm but subjective numbness still appeared prematurely. But it was not possible from these results to settle the important question whether traumatic Raynaud's phenomenon was merely associated with this peripheral nerve lesion or was caused by it. There was however, some evidence to support the latter view.

The subjective numbness which the men developed in their attacks appeared almost simultaneously with the whiteness and therefore could scarcely have been caused by the arrest of the circulation in the presence of normal nerves. Simple arrest of the blood-flow to a normal finger is only followed by numbness after half an hour or so. Likewise with objective sensory loss; Hunt (1936) pointed out that objective sensory loss was demonstrable a few minutes after the onset of ischæmia in the attacks of Raynaud's phenomenon. This development of both subjective and objective sensory loss pari passu with circulatory arrest to the part strongly suggests that there was a primary disturbance of nerve function not only responsible for the premature sensory impairment but also precipitating the vasospasm of the Raynaud's attacks. The alternative explanation was that the digital nerves were permanently abnormal and responded to the causally unrelated ischæmia of the Raynaud's attacks with premature conduction defects. The latter explanation seemed unlikely in view of the

fact that premature numbness developed also in the experiments with the nerve clamp when the circulation to the digits was unimpaired.

Further evidence on this point was that the numbness of the fingers could be greater in extent than the whiteness. One of our patients, who was a good observer, was quite certain that numbness extended at least an inch more proximal than the whiteness. Likewise Agate (1949) reported that "hypalgesia did not seem to be confined to the fingers which had been reported abnormal"—a finding which we confirmed in our series.

A consideration of the paraesthesiae experienced by some people is also pertinent to this problem. 5 persons noted severe pins-and-needles at the onset of the attacks. Arrest of the circulation to the finger alone produces, if anything, only the mildest of pins-and-needles; nor is it likely that the paraesthesiae which they experienced were "cold pins-and-needles," because these also are a slight phenomenon not observed until the temperature of the hand has fallen to 12°C. Similar considerations also apply to the paraesthesiae which developed as the attacks were passing off. These, according to the men examined in this survey, were as severe as, if not more severe than, those following the cuff test. The postischaemic paraesthesiae following arrest of the circulation to a finger, if felt at all, are very mild, which fact suggests that it is not the return of blood to the finger alone that causes the paraesthesiae but some simultaneous event taking place more proximally in the limb.

The motor weakness found in these men also suggested the existence of a neurological lesion proximal to the ischaemic digital areas. Since both intrinsic hand muscles and long flexors of the fingers were involved, the causal lesion was clearly outside the fingers.

The sum total of this evidence suggests that there are disturbances in the peripheral nerves, and that these could possibly be the main cause of the simultaneous blanching of the fingers and the motor and sensory changes. Such damage or irritability on a nerve-trunk could well explain the permanent sensory and motor loss observed in this series and the intensification of the defect and the vasospasm seen in the Raynaud's attacks. This is not out of keeping with observations in peripheral-nerve injuries. Bumke and Foerster (1929) stated that vascular changes resembling those associated with Raynaud's phenomenon were sometimes found with peripheral nerve lesions, and Pollock and Davis (1933) recognised the existence of vasoconstrictor spasms associated with such lesions.

We therefore contend that a permanent sensory deficit is common in association with traumatic Raynaud's phenomenon, and that there is considerable evidence to suggest that proximal lesions in the peripheral nerves are associated with the condition and may well cause it. It seems also likely that further research into the aetiology of traumatic Raynaud's phenomenon might be profitably directed towards the peripheral nerves.

Summary

A clinical survey of 37 men with Raynaud's phenomenon due to the use of vibrating tools is reported.

There was evidence of persisting nerve damage in many of these men: motor weakness, sensory loss, and the development of premature numbness in response to ischaemia produced by cuffs and nerve clamps.

Damage to the peripheral nerves may be responsible not only for the neurological deficits but also for the vasospasm of the attacks.

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References at foot of next column

EFFECT OF CONTROLLED HYPOTENSION ON CEREBRAL FUNCTION AND CIRCULATION

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CONTROLLED hypotension brought about by methonium compounds and posture has proved of considerable value in many branches of surgery (McLaughlin and Watson 1951, Enderby and Pelmore 1951, Korkis 1951) but unfortunately has shown itself to be not without risk to the patient. Neurological complications have ensued (Goldsmith and Hewer 1952), sometimes causing death. For this reason some anaesthetists now consider the procedure to be unjustified, and Davison (1952) suggests that these neurological complications have been caused by cerebral ischaemia resulting from a postural redistribution of blood away from the cerebral circulation at the low blood-pressure used.

I have described (Saunders 1952) a method whereby adequate falls of blood-pressure can be produced and maintained, with the patient horizontal or very nearly so by administering hexamethonium bromide and applying pneumatic suction to the patient's legs. Bleeding and intracranial tension can be satisfactorily reduced with the patient horizontal. There is less danger of cerebral ischaemia in this position than when the hypotension is produced by tilting the patient. This is probably because there is no postural redistribution of blood away from the head, such as takes place with the patient tilted. This technique has proved very satisfactory for neuro-surgical work (James et al. 1953) and has been used also during facial, eye, ear, and orthopaedic operations in the Dunedin Hospital.

In the study reported here the cerebral arteriovenous oxygen difference was measured in patients with low blood-pressure induced during anaesthesia, and from it the cerebral blood-flow has been calculated. The hypotension was produced with hexamethonium bromide and by suction to the legs, with the patient kept horizontal or very nearly so (average tilt 5°). Cerebral function during hypotension was studied in 10 conscious healthy people.

Methods

The samples of cerebral venous blood were taken from the cranial venous sinuses of 8 patients undergoing craniotomy for cerebral tumour or intracranial aneurysms. Very light anaesthesia was maintained with ether and oxygen. Arterial blood samples were collected from the femoral artery in heparinised syringes, all contact with air being avoided. The oxygen content was measured by a microgasometric method (Saunders 1954), the accuracy of which has been checked against a manometric Van Slyke apparatus using blood not exposed to ether. The apparatus has been shown to give accurate estimations of oxygen in blood taken from patients anaesthetised with ether. During an estimation, the

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CEREBRAL VENOUS OXYGEN

Patient no.	Systolic pressure (mm. Hg)	Oxygen content (vols. %)
1	55	14.2
2	65	13.2
3	40	13.7
4	50	12.5
5	50	15.5
6	50	13.1
7	60	13.4
8	65	10.3
Mean	54.5	13.2

oxygen is evolved by mixing the blood sample with a ferricyanide-bicarbonate-saponin mixture, to which an acid buffer is then added.

The ability to reason and remember was tested in 10 conscious healthy people whose blood-pressure had been lowered in the erect posture by the administration of hexamethonium bromide. The tests were simple (100-minus-7 test, Babcock sentence). The 100-minus-7 test consists in subtracting 7 from 100 repeatedly until zero is reached. The Babcock sentence is a sentence containing several confusing adjectives and must be memorised and repeated back to the examiner.

Results

CEREBRAL ARTERIOVENOUS OXYGEN DIFFERENCE

Samples of cerebral venous blood were withdrawn from 8 anaesthetised patients. The oxygen content of these blood samples, together with the systolic blood-pressure at the time of withdrawal, is shown in the accompanying table.

At a mean systolic pressure of 54.5 mm. Hg the mean cerebral venous oxygen content was 13.2 vols. %.

The arterial blood was found to be almost fully saturated with oxygen, with a mean oxygen content of 18.0 vols. %. This gave a mean cerebral arteriovenous oxygen difference of 4.8 vols. %. Kety and Schmidt (1948) found that, when healthy adults breathed 85-100% oxygen, the mean arterial oxygen content was 18.0 vols. %, and that the cerebral venous blood contained 10.9 vols. %, giving an arteriovenous oxygen difference of 7.1 vols. %. The arteriovenous oxygen difference of patients with brain tumours does not differ significantly from that of healthy people (Kety, Shenkin, and Schmidt 1948). The arteriovenous oxygen difference of the hypotensive patients in this series is thus decreased by 2.3 vols. % below that of healthy conscious people.

CEREBRAL FUNCTION IN CONSCIOUS PEOPLE DURING HYPOTENSION

The blood-pressure of 10 conscious healthy people aged 20-45 were lowered with hexamethonium bromide in the standing position. All of them tolerated a systolic pressure of 60 mm. Hg in the erect posture for five minutes without losing consciousness. In some the intellectual acuity was slightly impaired, as shown by simple tests (100-minus-7 test, Babcock sentence). 2 subjects, at systolic pressures of 45-50 mm. Hg in the erect posture, were unaware that their blood-pressure were below normal and performed the tests as well as before.

Thus, under these conditions, a healthy person can tolerate a considerable fall of systolic pressure. Ordinarily, however, slight signs of cerebral ischaemia are likely to appear when the blood-pressure falls to 60 mm. Hg systolic in the erect posture.

Discussion

Kety et al. (1950) have pointed out that the cerebral arteriovenous oxygen difference represents the ratio of cerebral metabolic demand to cerebral blood-flow. A decrease in the arteriovenous oxygen difference therefore indicates an increase in the ability of the cerebral circula-

tion to cope with the metabolic demands of the brain, even though it conveys no information about either the cerebral blood-flow or the metabolic rate separately. Thus in these anaesthetised hypotensive patients the cerebral circulation can more easily meet the demands of the brain for oxygen than in people under normal conditions.

This relationship has been expressed by Kety in the form of the following equation :

$$C.B.F. = \frac{CQO_2}{(A-V)O_2}$$

where C.B.F. represents the cerebral blood-flow, CQO_2 , the cerebral oxygen consumption per minute, and $(A-V)O_2$, the arteriovenous oxygen difference. The normal values in adults breathing 85-100% oxygen are C.B.F. 45 ml. per 100 g. of brain a minute; CQO_2 3.2 ml. of oxygen per 100 g. of brain a minute; and $(A-V)O_2$ 7.1 vols. % of oxygen.

Loss of consciousness or cerebral depression from many causes, including anaesthesia, leads to decreased cerebral oxygen consumption. Second-stage or third-stage thiopentone anaesthesia (Himwich et al. 1947, Himwich 1949, Wechsler et al. 1951) decreases the cerebral oxygen demand by about 30%. The patients in this series were lightly anaesthetised with ether and oxygen. S. S. Kety (personal communication) has shown that with light ether anaesthesia the cerebral oxygen consumption is similarly reduced by 30% from a normal value of 3.2 ml. of oxygen per 100 g. of brain a minute to about 2.25 ml. of oxygen per 100 g. of brain a minute. If this figure applies to the patients at present under discussion, who were also anaesthetised with ether, the cerebral blood-flow during the hypotension could be calculated, from the equation given above, as follows :

$$C.B.F. = \frac{CQO_2}{(A-V)O_2} = \frac{2.25 \times 100}{4.8} \\ = 46.9 \text{ ml. per 100 g. of brain a minute.}$$

This is approximately equal to that of a healthy person breathing oxygen (45 ml. per 100 g. of brain a minute).

Mechanisms exist in the body to safeguard the adequacy of the cerebral circulation and to compensate for any decreases of effective cerebral blood-pressure. Scheinberg (1949), using the nitrous-oxide technique, has shown that, when a healthy person is tilted to 65° from the horizontal, the effective mean cerebral arterial pressure falls by 34%, but the cerebral blood-flow falls by only 21%. This indicates that the cerebral vascular resistance has fallen, but that the compensation is insufficient to maintain a normal cerebral blood-flow at the lowered cerebral blood-pressure. This has been confirmed by Hafkensiebel et al. (1951) and Patterson and Cannon (1951).

When the blood-pressure is reduced by spinal anaesthesia, similar inadequate compensation takes place both in normotensives (Kety et al. 1950) and in hypertensives (Kety, King, et al. 1948). When, however, the fall of blood-pressure is produced by the administration of a vasodilator drug, the cerebral blood-flow is less affected by the blood-pressure fall. Hafkensiebel et al. (1950) reported that, with a mean blood-pressure fall of 38 mm. Hg produced by dihydro-ergocornine, the cerebral vasodilatation was sufficient to maintain the cerebral blood-flow almost exactly at a normal level. With papaverine the cerebral blood-flow was actually increased to 24% above normal despite a blood-pressure fall of 12% (Scheinberg et al. 1951) showing that the compensation had been more than complete.

It appears that the administration of these drugs with a generalised vasodilator action produces a degree of cerebral vasodilatation sufficient to maintain the cerebral blood-flow at a normal level, or even to raise it above

normal, despite a fall of effective mean cerebral arterial pressure. The blood-pressure fall accompanying either surgical sympathectomy or spinal anaesthesia to the mid-thoracic region results from denervation and dilatation of the blood-vessels in the lower part of the body only. The cerebral circulation retains its vasoconstrictor tone because it is not involved in this denervation; hence under those conditions a fall of effective blood-pressure leads to a decreased cerebral blood-flow.

The patients in this series show that hexamethonium bromide has a cerebral action similar to that of these other vasodilators; hence, when hypotension is brought about with hexamethonium bromide and by suction to the legs in the horizontal posture, the cerebral blood-flow of the anaesthetised patient remains normal and is adequate for the metabolic demands of the brain. This is in agreement with Crumpton and Murphy (1952), who found that, when the systolic pressure of conscious hypertensive patients was lowered with hexamethonium bromide in the supine posture, the cerebral blood-flow remained unaltered. In erect conscious normotensive people, however, some signs of cerebral anoxia often develop when the blood-pressure falls to 60 mm. Hg systolic. Hughes (1952) mentioned that samples of cerebral venous blood taken from hypotensive anaesthetised patients under his care were not all satisfactorily oxygenated. If these patients were in a tilted position with the head raised, any cerebral ischaemia was probably caused by a postural redistribution of blood away from the head. This appears to be avoided if the patient is kept horizontal.

Any estimations of cerebral blood-flow are open to the criticism (Hughes 1952) that some of the blood may be passing through arteriovenous shunts and not through the substance of the brain. Such shunts are known in other parts of the body (Chambers and Zweifach 1947). The supposed arteriovenous shunts found in the injected brains of mammals (Pfeifer 1928) and man (Pfeifer 1930) were considered by Campbell (1938) to be artefacts produced by faulty injection and interpretation. Campbell (1938), Wentzler (1936), Forbes (1938), Wolff (1938), and Scharrer (1940) could not find any arteriovenous shunts in the mammalian brain, and Scharrer concluded that if they exist at all they are so few that no physiological significance can be attached to them. It therefore seems likely that measurements of total cerebral blood-flow accurately represent the amount of blood actually available to the brain substance.

From the evidence at present available it therefore appears that, when the systolic pressure is lowered to 60 mm. Hg with hexamethonium bromide combined with suction to the legs, the cerebral blood-flow is not decreased and remains adequate for the metabolic needs of the brain.

Summary and Conclusions

Samples of arterial and of cerebral venous blood were taken from anaesthetised neurosurgical patients during controlled hypotension. The hypotension was produced with hexamethonium bromide and by pneumatic suction applied to the legs, the patients being kept horizontal or nearly so.

The arteriovenous oxygen difference (4.8 vol. %) was less than normal, and the estimated cerebral blood-flow (46.8 ml. per 100 g. of brain a minute) was about equal to that of a healthy person, showing that under these conditions the cerebral blood-flow remains more than adequate to meet the metabolic demands of the brain. This is partly due to a fall in cerebral vascular resistance brought about by the hexamethonium bromide and partly to a decreased cerebral oxygen demand occurring during anaesthesia.

Cerebral function during hypotension has been studied in conscious people in the erect posture. No loss of consciousness occurred at a systolic pressure of 60 mm.

Hg, but slight impairment of cerebral function appeared in some people at that level.

It is concluded that cerebral blood-flow and oxygenation remain adequate during hypotension when the patient is kept horizontal or nearly so, and care is taken that the systolic pressure is not reduced below 55–60 mm. Hg.

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HOW TO PREVENT CRIPPLING IN RHEUMATOID ARTHRITIS

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WHY do some patients with rheumatoid polyarthritis become bedridden? Are deformity and ankylosis of numerous joints inevitable, or can they be prevented? Usually the story the patient tells us provides us with the answers. Nine out of ten bedridden patients will relate the same sequence:

- (1) The knees became painful and swollen, and the quadriceps muscles wasted away.
- (2) The patient walked less and less, and sat in an armchair more and more.
- (3) He could not straighten his knees.
- (4) He could not walk, and took to wheel-chair or bed.
- (5) His arms became fixed and his hands powerless.

He takes to his bed for one reason only—a flexion deformity of the knees. If one knee can be straightened the patient will walk. Painful feet and ankles may bother him a bit; but they do not confine him to bed for long. The hips are not often involved; and ankylosis of both hips does not prevent walking.

When a patient has been in bed for years and has several ankylosed and deformed joints, these simple facts may be forgotten. While he can walk and dress himself daily he will do enough to keep his muscles active

and his other joints mobile. When he stops walking he sits or lies with his arms at his side, his elbows flexed, his forearms pronated, and his wrists dropped. The muscles waste away, bones are decalcified, and the joint capsules become fibrosed. Prolonged rest in bed is disastrous to muscles, bones, and joints. The feet need to bear weight that they may keep their shape; articular cartilage needs to bear weight to preserve its vitality. The posture of a joint is a delicate balance of muscular pulls and external forces. When the force of gravity is removed, the joints of an arthritic patient readily occupy new positions.

Most of the pain of rheumatoid arthritis is felt in the hands and the knees, and every patient is mortally afraid of two things:

1. That he will not be able to walk.
2. That he will not be able to use his hands.

He can be assured that he will walk so long as he can straighten his knees. And he can be assured that he will use his hands so long as he prevents his hands from drooping and facing downwards. He should be kept out of bed at all costs. He should never be sent to hospital merely for a rest, but only for a specific purpose—e.g., correction of a deformity. While in bed he should keep his knees extended (not flexed over a pillow) and he should get out of bed every day and walk.

Deformities can appear even when the arthritis has been suppressed by drugs, because the muscle balance has not been restored. The physician should acquire the habit of watching for extensor weakness, and he should be ready to support the weakened muscles at any time. A few weeks' inattention may lead to a serious disability.

The Knee which Can be Fully Extended

The knee which threatens deformity may be painful or painless, swollen or not swollen, fully flexible or not. But it always has a weakened quadriceps,

which must be strengthened. Flexion must be avoided at all costs, and the patient should concentrate on quadriceps drill. He should keep the knees straight when he is sitting or lying, and his chairs and bed should be raised on blocks. Physical treatment which puts the joint through its full range of flexion does harm by further damaging the inflamed synovial membrane.



Fig. 1—Band calliper, which allows limb to bear weight, fixed on with plaster bands in front and behind.

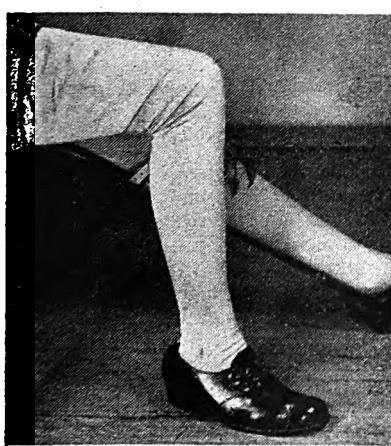


Fig. 2—Advanced arthritis showing range of flexion in right knee two years after immobilisation in extension for four weeks. Calliper on left leg.

A very weak quadriceps should be supported by a straight calliper with a band at the top instead of a ring (fig. 1). The leg bears its own weight, and walking is encouraged to strengthen the muscles and to preserve the articular surfaces. If the knee is not painful or swollen, the calliper may be removed at night, but it is better to wear it continuously for a week or two.

If the knee is painful and swollen, the calliper is fixed on, with the leg straight, for two to four weeks. Both knees can be treated thus at once, and the patient uses crutches. The pain disappears forthwith, and the swelling subsides rapidly, even though the limb is bearing weight. After two to four weeks the calliper is left off for two hours each day. This period gradually lengthens, and after about two months the patient is wearing the calliper at night only. If he cannot sleep in it, it should be worn during the day for a few hours. The quadriceps usually needs support for a few hours every day for four months.

Flexion always returns with ordinary use of the limb, and it should not be sought by forcible active or passive movements. Quadriceps exercises should be done, and low chairs should be avoided. There is no danger of ankylosis in extension.

The Knee which Cannot be Extended

If the patient cannot straighten his knee, it can usually be straightened under anaesthesia, the calliper fixed on, and the patient allowed to walk with crutches (fig. 1). The shoe should be left off for forty-eight hours, because a pressure sore may develop on the heel while the shortened flexors are being overcome. The lower leg is supported at the back by a padded plaster slab, and the lower ends of the calliper are kept apart with a wooden spreader. After forty-eight hours the shoe can be worn and the patient treated in the manner already described.

Swelling of the joint does not contra-indicate forcible extension; there is no severe reaction if the manipulation is confined to one strong movement and the leg is fixed firmly in the calliper. All swelling subsides very soon. If it is a slight and recent deformity (within three years), and if the joint cartilage is intact, a good range of flexion will return when the calliper is removed. If the joint had been disorganised before, the operation is performed with the hope of achieving a stable ankylosis in extension. In many of these cases, however, a surprising amount of painless flexion returns (fig. 2).

If too much force is used, fragile bones may break and nerves and vessels may tear. A deformity too gross and too old cannot be treated in this manner. If it can be partly corrected it may be fixed in its new position and fully corrected a few days later. Gradual correction by traction or by wedging of plasters has always failed because the patient cannot bear the prolonged drag on the posterior ligaments. Any procedures, moreover, which necessitate long-continued rest in bed are inadvisable. The patient is kept at his job, and other joints are not likely to be involved.

For several years I used cylindrical plasters and allowed the patient to walk on the straight leg. But the band calliper is superior because it prevents pressure sores and peroneal palsy: and it is superior to the ring calliper because it can be fitted without any bother. A slipper is provided with it to be worn at night.

The Hands

In arthritis more pain is felt in the hands than in any other joint. The whole hand may be swollen, and the fingers may droop and go straight; the hand cannot be closed or supinated. The elbow and the shoulder cannot be moved, because of the pain in the hand, and the whole arm becomes fixed.

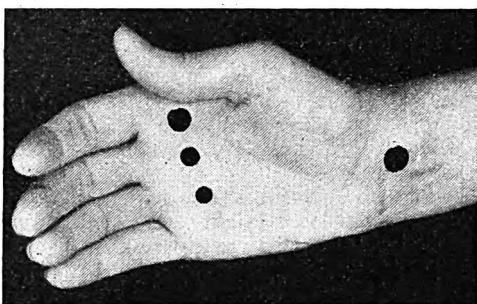


Fig. 3—Dark areas show localised tenderness in arthritis of wrist and metacarpophalangeal joints.

A good deal has been written about reflex swelling of the hands through remote vasomotor effects. But a local cause is more likely. We know well how a furuncle or a septic infection of the wrist or palm may cause intense swelling of the whole hand. A localised arthritic lesion can do the same. When a painful hand is carefully palpated it may be diffusely tender, but acute tenderness will usually be found confined to the wrist or to a metacarpophalangeal (basal) joint (fig. 3). Arthritis of either the wrist or the basal joints may cause inability to close the hand, but arthritis of the wrist causes more damage.

Arthritis of the Wrist

If the inflammation of the wrist is mainly on the volar aspect, local swelling is prevented by the tough capsular ligaments and is masked further by the transverse carpal ligament, which covers the flexor tendons and the median nerve. Pain may be referred wholly to the fingers. Diagnosis is all-important and depends on localised tenderness. Irreparable harm may be done by allowing a painful wrist to droop in pronation for a few weeks. This can be avoided if it is fixed in the correct position and the fingers and thumb are left free (fig. 4). Rotary movements will be unhampered if the cast is applied with the wrist midway between supination and pronation and the styloid processes are padded with felt.

The pain in the fingers disappears as soon as the wrist has been fixed, and the patient can use his hand. If he uses his hand he must use his whole arm, and the elbow and shoulder usually improve. After three or four weeks the splint is taken off, and a removable cast or a stiff leather support is worn for diminishing periods. It may have to be worn at night for a long time. The wrist and the basal joints usually increase their range after continuous fixation. Ankylosis never follows.

When the wrist is not splinted, the patient should be instructed to prevent it at all times from drooping. When resting it should be either supported or allowed

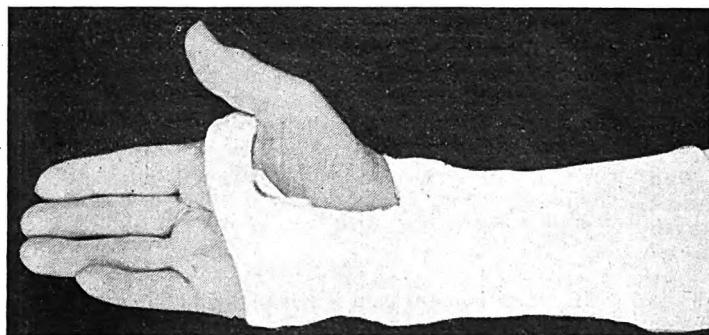


Fig. 4—Plaster for arthritis of wrist permits full supination and free movements of thumb and fingers. Forearm when hanging vertically is inactive; when horizontal it is active.

to hang in supination. Gripping and twisting exercises should be done every hour.

Metacarpophalangeal Joints

If the hand is painful and swollen and the wrist is not tender, careful examination of the hand may reveal acute tenderness of one or more basal joints. An inflamed basal joint tends to flex, with extended phalangeal joints. If several basal joints are involved, the hand cannot be closed. The delicate balance of muscles is upset, and various deformities of the fingers may result. Ulnar deviation is a sequel to ineffectual attempts to close the hand when the interphalangeal joints cannot be flexed.

A plaster cast should be applied which extends the basal joints and leaves the phalangeal joints free (fig. 5). and the hand should be used. If the hand is very painful, the plaster cast may be worn continuously for two to four weeks, and then intermittently for a long time.

Two Mistaken Beliefs

Rheumatic patients suffer a great deal from two mistaken beliefs:

- (1) The belief that they should put their painful joints through their full range every day.
- (2) The belief that their joints will ankylose if they are completely immobilised for a few weeks.

Danger of Indiscriminate Movements

The synovial membranes are inflamed and friable, and excessive movements intensify the inflammation. We



Fig. 5—Plaster for arthritis of basal joints terminates $\frac{1}{2}$ in. short of middle joints of fingers.

should think of the function of each joint and try to preserve that. The knee is intended to bear weight and the wrist is intended to be a stabiliser and a pivot for the hand. The knee does not need the 150° of flexion which is sought so persistently. And the wrist does not need much flexion and extension so long as it can be rotated and the fist can be clenched. Plenty of exercise of the limb is necessary, but the damaged joint should be rested. When the splint has been taken off, the range of the joint will increase gradually so long as it is not forced.

Continuous Immobilisation

Immobilisation for five weeks never causes ankylosis of the knee if the cartilage is intact. Rather it increases the range, because the inflammatory process goes into reverse, and pain and muscular spasm are reduced. When the cartilage has gone ankylosis may occur in a good position, and the patient is extremely grateful.

Continuous fixation has never been popular, because the treatment of joint diseases has been haunted by the shadow of ankylosis. Hunter (1837), Hilton (1860), and Thomas (1878) have arisen successively to advocate rest for arthritic joints; among the few who listened were Phelps (1890), Robert Jones (1909), and Aitken (1935).

Coates (1933), Kindersley (1936, 1938), Tippett (1940), Bell (1940), and Duthie (1951) have shown more recently that the fears of ankylosis are idle.

At a discussion at the Royal Society of Medicine in 1935 some speakers said that Kindersley's important findings were difficult to apply in practice, because it was not always easy to get a patient to walk who had been in bed for several weeks with his knees in plaster. This difficulty can be overcome if the patient is not put to bed but is encouraged from the beginning to walk on his extended knees.

Summary

In rheumatoid arthritis it is supremely important that patients should be able to walk and to use their hands.

If flexion deformities of knees and wrists are prevented, arthritic patients will never become crippled.

Deformity of the knee can be prevented by keeping it extended in a calliper and encouraging the patient to walk.

Deformity of the wrist can be prevented by continuous immobilisation in plaster splints which allow the fingers to be used and the hand to be rotated.

Arthritic joints which are immobilised for a few weeks do not ankylose.

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CLINICAL APPROACH TO INFERTILITY

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THE husband and wife who consult their practitioner or gynæcologist on account of infertility are primarily concerned to obtain advice or treatment which will enable them to have a child, and there is a tendency to assess the success or failure of the investigation and treatment of these cases solely on the proportion of wives who become pregnant. Barns et al. (1953) conclude from a statistical analysis of 1200 cases of primary infertility that in few cases can a subsequent pregnancy be attributed to treatment, and this knowledge must cast doubt on the value of work done in infertility clinics. It is important, however, that practitioners and gynæcologists who undertake infertility work should appreciate that careful, sympathetic handling of the childless couple, even though it may not have the material effect of producing a pregnancy, is likely to assist husband and wife to face their problem; whereas imprudent management of the case may bring much unhappiness and tension to the marriage. These points are illustrated by the following three cases.

Case-reports

Case 1.—Mr. and Mrs. S, after two years of married life, consulted their doctor because they had failed to have a child;

no contraceptive measures had been used. The doctor made a pelvic examination of the wife and obtained a sample of semen from the husband. The couple were told that the husband was "below normal." This news was a great blow to the husband, and from this point onwards, because of premature ejaculation, he experienced difficulty in carrying out the sexual act. Mrs. S, an intelligent woman, tried to help her husband, but over a period of years the difficulty became more marked and husband and wife suffered considerable emotional distress. After seven years of marriage they were referred to an infertility clinic. A few simple investigations were carried out on Mrs. S and no abnormality was discovered. The quality of the husband's semen was shown to be within normal limits. The findings were discussed with the couple, and they were very relieved to hear that there did not seem to be any abnormality on either side. They agreed to artificial insemination with the husband's semen and were overjoyed when conception occurred after the sixth insemination. A healthy child was subsequently delivered, and within a few months of the confinement normal sex relations were established.

Case 2.—Mr. and Mrs. M were married in India during the late war, whilst they were serving in the Forces. When, after two years of marriage, no pregnancy had occurred, they consulted the Service medical officer and were told that the husband was subfertile. This was a great disappointment to the couple, and when they were examined at an infertility clinic four years later Mrs. M stated that the knowledge that her husband was unlikely to give her a child had caused her to feel some resentment and this had worried her a great deal. The husband had sensed this change in his wife's attitude, but neither had ever discussed the matter with the other. Each felt that their relationship had become strained after the disclosure that the husband was subfertile. The investigations at the infertility clinic showed that the husband's semen was within the normal range, and the couple were reassured. Conception took place within a few weeks of the investigations being completed, and a live healthy child was delivered to very grateful parents.

Case 3.—Mrs. F was referred to the infertility clinic by her practitioner after she and her husband had been trying to have a child for three and a half years. Postmenstrual insufflation and hysterosalpingography suggested that the fallopian tubes were blocked; no other abnormality was discovered. The findings were explained to the patient. In the meantime her husband had been interviewed and arrangements made for him to bring a sample of semen for analysis; he failed to attend even though several alternative appointments were offered to him. Mrs. F attended the follow-up clinic and explained that her husband, on hearing that her fallopian tubes were blocked, concluded that she was responsible for the failure to conceive. He persisted in this attitude; and although his wife was anxious to have surgical treatment, if it were thought advisable, he refused to have a semen specimen analysed. Mrs. F was seen at intervals over the following year, and it was obvious that her husband's attitude was causing her much distress; she felt that her marriage was a failure and that the fault was hers. Relations and friends had been told by the husband that the responsibility for the childlessness lay with his wife; the fact that he had several brothers and sisters with large families added weight to his story.

Discussion

Infertility clinics today are largely concerned with mechanical investigations, and little attention is paid to the reaction of husband and wife to the manner in which their case is managed. The experiences of the three couples described here show how allocation of responsibility to one or other partner can bring much unhappiness to a marriage. Our criticism of the management of the first two cases is not that an error was made in the assessment of the fertility of the husbands, but that the men were told that they were responsible for the failure of their wives to conceive. In the third case we believe that it was a mistake for the wife to be told that the fallopian tubes were blocked, since she then accepted responsibility and her husband refused examination.

In our clinic we now have records of many cases where trouble has followed the allocation of blame, and we are

convinced of the need for discretion and tact in deciding how much information is given to patients after investigations have been completed. The reaction of husband or wife to the knowledge that he or she is subfertile should always be balanced against the value of the treatment that can be offered; when some condition has been discovered that bears a doubtful relationship to fertility, or when the value of treatment is equivocal, we can see no advantage in placing responsibility clearly on one or other partner.

In many clinics the wives are examined by a gynaecologist, while the husbands are referred to a pathologist or urologist. This approach suggests failure to appreciate the single nature of the problem of infertility; and it is more likely, we believe, to give rise to difficulties of the type described here. At the Royal Victoria Infirmary, Newcastle upon Tyne, the clinical management of these cases has been studied carefully by the medical staff, and the following plan has been introduced.

The initial contact with the couple is made through the wife, who is referred by her general practitioner to the gynaecological outpatient department. At this visit it is explained to the patient that involuntary childlessness concerns her husband as much as herself, and an appointment is made to see them together one evening. At this evening interview the combined nature of the problem is emphasised and the necessary investigations are outlined. Appointments are made for the husband and wife to attend separately, and the investigations are kept to a minimum. A careful history is taken from husband and wife, and each has a general medical examination and a local examination of the genital organs. The husband's semen is analysed, and this test may have to be repeated once or twice where the initial analysis shows a poor quality of semen. Premenstrual curettage and postmenstrual tubal insufflation are carried out on the wife. In certain cases where there is doubt about consummation of the marriage, intercourse is advised the night before the woman is admitted for premenstrual curettage, in order that a check can be made that semen is being deposited in the vagina. Occasionally it may be necessary to repeat either of these examinations on the wife. In most cases these few simple investigations suffice, and once they have been completed a second evening interview with the couple is arranged and the results of the investigations are then presented in one of three ways:

1. No reason has been found for the failure to conceive, and they are reassured that there is therefore a good chance that a pregnancy will occur.
2. One or more factors capable of delaying conception have been found, but there is the possibility that a pregnancy will occur.
3. Some condition is present which, in the light of present knowledge, precludes a pregnancy.

When the couple are in need of help on matters such as the frequency of intercourse, or when sex difficulties are present, advice is given. Allocation of responsibility for the failure to conceive is avoided unless some condition is present which clearly merits active treatment—e.g., fibroids or tuberculous endometritis. Care is taken not to draw attention to conditions which bear a doubtful relationship to fertility—e.g., retroversion of the uterus or apparent blockage of the fallopian tubes. The treatment of established subfertility in the male is so unsatisfactory that we are reluctant to draw attention to this finding. The examination of the husband may appear to be pointless, but a knowledge of his standard of fertility is essential if the couple are to be given a worth-while prognosis; in addition it has the value of bringing home to husband and wife that childlessness is a problem which they must face together.

By this plan husband and wife are investigated in the department of gynaecology; we have been responsible

for the evening interviews, and, although at present the semen analyses are done by one of us (J. K. R.), this work might equally well be done by a technician. This method of dealing with the husbands is considered preferable to referring them to another department for semen analyses.

These observations are made from the viewpoint of the clinician and deal with the clinical approach to the routine investigation of involuntary childlessness. We are aware that many pathologists, urologists, endocrinologists, and research-workers are interested in certain aspects of infertility, and it is not our intention to belittle the value of their work. We do suggest, however, that it is particularly important that those whose interest in infertility lies in a narrower field should remember always that they are dealing with a marriage rather than an individual.

Summary

The success or failure of work at an infertility clinic cannot be assessed solely by the proportion of women who become pregnant.

When the problem is viewed as a combined one affecting a marriage rather than individuals, and when discretion and tact are shown in the clinical management, then the couple are likely to face the future with greater assurance and understanding.

When little regard is shown for the emotional reaction of patients to the manner in which their cases are handled, investigation of involuntary childlessness may bring much unhappiness and distress.

The plan of approach instituted at the infertility clinic in the Royal Victoria Infirmary, Newcastle upon Tyne, is described.

We should like to thank Prof. H. Harvey Evers and Mr. Frank Stabler for the many helpful suggestions and criticisms they have offered, in the course of numerous discussions.

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SEVERE ASTHMA TREATED WITH CORTICOTROPHIN

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THERE have been several favourable reports of the treatment of asthma with corticotrophin and cortisone; but the results of any new treatment of asthma are notoriously difficult to assess. For this reason a controlled trial of corticotrophin was made in patients with severe chronic asthma which had not responded to any other forms of treatment.

Only patients whose asthma had been persistent for at least three months, without more than two weeks' complete remission during this time, were admitted to the trial. Patients with other major diseases were excluded, apart from 2 patients with mild hypertension. Of the 13 patients in the trial only 2 had had symptoms of chronic bronchitis before the onset of their asthma.

The Trial

Corticotrophin and saline solution were put up in identical bottles. Each patient was given a reference number, and the hospital pharmacist allocated him to one or other treatment group on reference to a list prepared beforehand by marking corticotrophin or saline solution at random against a series of consecutive numbers. No person dealing with the patient knew which substance was being given. Each patient was observed for a few days before entering the trial. During this time a full history was obtained—the mode of onset of the

asthma, the duration, the period of full disability, precipitating factors, any history of allergy, and the treatments previously given were all recorded. Each patient underwent radiography of the chest, examination of the sputum, a white blood-cell count, an absolute eosinophil-count, and electrocardiography. Serial records of the blood-pressure, weight, and sputum were made.

A daily assessment was made of the degree of spasm (mild, moderate, or severe) on auscultation of the chest with the patient breathing normally; the number of attacks severe enough to require an injection of adrenaline or of aminophylline; and the presence or absence of heart-failure.

The injections were given six-hourly for seven days, eight-hourly for two days, and twelve-hourly for three days. Each injection of corticotrophin contained 25 mg.; hence the total dose was 1 g. in twelve days. In 2 patients only half the standard dose was ordered, because they also had hypertension.

Those whose asthma did not adequately respond to the unknown substance were later put on to known corticotrophin, and the effects were compared. Those who responded to the unknown substance were followed

TABLE I—DETAILS OF CONTROLS AND OF PATIENTS TREATED WITH CORTICOTROPHIN

	Controls (7 patients)	Corticotrophin (6 patients)
Age	33-62	30-62
Sex	Average 47.4 6 F, 1 M,	Average 46.7 5 F, 1 M,
Total length of history (yr.)	1/4-34	1-12
Length of severe disability (yr.)	Average 16.5 1/4-2	Average 6.1 1/4-3
Family history of allergy..	Average 8.1 mos. Positive 2 Negative 5	Average 15.5 mos. Positive 2 Negative 4
Personal history of allergy	Positive 1 Negative 6	Positive 2 Negative 3 Doubtful 1
Associated hypertension..	1	1
Chronic bronchitis preceding asthma	0	2

up to determine the length of their remission. Those who relapsed were put back on treatment with the unknown drug to which they had previously responded.

After the trial had been in progress for nearly fourteen months 13 patients had been included. In addition, 7 other patients were treated with known corticotrophin because they were considered to be too ill to go into the trial. During this period there had been 132 admissions to the hospital because of asthma; hence it was only a small percentage whose asthma was considered severe and persistent enough to be included in the trial.

By this time there was a strong clinical impression that some patients were responding much better than others. Moreover 3 patients had died in severe asthma while under observation preparatory to entering the trial. The apparent effectiveness of the injection given to each patient was then assessed and the trial was closed.

Results

The details of the two groups are given in table I. The only striking difference between the two groups lies in the duration of the asthma. In the patients treated with corticotrophin the total duration was considerably shorter, yet the period of severe disability (during which

TABLE II—IMPROVEMENT OF CONTROLS AND TREATED PATIENTS

Improvement	Saline (7)	Corticotrophin (6)
Much	1 } 29 %	3 } 83 %
Moderate	2	0
Slight	3	1
None		

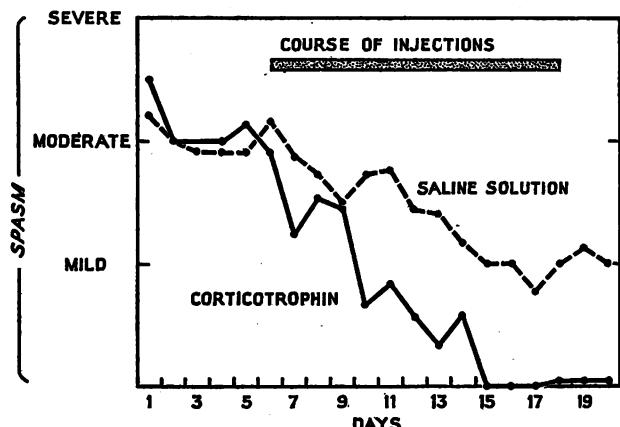


Fig. 1—Effect of treatment on spasm (all cases in each group combined).

only occasional short remissions occurred) was almost twice as long as in the controls. This does not mean that the corticotrophin group had less severe asthma, however, since it has been shown that most deaths in asthma take place in patients whose disease has lasted less than five years (Earle 1953).

EVIDENCE OF EFFECTIVENESS OF CORTICOTROPHIN *Assessment of Unknown Substance*

The substance which the patient had been given was correctly estimated in 12 out of 13 cases (1 patient improved on saline solution and was thought to have had corticotrophin). Although the degree of improvement was the most striking difference between the two groups and was the basis of deciding which substance had been given, certain side-effects occurred mainly in those receiving corticotrophin; these were a considerable increase of weight and evidence of fluid retention.

5 patients receiving corticotrophin but only 1 receiving saline solution gained more than 4 lb. in weight; and 3 receiving corticotrophin but none receiving saline solution showed manifest evidence of fluid retention.

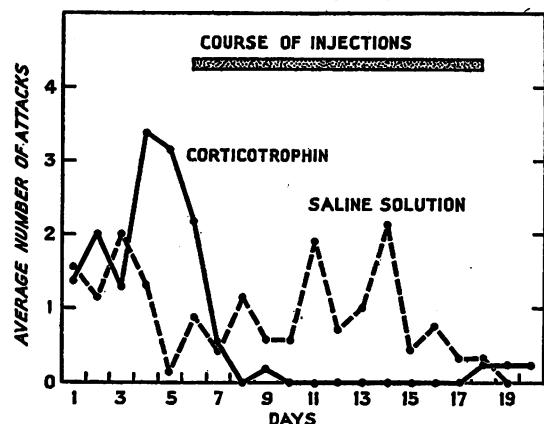


Fig. 2—Effect of treatment on average number of attacks of asthma requiring injection of either adrenaline or aminophylline (all cases in each group combined).

Degree of Improvement

Of the 7 patients receiving saline solution only 2 showed moderate or much improvement, against 5 of the 6 receiving corticotrophin (table II).

Effect on Asthma

Combined graphs have been made to show the degree of spasm recorded each day (fig. 1) and the daily number of attacks of asthma requiring an injection of either

adrenaline or aminophylline (fig. 2). The spasm diminished considerably faster in the patients receiving corticotrophin than in those receiving saline solution. Unfortunately the number of attacks requiring injections in the two groups was considerably different before the trial started (presumably a chance finding due to the small number of cases in the trial). Nevertheless, whereas the number of injections required by the patients receiving corticotrophin rapidly decreased almost to zero, little over-all change occurred in the number required by those receiving saline solution.

Change from Saline Solution to Corticotrophin

3 of the patients in the saline group who did not improve were given known corticotrophin, and all were much improved. 1 who improved moderately on saline solution relapsed soon after and was later given known corticotrophin, on which she is now maintained with almost complete freedom from asthma.

1 patient receiving saline solution has not relapsed after ten weeks. Another patient relapsed but did not return for further treatment. Yet another, whose asthma was complicated by purulent bronchitis, died a few days after the injections of saline solution were stopped.

Relapse after Withdrawal of Corticotrophin

Of the 6 patients receiving corticotrophin 3 relapsed one, eight, and twenty-three days after the end of the twelve-day course; they were put back on corticotrophin therapy when it was apparent that the relapse was complete, and satisfactorily improved again. 2 patients have not relapsed eight weeks and thirteen months after the end of the treatment. 1 patient died with cor pulmonale nineteen days after the end of the course.

Maintenance Treatment

7 patients in the trial group and 5 patients with status asthmaticus have been maintained on corticotrophin for one to thirteen months (average six months). Most of them have responded well, and any attempts to reduce the dose too quickly, to substitute saline solution for corticotrophin unknown to the patient, or to omit the injection altogether have almost always led to relapse.

Many of the patients still have some bronchospasm, but most of them can now do their own housework or light work outside, which they had not been able to do before the start of treatment. Severe asthma has usually been converted into mild asthma.

The daily requirements have been 20-80 mg., usually given in two doses by the patient. The night dose is generally the larger, to prevent nocturnal attacks. An increased dose is often required to suppress asthma when the patient has a cold. There is no real evidence of increasing resistance to corticotrophin in these patients, but it is too early to say that this will not develop. Most of the patients are now being maintained on cortisone by mouth.

Status Asthmaticus

Apart from the patients in the trial series 7 patients were treated with known corticotrophin because their condition was too desperate for inclusion in the trial. Of these, 3 improved immediately and dramatically, 3 improved slowly (but this improvement could not be attributed with any certainty to corticotrophin), and 1 died twenty-four hours after the onset of treatment.

DEATHS

That deaths in asthma are not rare is being more widely recognised. 3 patients died in severe chronic asthma while under observation preparatory to entering the trial. Though in severe spasm, they were not considered

to be desperately ill, and each of them had been seen in equally bad attacks on previous occasions. Morphine had not been given.

2 deaths took place in the controlled trial:

A labourer, aged 56, had had asthma for thirty-four years, and purulent bronchitis had developed. He was severely ill and had not responded to the usual treatment. He received saline solution in the trial, did not improve, and died a few days later.

An optician, aged 52, with thirty-two years' history of chronic bronchitis had had severe asthma for ten years. There was evidence of severe emphysema. His spasm diminished after treatment with corticotrophin, but his dyspnoea increased, and he developed congestive heart-failure. He died nineteen days after the cessation of treatment.

2 patients died who had been treated for status asthmaticus :

A doctor, aged 70, who had not responded to orthodox therapy, succumbed twenty-four hours after starting treatment.

A prison officer, aged 50, had had asthma for only a month before admission. He was in severe distress and only slowly improved under treatment with corticotrophin, which was later discontinued. He died in a severe attack a few days after leaving hospital.

Discussion

It is difficult to make a proper statistical estimate of the significance of the results, because the side-effects of corticotrophin make it hard to ensure that the observer's assessment was entirely without bias. The correct assessment of 12 out of 13 patients as belonging to either the controls or the treated group is certainly beyond the limits customarily accepted as attributable to chance, but it is impossible to be certain how great a part observation of the side-effects of corticotrophin therapy had in enabling the observer to make his assessment. All that can be said is that he was aware of this danger and tried to make the assessment mainly on the basis of the response of the patients' asthma. Nevertheless, there is a strong clinical impression that corticotrophin is valuable in the treatment of most patients with severe chronic asthma. In some of them the effect seems immediate and dramatic, corticotrophin appearing to be life-saving, whereas in others the improvement is slower. Corticotrophin 25 mg. every four to six hours is usually required in patients with status asthmaticus, but the dose can often be reduced within forty-eight to seventy-two hours, by which time, in most cases, improvement has taken place. Less urgent cases may respond to smaller doses.

Maintenance therapy is indicated in patients with severe asthma who cannot be relieved by orthodox treatment. There is no indication for such powerful drugs in milder cases which can be adequately controlled with simpler and cheaper remedies. Other forms of treatment, especially breathing exercises, should not be forgotten in patients responding well to corticotrophin.

The only serious side-effect of corticotrophin, noticed in 3 patients, was the development of severe retention of fluid with signs of congestive heart-failure. Low-salt diets and mercurial diuretics may be required. Patients who are well enough should be weighed daily so that this complication can be foreseen.

Some workers recommend the routine use of an antibiotic to suppress secondary infection when either cortisone or corticotrophin is used. We have not done so in patients who did not have a purulent sputum, and we have found no evidence of an increased tendency to respiratory infection. A larger controlled series might have produced results of greater statistical significance; but, since we were treating a condition with a considerable mortality, it was not felt justifiable to continue to withhold corticotrophin from severely ill patients. Moreover we have found it very hazardous to make a prognosis

in patients with severe asthma. They may have recovered from attacks of similar severity in the past, yet for some unknown reason they may suddenly die.

Summary and Conclusions

13 patients with severe chronic asthma were given either corticotrophin or saline solution by injection for twelve days. No-one in charge of the patients knew which substance was being given. Of the 6 patients receiving corticotrophin 5 showed moderate or much improvement, compared with 2 out of 7 patients receiving saline solution.

Much improvement took place in 3 of 7 patients with status asthmaticus treated with corticotrophin.

12 patients with severe asthma were maintained on corticotrophin with satisfactory results. Usually their asthma became mild.

Death is likely in patients who have repeated attacks of status asthmaticus. Corticotrophin (or alternatively cortisone) should be made available for all such cases.

This paper represents the combined work of a number of people. The trial was planned with Dr. B. Hirschowitz and Dr. H. Joules, and with Dr. R. Doll who in addition helped with the analysis of the results. Grateful acknowledgment is also given to Dr. R. A. J. Asher for his advice, to Dr. K. Baker and Dr. S. Kuper and other members of the medical and nursing staff for help in running the trial, and to Miss M. Barron-Boshell and her colleagues in the pharmaceutical department for their co-operation. Corticotrophin was supplied by the Medical Research Council.

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HÆMATOMATA OF RECTUS SHEATH

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HÆMORRHAGE into the rectus sheath is uncommon, and when it occurs is very unlikely to be diagnosed. Indeed, in a review of 21 cases of this condition Kapsinow (1946) found that only 2 were correctly diagnosed before operation.

A most comprehensive survey of all aspects of this lesion in its various forms was made by Payne (1938), who stated that it was known to Hippocrates, Galen, and Leonardo da Vinci, and that more than 300 cases were reported between 1880 and 1938. The picture always seems highly characteristic in retrospect but does not stand out so clearly beforehand.

3 cases have recently been observed in the Wolverhampton area, all with signs of extravasation of blood into the abdominal wall either immediately or after an interval of a few days: 2 around the umbilicus, and 1 far out in the right iliac region.

Case-histories

Case 1.—A stout bronchitic hypertensive man, aged 54, said he had been awakened from sleep by a sharp pain in the region of the right iliac fossa at 3.30 A.M. the night before admission. This grew steadily worse and spread all over the abdomen and was followed a few hours later by the appearance of a lump on the right side. He had had three similar but milder attacks of similar pain, without any lump, in the last two years. In the previous two weeks he had had twinges of pain and a feeling of soreness in the same place but had been able to work. Apart from breathlessness on exertion he showed no other evidence of disease.

On examination he was stout and wheezy and had bad teeth and blood-pressure 210/120 mm. Hg. His pain was now moderate. A firm, dull, elongated, and rather reniform mass was present in the right middle and lower abdomen. It was not ballotable and could not be palpated in the loin. It was a

little tender, but there was no guarding or rigidity around it. Straight radiography showed gas in the cæcum, which was normal in position and shape. Intravenous pyelography was normal. The white blood-cell count was 11,400 per c.mm. (polymorphs 90%). His temperature fluctuated between 98° and 100°F and his pulse-rate between 80 and 100. The lump persisted, always somewhat obscurely owing to his fatness. His bowel was prepared during the investigation, and on the fifth day of illness he was taken to the operating-theatre. Here a yellow-green patch of ecchymosis was seen above the right anterior superior spine. It was clear that there was some bloody extravasation in the abdominal wall, and some form of pancreatitis was suspected.

Operation.—A right paramedian incision was made over the prominence of the swelling. Everything was normal till the rectus muscle was reflected, when a huge clot was revealed. This was evacuated, and no bleeding point was found. The wound was closed over a small drain without opening the peritoneum. Recovery was uneventful. Postoperative inquiry showed that, in fact, a cough had awakened the patient from sleep, and that the pain had followed a violent bout of coughing.

Case 2.—A stout and slightly bronchitic woman, aged 68, was, in the course of her daily duties, suddenly seized with severe lower abdominal pain and vomiting on the morning before admission. Almost exactly a year previously she had had a conservative resection for a carcinoma of the rectosigmoid junction.

Examination revealed slight generalised abdominal distension and local tenderness in the left iliac fossa and a striking flame-shaped patch of dark-red mottled ecchymosis spreading out in all directions from the umbilicus and around the paramedian scar. It was thought to have some origin from the old lesion and anastomosis.

Operation.—Incision into the left rectus sheath revealed a large blood-clot. When this was cleaned out, the epigastric artery was found torn and was ligated, a small drain was inserted, and the wound was closed. Recovery was straightforward. The patient could not remember that any unusual strain or cough had preceded the pain, but a little cough and moving and lifting things were all part of her daily routine and unless severe would have passed unnoticed.

Case 3.—A stout bronchitic woman, aged 51, was admitted with six days' history of severe persistent abdominal pain of sudden onset in the left hypochondrium. Relief was obtained only by lying in bed. On the day before admission the pain had become generalised and passed into the right iliac fossa. Apart from slight nausea there were no other associated symptoms; but there had been several similar minor attacks in the last six months.

Examination showed her to be well, though her systolic blood-pressure was just over 100 mm. Hg. Her abdomen was diffusely tender, especially low on the right side. There was a striking blue-green discolouration around the umbilicus. Three days later a clearly defined tender mass was present in the left hypochondriac region. The mass seemed fixed and was elongated in the axis of the rectus muscle. It persisted four or five weeks and for some time after the umbilical discolouration had faded. No evidence was found in repeated estimations of urinary diastase to support the diagnosis of pancreatitis.

Operation.—A year later laparotomy was done because of increasing distension, and a large loculated ovarian cyst was removed. The pancreas and gall-bladder were normal. It seemed clear, after the experience of the two cases outlined above, that the acute incident in the previous year had been due to a rupture in the left superior epigastric artery rather than to any complication of the cyst or disease of the pancreas.

Discussion

Rupture and haemorrhage from either the superior or inferior epigastric artery may take place with any degree of severity from the tiniest tear and leak to complete rupture and massive bleeding. The clinical picture can simulate almost every acute or subacute abdominal lesion. Nausea, vomiting, and severe prostration suggesting intra-abdominal disease may be prominent especially when the haemorrhage is in the lower part below the semilunar fold of Douglas, where the posterior rectus sheath is absent and the blood can irritate the

peritoneum, as in case 2. The large haemorrhages give rise to masses often delineated by the rectus sheath, but in the lower part these can diffuse widely into the flanks or deep into the pelvis and be palpable per vaginam (Payne 1938). So also can the ecchymosis following the extravasation of the blood pass into the flank (case 1) like Grey Turner's sign, or around the umbilicus (cases 2 and 3), called Laffont's sign (here the route is possibly along the obliterated hypogastric artery, if due to a lesion of the inferior epigastric artery), or even at times to the perineum (Payne 1938).

In minor incidents, or before the appearance of surface discolouration, diagnosis is especially difficult. The absence of real rigidity or of guarding, an awareness of the possibility of the condition, and the type of patient in whom it occurs are all a great help. It is usually in middle-aged or elderly people with arterial disease (hypertension or palpable arteries), with distension (adiposity, fluid, cysts, &c.), often with septic foci (foul teeth especially) and a trigger mechanism—e.g., cough from chronic bronchitis or any sudden strain. It usually develops on the right side, because all strains are greater on that side which is used more. In case 2 the occurrence on the left side was probably related to abnormal fixity of the vessel at one point owing to the previous paramedian incision. Previous minor attacks are common, suggesting subjacent disease, which may of course coexist. Soreness for a week or two beforehand, due to

minor vascular incidents, may be premonitory of the major rupture.

Treatment

Operation is advised by all who have written on the subject, and the sooner the better because delay may allow repeated massive haemorrhage or infection—two grave complications—to take place. The only other cause of the very infrequent deaths has been intestinal obstruction (Payne 1938). The peritoneum need not be opened unless some intra-abdominal disease is known to be present and to require surgery. Drainage should be instituted in the acute cases, but is unnecessary, though probably safer, in the subacute types in which bleeding has ceased spontaneously.

Summary

3 cases of haemorrhage into the rectus sheath are described.

A greater awareness of the features, frequency, and degrees of severity of the lesion would explain many otherwise mysterious but spontaneously resolving abdominal syndromes.

I wish to thank Mr. W. R. S. Hutchinson, F.R.C.S., who operated on case 2, for permission to publish these cases.

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Preliminary Communication

A MODE OF DRUG ACTION

WE have very little knowledge regarding the method of much drug action, and any suggestions based on experimental evidence are of interest. In the last few years it has become recognised that there exists in cells a so-called sodium pump which extrudes sodium and is responsible for the great difference between the concentration of this ion in and outside cells. Since the work of Fenn and Cobb,¹ it has been realised that anoxia or electrical stimulation causes striped muscle to take up sodium, and more recently Hodgkin and Katz² have demonstrated that the action-potential of nerve is due to a temporary sodium shift. The operation of the sodium pump has been studied in blood-cells, yeast, and frog's skin; and it has been found that many substances, including many salts, azides, and cyanides, may poison the enzyme system and allow sodium to enter the cell.

We now suggest that various well-known drugs cause an accumulation of sodium at specific receptors. The first indication of this came from the finding that when the isolated rat diaphragm³ or the isolated rat ventricular strip⁴ is depressed by anoxia, it can be revived by reducing the sodium of the environment, the osmotic pressure being maintained by sucrose; or by adding strophanthin (2 µg.). A similar resemblance between the beneficial effects of low sodium and strophanthin levels had been noted by Clark⁵ and Clark and Daly⁶ in the frog heart which had been made hypodynamic by prolonged perfusion. Changes in potassium do not have such a beneficial effect.

A new study of the effect of drugs on the smooth muscle of the uterus has revealed that reduction by half of the sodium in the external solution restores the normal response to acetylcholine or histamine in guineapig uterus in Krebs's solution (50 ml. bath) which has been previously rendered insensitive by a large dose (1000 µg.) of these

substances (tachyphylaxis).⁷ Response is similarly restored if the histamine reaction has been abolished by an anti-histamine drug (mepyramine maleate 1 µg.), and the acetylcholine (5–10 µg.) response by a minimum dose of atropine (2·6 µg.). Alternatively, a dose of anti-histamine or atropine which has been effective in normal Krebs's solution is no longer so if the sodium is reduced. Further, after the response has been restored it may again disappear if the preparation is placed a second time in normal Krebs's solution although no atropine has been added to the bath. Admittedly this is most difficult to understand.

In view of the effects of the anoxic heart, the effect of strophanthin (2 µg.) on the uterus was studied; and, as expected, this drug was found again to act like low sodium and to abolish the action of the anti-histamine drug and atropine in appropriate doses.

Also, a dose of anti-histamine or of atropine which has been found in the preparation to abolish the action of histamine and acetylcholine is no longer effective if the strophanthin is added at the same time. The action of strophanthin in enhancing the normal action of histamine and acetylcholine on the uterus is only slight, and is not comparable with that exerted after the blocking agents.

In all experiments Krebs's solution was used, and not Ringer's solution as in most previous work. Special attention also must be paid to the exact dosage, for a very large dose of atropine will abolish all response to acetylcholine even in low sodium, while a very large dose of acetylcholine can overcome a small dose of atropine. A larger dose of strophanthin has a paralysing effect on the preparation.

In conclusion, we suggest that large doses of histamine and acetylcholine and some blocking drugs, such as mepyramine and atropine, act by causing sodium accumulation at specific receptors; while other drugs, such as strophanthin, have the reverse action. These results are of considerable clinical significance.

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New Inventions

A DRIP ALARM

BECAUSE of the shortage of nurses and the pressure which devolves upon the limited numbers in a small general hospital, it has proved not uncommon for a drip-transfusion bottle to become empty and remain so for some time before being noticed. A simple form of alarm to sound just before the bottle becomes empty was designed, and has succeeded in its objects of saving discomfort for the patient and preventing recrimination among doctors and nurses.

The device consists of a weight-operated spring switch

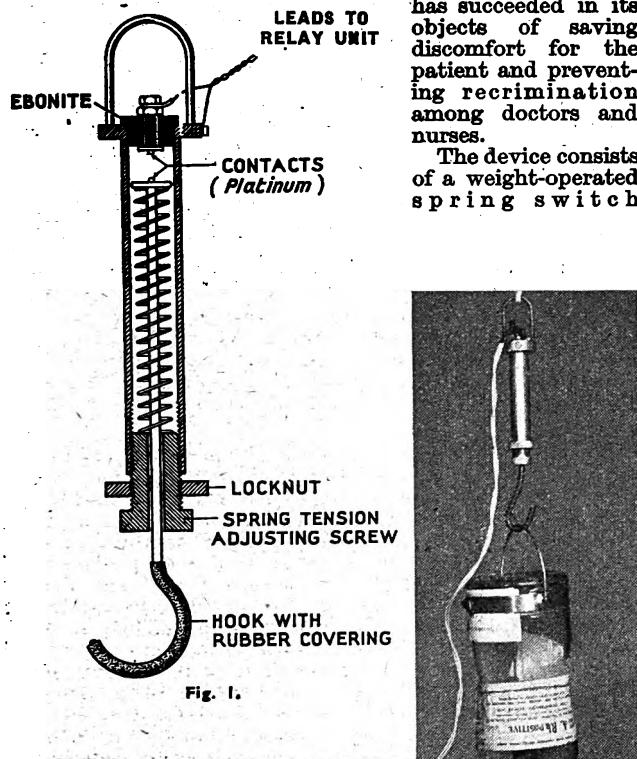


Fig. 1.

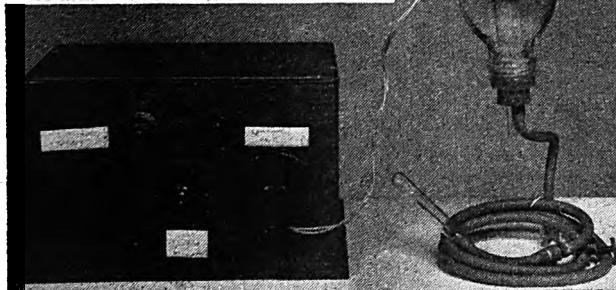


Fig. 2.

(fig. 1) which energises a relay on closure. The latter makes connections which illuminate a red light and sound a buzzer at the same time as extinguishing a green pilot light. The general lay-out of the apparatus may be seen in fig. 2. A remote buzzer may be operated away from the patient by using the "extension buzzer" plug. Although normally worked from the main 240 V A.C. supply (using a transformer with a 6 V output) the device could easily be adapted for use with dry batteries.

The system is simple to use, is safe, and has proved useful and popular with nurses.

I am indebted to Mr. George White, of Commercial Cable Co., for technical assistance with the apparatus, and I thank the consultants of Hounslow Hospital for allowing its use in the treatment of their patients.

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Reviews of Books

Manual of Urology

ALEC W. BADENOCH, M.A., M.D., CH.M. Aberd., F.R.C.S., surgeon, St. Peter's Hospital for Stone and other Genito-urinary Diseases. London : Heinemann Medical Books. 1953. Pp. 555. 10s.

UROLOGY is one of the newest but at the same time one of the oldest branches of surgery. In its long history it has accumulated not only a corpus of lore but a heap of lumber, from which it is now shaking itself free and emerging gleaming and streamlined. Mr. Badenoch has set out to provide the essentials of symptomatology, pathology, investigation, diagnosis, and treatment in the specialty. His book is planned on orthodox lines, starting with development, anatomy, and physiology, and the examination and investigation of a urological patient, and then dealing with the various diseases of the genito-urinary system, arranged for the most part regionally. An unusual feature is a separate chapter at the end of the book on operative urology. The approach is practical and the viewpoint that of the British school. He avoids dogmatism and discusses other views, but at the same time gives definite opinions. In all important respects his book is good. It is clear, concise, consistent, and covers much besides the mere essentials. The metabolic aspects of renal disease are perhaps given less space than they deserve ; and there is a good case for introducing, in a modern textbook, the milli-equivalent notation for electrolyte concentration, if only as alternative, since it has certainly come to stay and is gaining ground. In so practical a book it is disappointing to find hardly anything about the varieties, qualities, use, and care of ureteric catheters, especially as a good deal of attention is given to other urological instruments. Omissions, however, are inevitable in a book of moderate length. The illustrations are good and plentiful, and this book is a pleasure to handle.

Retinal Circulation in Man and Animals

I. C. MICHAELSON, PH.D. Glasg., F.R.F.P.S., D.O.M.S., advisor in ophthalmology to the Government of Israel. Springfield, Ill. : Charles C. Thomas. Oxford : Blackwell Scientific Publications. 1954. Pp. 146. 50s.

THE extensive studies recorded here on the developing vascular system of the retina were carried out on different vertebrates, special attention being paid to representative species like the eel, frog, pigeon, and some mammals. They amplify the rather sparse knowledge on the choroidal circulation and the vascular system of the vitreous in nourishing the retina. In addition, Michaelson brings forward much new and detailed work on the uneven rate of vascularisation of the retina during development, and on the uneven vascular development in different parts of the retina—work which leads him to the assumption that there is a local factor in the retina which influences vascular development and is capable of affecting growth of new vessels. This small book is profusely illustrated and clearly documented.

Atlas of Pelvic Operations

LANGDON PARSONS, M.D., professor of gynaecology, Boston University School of Medicine; HOWARD ULFELDER, M.D., assistant clinical professor of gynaecology, Harvard Medical School. Philadelphia and London : W. B. Saunders. 1953. Pp. 231. £4 10s.

THIS substantial volume weighs 4 lb. 13 oz. Its purpose is to teach by means of illustrations the technical details of pelvic surgical procedures, as practised and tried in the Harvard and Boston schools of medicine. The format is designed to permit a surgeon to follow a detailed description of the operation by word as well as by drawings, or to combine the two if he chooses. There are 197 plates, each of which contains from 3 to 13 separate drawings, and each drawing illustrates a definite step in an operation. All the ordinary gynaecological operations are described, as well as many of the more unusual ones (e.g., the Marshall-Marchetti operation for stress incontinence). Some operations not strictly gynaeco-

logical—such as large-bowel resection and anastomosis and excision of rectum—are also described and illustrated. The modern extensive operations for malignant disease of cervix and vulva are fully shown. The atlas is carefully written and beautifully illustrated: its careful study should certainly improve a surgeon's skill and on occasion enable him to carry out safely a procedure with which he may not be very familiar. Therein lies a danger: the atlas makes pelvic surgery look almost too simple.

Peripheral Circulation in Man

A Ciba Foundation Symposium. Editors for the Ciba Foundation: G. E. W. WOLSTENHOLME, O.B.E., M.A., M.B.; JESSIE S. FREEMAN, M.B., D.P.H., assisted by JOAN ETHERINGTON. London: J. & A. Churchill. 1954. Pp. 219. 25s.

ON the first page of the first number of the *British Journal of Experimental Pathology*—which saw the light in February, 1920—the late W. M. Bayliss, then probably the most outstanding British physiologist, posed the question "Is haemolysed blood toxic?" In giving a negative answer—which certainly delayed our knowledge of the renal effects of haemolysed blood—he was careful to point out that the results obtained in the rabbit were not, for reasons special to that animal, to be applied to other species. Generalisations from findings in animals, under conditions of experiment, in the physiological laboratory, are more guarded today; yet Professor Edholm, in opening the Ciba symposium on the peripheral circulation, was constrained to say: "Human physiology is still regarded with some suspicion by a number of physiologists . . . it is harder to work on man than on isolated pieces of tissue." A remark which is at once a warning and a stimulus.

The cogency of this warning was well borne out by the opening paper in which Prof. A. C. Burton surveyed the methods of measuring human peripheral blood-flow. Indeed he made the difficulties seem so formidable that some of the audience may well have wondered, at this stage, whether a conference held upon such shifting sands was worth pursuing. Pace these philosophic doubts, it seems to have been generally accepted that venous-occlusion plethysmography is a reliable method; even if one is left wondering whether the rate of filling an artificially emptied blood system may not be a different thing from the rate of flow under normal physiological and psychological conditions—if such exist.

Though much of this symposium was concerned with the measurement of blood-flow and is for the expert physiologist and physicist to evaluate, the report contains much good biological reading—including, for example, work on the observation of living tissues, the physiology of adrenaline, the nervous control of blood-vessels, afferent effects by sympathetic trunks, reaction and adaptation to cold, reversed blood-flow in arteries, and various aspects of the pathology of the peripheral circulation, contributed by some thirty scientists drawn from eight nations.

The Ciba Foundation deserves credit for its notable example of the beneficent activity of free enterprise in the world of medical science. In the choice of the subjects for its conferences, in the rigorous limitations in size, in the careful selection of the participants, and in the excellence of the organisation, it shows an element of benign autocracy which makes a refreshing contrast to the compromises of committees. The matter does not end with the closing of the foundation's doors on the last departing participant, but goes on to the production of a monograph such as the one we are reviewing, which bears witness to the efficient though unostentatious recording done during the conference and the admirable editing by the foundation's director and his staff.

Hospital Accounts and Financial Administration

3rd ed. Capt. J. E. STONE, C.B.E., M.C., F.S.A.A., F.H.A. London: Faber & Faber. 1954. Pp. 866. 6 guineas.

ALL concerned with the financial side of hospital life will welcome the publication of this entirely new and enlarged edition of a well-known standard work.

The first part is a section on general accounting; the second part discusses the financial control of hospitals; and other sections include a detailed study of the National Health Service

Act and the problems of departmental accounting. The appendices reproduce important statutory instruments and many valuable forms. The publication is remarkable for its completeness and contains extracts from all circulars published by the Ministry of Health relating to accounts and costing. There is a useful summary of law cases relating to legacies, and this is to be kept up to date by the issue of supplements. One section of the book sets out a summary of the system in Scotland, and for those working in England the differences can be instructive. Occasionally the author appears to be just a little out of touch with common practice. Thus, he says that the practice of signing for wages is almost obsolete, but we understand that it is in fact still quite common. He recommends the use of an official invoice form provided by the hospital, but this is not in general use and indeed was the basis of one of the well-known frauds in local government. Continuous stocktaking throughout the year is recommended, and this is indeed a very good practice; but unfortunately the financial regulations require stocktaking of everything at the end of the year.

Despite the high price of the publication, it is one that every hospital management group should possess.

Narcotics and Narcotic Addiction

Prof. DAVID W. MAURER, PH.D., lecturer on narcotic addiction and criminal argots, Southern Police Institute, Louisville, Kentucky; VICTOR H. VOGEL, M.D., medical officer in charge, European Activities, U.S. Public Health Service, Paris. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954. Pp. 303. 54s.

ACCORDING to Osler, man is a medicine-taking animal; and this book on drug-addiction is welcome. The authors have not limited themselves to narcotics, as the title suggests. The commonest form of addiction in America is the use of marihuana; but "more dangerous," they say, are "recent products of medical and pharmacological research," and they emphasise that "any drug which will substitute smoothly for an addicting drug is equally as addicting as the primary drug." The authors stress the high incidence of barbiturate addiction—often induced by medical treatment—alone or in combination with amphetamine, alcohol, morphine, or other drugs. That "more deaths are caused by barbiturates, either accidentally or deliberately ingested, than by any other poison" applies to this country as well as to America; and it is sobering to read that even heroin, dihydro-morphinone, cocaine, and recently pethidine were considered free from dangerous addicting properties when first introduced. In this way "addicts were literally made by the millions."

Dr. Vogel finds that drug-addicts need to be segregated for a minimum of 4½–6 months, preferably in special institutions; and even then results are poor in thoroughly established cases. The recognition of addicts is discussed in a special section, because the authors have found that even responsible persons have "fantastic ideas of what the symptoms of addiction are." Stress is rightly laid on difficulties of diagnosis: in most cases it has to be made on withdrawal symptoms rather than from symptoms of intoxication. Many addicts go undetected for a long time while supplies are unfailing, and the many different symptoms with which they present often deceive their physicians.

A chapter on legal controls for drugs of addiction refers mainly to American law. The last part, devoted to the argot of narcotic addicts, gives an interesting if horrifying glossary of terms used in the American underworld, intended for the guidance of "Government Officials and Law Enforcement Officers," to whom this book is primarily addressed.

The Yearbook of the Universities of the Commonwealth 1954 (London: Association of Universities of the British Commonwealth. 1954. Pp. 1916. £3 3s.)—The 31st edition contains only one new institution, the Nova Scotia Agricultural College. News came too late for the inclusion of the University of Rajshahi in East Pakistan and of Rhodesia University College at Salisbury. A new feature is a statement of the numbers of foreign students attending each university. Perhaps the most useful item is the index containing about 30,000 names of "staff and officials."

For Students only! the last minute cram



THE FEEDING OF NORMAL INFANTS FROM BIRTH

BREAST FEEDING

A normal infant should not be put to the breast until 6-12 hours after birth. In the case of a premature, this period should be longer.

He should then be put to the breast every 3 hours for 5 minute periods, gradually working up to 10-15 minutes.

On about the 4th day, the flow of milk should be established.

At the end of a week's feeding, he may take 20 minutes to empty a breast. In such cases, only one breast should be used at each feed.

1-2 ozs. of glucose water in 5% mixture should be given after each feed until the 5th day.

At this stage, a test feed should be given to see how much milk the child is receiving after each feed for 24 hours and the average per feed estimated.

He should receive 2½ ounces of milk in 24 hours for every pound of body weight.

Should the supply of breast milk prove insufficient, the deficit should be made up with Half Cream Cow & Gate until 2 months and then Full Cream.

When breast feeding has been established, the child should gain 4-6 ozs. per week.

Breast feeding may be continued until 9-10 months, but weaning should be started when the child is 4-5 months old or weighs 15 lbs.

ARTIFICIAL FEEDING

It is usual to give Half Cream Cow & Gate until the child is 2 months old, but some are able to take the additional fat in Full Cream almost from birth.

When it is decided to change from Half to Full Cream, an abrupt change should not be made. One measure of Full Cream should be substituted for one of Half Cream at first and gradually stepped up until the child is on Full Cream only. This change over should take about 5 days. Although the average child requires 2½ ozs. per lb. of body weight in 24 hours, this amount should be varied to suit each individual child.

Signs of Underfeeding.

Crying, failure to put on weight, green stools and constipation.

Signs of Overfeeding.

Vomiting, putting on too much weight, constipation.

If the child is below weight, feed up to the expected body-weight, e.g., suppose a child weighs 9½ lbs. and should weigh 10 lbs., then he will require 10 x 2½ ozs. of milk in 24 hours.

Weaning should begin as in breast feeding, using Cow & Gate CEREX.

Further information about our products is freely available.

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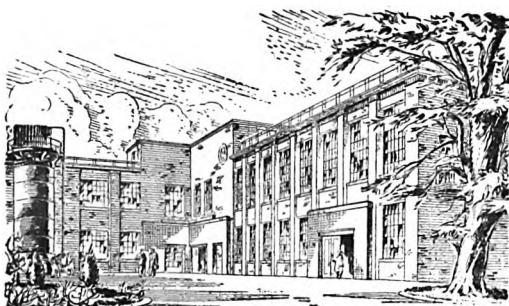
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THE LANCET

LONDON: SATURDAY, JUNE 5, 1954

The Unruly Member

Most people, as they go through life, prefer to hear nothing but the truth from those they like and trust ; but they do not necessarily require the whole truth. On p. 1161 Dr. RUSSELL and Dr. MITCHELL remind us of the responsibility that lies on us as doctors in our handling of truth.

One error is to say too little ; and though we are growing out of the undesirable professional habit of using silence to mystify the patient, some of us are still not punctilious enough about giving such plain explanations as will do nothing but good. Apart from the major anxieties (so often unexpressed) which need relief, there are often minor questions which the patient would like to ask, but does not—whether he can go on playing golf, whether he should change his job, and so on. In a recent lecture Dr. C. F. HAWKINS mentioned his practice of getting patients to write down such questions, so that he can answer them on his next ward round. This not only helps the patient but is also instructive for students, and it is a practice which might well be generally adopted. Moreover, it throws on the patient the onus of seeing that he gets the information he wants : he does not then complain "they tell you nothing."

But there is also the opposite error of saying too much—of telling the patient everything one knows or surmises about his case, without regard to the possible effect of loquacity upon his fears. This is illustrated by RUSSELL and MITCHELL's account of what sometimes happens when the partners of a marriage come for advice about sterility. The mere fact that they have come for this purpose indicates their deep desire to have a child ; and if the doctor lays their failure at the door of one or the other he inevitably provokes guilt and shame in that one, and resentment, pity, or superiority in the other. Pride in successful procreation is even older than mankind, and so deep and primitive an emotion cannot be argued with : it must be accepted as a dynamic factor in the situation. In practice, RUSSELL and MITCHELL say, no opinion on the cause of sterility should be offered to either partner until both have been examined. It may then be possible to assure them that no cause has been found, and that there is a good chance that they will yet have a child. (This is good treatment in itself, for relief of anxiety can be followed by conception : as is illustrated in cases where a couple give up worrying and adopt a baby—only to find, after a few months, that the wife has become pregnant.) If one or more factors capable of delaying pregnancy are present, then the couple can be told that conception is not impossible. Unless action is recommended attention should never be drawn to conditions which bear a doubtful relation to fertility—such as retroversion of the uterus or apparent blockage of the fallopian tubes. And even when, according to present knowledge, pregnancy is judged very unlikely, or even impossible, this information will not necessarily be helpful. To tell a husband

that he is subfertile is a serious blow to his self-confidence, however well he and his wife may accept it at the conscious level. It is equally hard on the wife to learn that she is barren, however kindly the hard word is avoided ; and unless she has some condition which demands treatment, RUSSELL and MITCHELL believe she should never be given cause to think herself so. By taking thought we can sometimes avoid creating a situation in which the husband is content to blame his wife, or the wife feels—whether she expresses it openly or not—resentment towards her husband.

Indeed the subject of what not to tell patients generally deserves much more consideration than we are apt to give it. To say too much is as bad as to say too little ; and judging well how much to say depends on an unlimited exercise of insight and imagination, as well as on the guidance offered by those—like RUSSELL and MITCHELL—with special experience. In particular, perhaps, some lessons can be learnt from psychiatric practice. The psychiatrist, by listening more than he talks, is able to locate with some accuracy the springs of a patient's discontent, and can thus direct his reassurances where they will do most good. He also explains, as well as he can, whatever he is asked to explain ; but his chief efforts are directed to getting the patient to seek his own way out of his difficulties. Reasonable people need reasonable explanations of what is going on in their bodies, and of what is being done to help them. Given this much, they will usually face their fears well. What they do not want—and this is as true of doctor patients as of others—is to be loaded down with their medical adviser's own doubts and anxieties about their diseases. It requires self-control, at all times, to keep these doubts back ; and the test comes when an intelligent and persistent patient sets himself to nag us into disclosing them. Something he must be told, or he will conjure up threats to his safety out of our evasions ; but when enough has been said, when he has been given sufficient factual information to feed his intelligence, and enough justified reassurance to check his fears, the time has come to refuse further cross-examination until that much has been thought over and digested. At this point the doctor should take his hat and go.

The danger of inducing illness by injudicious remarks is, of course, very great. The boy who is told to "take things easily," because there is some doubt about the significance of a cardiac murmur, may take them so easily that he grows up a cardiac invalid. An innocent murmur should never be mentioned to the patient ; indeed no abnormal physical sign ought to be mentioned unless the doctor regards it as significant. A high blood-pressure is a finding which, even today, we cannot accurately interpret : people with "benign" hypertension have little or nothing the matter with them, and commonly live a normal span ; so there is nothing to be said for telling them that their pressure is "high," and still less for telling them what the reading is. In the same way, early signs of a disease for which there is no successful treatment, but which has as yet caused no trouble, should be recorded only in the doctor's notes, not mentioned to the patient. Even if it takes years to develop, he will know about it quite soon enough. Abnormal signs in children should seldom be discussed

with the parents unless they are treatable, and they should never be spoken of before the child. Children are too often labelled undersize or underweight, and regarded with anxiety on that account for years; but at adolescence they may shoot up like fountains and feed like giants, and reach the average stature for the race in a matter of months. Some children are small and thin: that is the truth of the matter. It does not necessarily mean there is anything wrong with them, and the doctor's part, when they are brought to him, is to make sure they are healthy and tell the parents so. If he does the opposite—draws attention to their smallness, and urges care and to watching—he is doing a bad turn to all concerned, especially the child.

People who are about to die, or who first present themselves to their doctors with a fatal disease, offer a special problem. The Churches hold that a professing Christian has a right to be told when he is dying: he has spiritual affairs to attend to. Sometimes a man whose temporal affairs need settling in order will also be glad to be told. But many—perhaps most—people would rather be spared too much frankness, preferring not to have their unspoken fears confirmed. Much, of course, depends on the patient—and hence on the doctor's judgment.

Perhaps the most damaging way of telling a patient more than he should hear is to stand at his bedside and instruct, as though across a stone effigy, a class of students in the variety of misfortunes to which his disorder lays him open. Scientific terms—used somewhat in the spirit of "always speak French before the servants"—are no sort of safeguard. Either the patient understands them, and is justly alarmed; or he does not understand them and—thanks to his imagination—may be alarmed quite needlessly. Besides, some fool of a student may at any moment disclose a dire possibility in plain English. Only one course is safe: once the physical signs have been demonstrated, bedside teaching should be conducted elsewhere than at the bedside.

Cerebral Circulation

IN 1855 ADOLF EUGEN FICK,¹ then a demonstrator of anatomy at Zürich, published the account of diffusion in fluids which has since brought him eponymous fame among physical chemists. In 1870² the same versatile thinker enunciated to the local learned society at Würzburg the "principle" which has made his name familiar to medical students. He pointed out to his audience that, if one could determine the oxygen-content of the blood (*a*) in the pulmonary artery and (*b*) in the aorta, then the quantity of blood traversing the lungs (i.e., the cardiac output) could be deduced from the subject's consumption of oxygen during a given period. He apologised for the fact that technical difficulties prevented him from presenting any results on man, but he made some illustrative calculations using published data obtained on dogs. It is interesting, though irrelevant, that a young physicist named RÖNTGEN was introduced as a new member at the same meeting of the Würzburg Physico-Medical Society.

1. Fick, A. E. *Phil. Mag.* 1855, 10, 30.

2. Fick, A. E. *Verhandlungen der Physikal-Medizin Gesellschaft in Würzburg.* July 9, 1870.

It was not until 1945, however, that KETY and SCHMIDT³ produced their ingenious method of applying an extension of Fick's principle to the measurement of blood-flow through the living human brain. They then demonstrated that, if a subject breathed a gas-mixture containing some 15% nitrous oxide, it was possible, by analysing blood from his internal jugular vein and comparing its content of nitrous oxide with that of the arterial blood, to compute the cerebral blood-flow. To do this it was necessary to know how much of the gas was taken up by the brain in a given period of time, and they showed that this could be calculated from the solubility of the gas in brain-substance, once equilibrium had been established. In practice, since the arterial and venous concentrations of nitrous oxide have to be measured while they are rising—instead of being steady as in FICK's classical instance of the cardiac output—serial samples are required so as to estimate the rate of rise, and some mathematical complexities are added from this cause. None the less the figures can be simply manipulated graphically, and the results so obtained check well with other methods of estimating cerebral blood-flow in man and animals. The results of such determinations are generally expressed per 100 g. of brain, since the solubility of the gas where it enters into the calculation is itself expressed in these terms; for most purposes this value as a function of weight is perfectly satisfactory, but an approximate estimate of the total flow through the organ can be derived from it by assuming an average brain-weight (1400 g. for an adult male) not forgetting, however, that the range of brain-weights extends from under 1000 g. to over 1800 g.⁴

During the decade since the introduction of the nitrous-oxide technique, measurements of the cerebral blood-flow (C.B.F.) have played a part in many studies of brain disorders. In particular, when taken in conjunction with measurements of oxygen utilisation and glucose uptake, they have thrown light on the metabolic activities of the brain, and the results of such studies were recently discussed in these columns in relation to the pathogenesis of coma.⁵ Also, when combined with measurements of blood-pressure, the C.B.F. may be used in haemodynamic calculations, and such an application is exemplified in a study by SHENKIN and NOVACK⁶ of the behaviour of the cerebral vessels in several groups of hypertensive patients.

This study revealed that hypertension unaccompanied by arteriosclerosis is characterised by a rise in cerebral vascular resistance (C.V.R.) (which is the ratio of mean arterial blood-pressure to cerebral blood-flow) without any change in the C.B.F., whereas in the presence of coexisting arteriosclerosis the C.B.F. was itself significantly reduced. Arteriosclerosis was diagnosed in this series of cases either on radiological or ophthalmoscopic evidence or on a history of vascular occlusion, and, when present without concomitant hypertension, it had no significant effect on either C.V.R. or C.B.F. SHENKIN and NOVACK went on to investigate the reversibility of the cerebral vasoconstriction found in their hypertensives, and by

3. Kety, S. S., Schmidt, C. F. *Amer. J. Physiol.* 1945, 153, 53.

4. Gray's Anatomy. London, 1949; p. 1040.

5. *Lancet*, March 20, 1954, p. 607.

6. Shenkin, H. A., Novack, P. *Arch. Neurol. Psychiat.* 1954, 71, 148.

administering carbon-dioxide inhalations they showed that this vasodilator substance was capable of lowering the otherwise raised C.V.R. by some 20%. In their normotensive arteriosclerotic subjects excess carbon dioxide did not produce a reduction in C.V.R. as it does in normal healthy people, but reduction of arterial carbon-dioxide tension by overbreathing did increase the C.V.R. in the arteriosclerotic patients. This latter finding is taken to indicate that in arteriosclerotic persons the cerebral vessels are probably maximally but not irreversibly dilated. SHENKIN and NOVACK also refer to other studies in which a number of reputedly vasodilator drugs were tested for their effects on the C.B.F. Among these nicotinic acid and aminophylline gave negative results but papaverine did appear to increase the flow. Opinion is divided on the action of tolazoline, for, while DEWAR et al.⁷ have reported that it caused an increase of C.B.F. in each of six patients with stenosis, SCHEINBERG et al.⁸ obtained rather variable results from somewhat larger doses of the same compound in persons without circulatory embarrassment.

On another page in this issue Dr. J. W. SAUNDERS reports upon the effect of hexamethonium bromide upon the C.B.F. In his work the hypotensive drug was combined with the application of negative pressure to the legs, so as to impede venous return, as a means of reducing bleeding and intracranial pressure in connection with neurosurgical operations. For determining the C.B.F. in the hypotensive phase, SAUNDERS relied on measurements of the arteriovenous oxygen-gradient across the brain and calculated the actual blood-flow by using figures supplied by KETY for the oxygen consumption of normal brain tissue under comparable conditions of light anaesthesia. In this way he arrived at the conclusion that the C.B.F. was not seriously reduced when the systolic blood-pressure fell to the region of 55 mm. Hg. This means that a considerable fall in C.V.R. must have accompanied the onset of arterial hypotension, with consequent safeguarding of the cerebral blood-supply. The adequacy of the latter in the presence of hypotension was confirmed in SAUNDERS's study by the fact that normal subjects could sustain a fall of systolic arterial pressure to around 60 mm. Hg, for at least five minutes without loss of consciousness or serious impairment of intellectual acuity. Estimates of C.B.F. based solely on arteriovenous oxygen differences were used in 1939 by WILLIAMS and LENNOX⁹ to study its relation to hypertension, and, though all such estimates of C.B.F. must rest upon an assumed value for the actual oxygen-requirement of the brain, and have been much criticised,^{10 11} it is notable that the conclusions of WILLIAMS and LENNOX were in good general agreement with the more exact findings of SHENKIN and NOVACK. A further point which merits some consideration in relation to all measurements of C.B.F. is the possible variation resulting from different sites of sampling on the venous side. KETY and SCHMIDT¹² are at some pains to point out that there is remarkably little difference in oxygenation

between blood taken from the right and left internal jugular veins of the same subject, but HIMWICH and his colleagues¹³ have claimed that there is a significant difference which can be attributed to the fact that the vein on one side drains mainly cortical blood via the superior sagittal sinus, while the other receives blood mainly from subcortical areas via the straight sinus. In SAUNDERS's work blood was obtained from an unspecified sinus and may not therefore have been representative of the whole effluent from the brain; but the variations which have been recorded are hardly great enough to affect his main conclusion. However, in many animals, such as the cat, which is a favourite species for neurophysiological work, there are extensive intercommunications between the intracranial and extracranial vasculature¹⁴ which create great difficulties in venous sampling.

The general applicability of the nitrous-oxide technique might be questioned because of the rather complex manipulations involved, but SCHEINBERG and his associates¹⁵ in Florida have lately employed it with success to investigate the effects on the C.B.F. of vigorous exercise on the treadmill. Having shown previously that change from the supine to the erect posture generally induced a fall in C.B.F. they went on to demonstrate that this fall did not occur in the exercising subject; moreover, the C.V.R. decreased during exertion. They noted an inverse relation between the C.V.R. and the cerebral metabolic rate and reach the conclusion, with which it is difficult to disagree, that the "chemical regulation of the cerebral circulation is complicated."

Although the nitrous-oxide technique has achieved great popularity, other methods of measuring C.B.F. have also been tried, incorporating modifications of instruments conventionally used for measurements of circulation-rate in other parts of the body. These include thermo-electric techniques such as that of GIBBS¹⁶ in which a small heated junction is placed in the internal jugular vein, and which in fact provides a good indication of changes in the C.B.F. without, however, directly measuring absolute rates. Even plethysmography has been employed, in a thinly disguised form, by measuring the rate of displacement of cerebrospinal fluid after occluding the jugular veins. Unfortunately simultaneous compression of the vertebral veins is not practicable, and, probably for this reason, the plethysmographic method has, in the hands of FERRIS,¹⁷ yielded unduly low estimates of the C.B.F. Yet another quite different approach is involved in the latest method devised by GIBBS¹⁸ in which the aim is to measure the extent of dilution of an injected dose of some recognisable material as it passes through a given vascular territory. This idea was developed as early as 1897 by STEWART¹⁹ in his measurements of cardiac output, and, as applied to the C.B.F., it requires the injection of azovan-blue (Evans blue) into the carotid artery and subsequent analysis of jugular venous blood. In the opinion of

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- 16. Gibbs, F. A. *Proc. Soc. exp. Biol. N.Y.* 1933, 31, 141.
- 17. Ferris, E. B. jun. *Arch. Neurol. Psychiat.* 1941, 46, 377.
- 18. Gibbs, F. A., Maxwell, H., Gibbs, E. L. *Ibid.* 1947, 57, 137.
- 19. Stewart, G. N. *J. Physiol.* 1897, 22, 159.

SCHMIDT¹⁰ this offers considerable promise, though the necessity for the intracarotid injection will limit its appeal.

It is evident that measurement of the cerebral blood-flow is becoming established, alongside measurement of the renal and hepatic blood-flows, as a recognised procedure in clinical research. Unlike FICK, the modern reviewer is more embarrassed by the plethora than the paucity of experimental data.

The Disabled

ALL those who have to do with the care of disabled people seem agreed on one thing—that the services designed for their benefit are at present chaotic. The Central Council for the Care of Cripples¹ (C.C.C.C.) the British Rheumatic Association² (B.R.A.), and even the London County Council³ (L.C.C.), in the evidence they have submitted to the Interdepartmental Committee of Inquiry on the Rehabilitation of Disabled Persons (the Piercy Committee), mention formidable gaps in existing arrangements. It is worth recalling what these arrangements are.

The Disabled Persons (Employment) Act, 1944, provides for the maintenance of a register of disabled persons suitable for employment, and requires all employers of more than 25 people to give work to a quota of such people (at present 3%). Moreover it provides for the reservation of certain categories of work for the registered disabled, for the establishment of rehabilitation and training centres, for sheltered employment in factory and at home by the formation of limited companies, and for the appointment of disablement resettlement officers (D.R.O.). In addition, the National Health Service Act, 1946, its Amendment Act, 1949, and the National Assistance Act (Part III), 1948, provide between them for the supply and maintenance of appliances, for the well-being of people temporarily or permanently disabled, and for the home care of the sick.

Registration, however, has some drawbacks of its own. If, for instance, a registered disabled man earning trade-union rates has to call in a fellow-worker, occasionally, to help him with some task, he causes this helper to lose time and hence money; and so may meet a surly response. A system intended to make for equity may in fact penalise anyone who feels inclined to give a disabled workmate a helping hand. Again, the provisions made for different kinds of disability vary greatly. Strong voluntary associations, as well as statutory provisions, give reasonable support to the blind and the deaf; but the tuberculous and the epileptic are not so well served. Many people dislike working alongside such patients; and people with these disabilities are therefore apt to avoid registration and conceal their disorders as long as they can. Many infective tuberculous patients, the L.C.C. believes, are at work in industry without either their employers or their workmates knowing anything about it. The Ministry of Health⁴ has recommended that people with known infective tuberculosis should be employed in normal industry provided that they, and their conditions of work, are under medical supervision; but some chest physicians think there must be a change of attitude among employers and

workmates before this will be practicable. Certainly such a plan would expose susceptible workers to more chances of encountering the disease—which might mean a greater danger of spread. The L.C.C. is confident that if enough alternative sheltered employment, offering satisfactory pay, were available, most of the patients now engaged in work which is unsuitable for them would come forward, and be glad to change. It would like to see more Remploy factories for these patients, and it also suggests that both Government factories and factories owned by private firms should set aside sections where people disabled by tuberculosis could be employed.

Those disabled by the rheumatic diseases also need much more help than they are getting. Last year, in the Survey of Sickness,⁵ rheumatoid arthritis was reported in 1·4-1·6 men, and 6·7 housewives, per 1000 people (over 16 years of age) who were interviewed; and the comparable figures for chronic rheumatism were much higher—41·67 men and 157 housewives, per 1000. Many people disabled by these diseases would be capable of doing part-time work, if this were to be had; many would be less disabled if their disease had been treated in its early stages; many are occupying hospital beds from which they might have been excluded, either temporarily or permanently, by active treatment; and many could do more if they had appropriate appliances.

The problem of appliances, indeed, badly needs reconsidering. Prof. THOMAS FERGUSON⁶ has reported that the lack of much-needed appliances, and of adequate treatment, was a cause of the weariness and dislike with which many of the disabled youths in his Glasgow study regarded doctors and hospitals; it also partly accounted for a high unemployment-rate among them. The C.C.C.C. mentions the time wasted when an appliance needs repair: even if it only needs a new screw or strap, the patient has to "see the doctor" in hospital before he can be given a chit to take to the workshop. The medical interview might surely be waived when the lesion is not in the patient but only in the instrument. The C.C.C.C. also recommends that the schedule of appliances should be extended to include such things as stocking-gadgets, which enable the patient to dress himself, and such special kitchen or other equipment as a housewife needs to carry out household tasks. Moreover, it suggests that disabled people whom a consultant thinks unfit to use public transport should be entitled to have motor chairs.

It is still not easy to find jobs for the disabled. The quota system works well up to a point, but the C.C.C.C. finds that some employers make up the quota by engaging people whose disability does not hamper them for the work in hand: a bank clerk with a gastric ulcer, for instance, is not disabled for his task and should not count towards the quota. The regulations might well be tightened so that those disabled people whose prospects of getting work are poor are given fairer opportunities under the quota system. All parties seem agreed that training courses are very inadequate at present. Professor FERGUSON has emphasised the need for more courses for disabled young people leaving school, when most of

1. Obtainable from the Central Council for the Care of Cripples, 34, Eccleston Square, London, S.W.1. Pp. 12.
2. Memorandum and Evidence submitted to the Piercy Committee, British Rheumatic Association, 5 Tite Street, S.W.3. Pp. 34.
3. Report of the General Purposes Committee (no. 2), Agenda for May 4.
4. Circular no. 7152.

5. Brooke, E. *Mon. Bull. Minist. Hlth. Lab. Serv.* 1953, 12, 114.
6. M.R.C. Memorandum no. 280. 1952. See *Lancet*, 1952, ii, 120.

them have a positive and enthusiastic attitude to work. Only too often they are allowed to drift into unskilled manual labour, to which they are unsuited but which is comparatively well paid. If they are then urged to go into skilled work, where the pay is less during training, they often think themselves better off where they are. It is only later, when they see their friends in skilled work earning higher wages, that they realise their own chance has been lost; and "the crisis of school leaving is never repeated."

Disabled school leavers are mainly handicapped by congenital disorders; and they need, as the C.C.C.C. says, an education which will equip them mentally, and as far as possible physically, to enter industry when they leave school. People disabled later in life need a course of reablement which will give them a new outlook on work. Even when courses are provided these may not suffice to launch the trainee successfully. Some trade-union organisations are reluctant to admit those whose training has been shorter than that of able employees, no matter how high the standard of proficiency reached. But, in fact, it is not wholly a question of proficiency: a severely handicapped young adult entering employment for the first time may need as long as three years at a training college to fit him for life in open industry. The C.C.C.C. therefore believes that substantial encouragement should be given to employers to train within industry; and it doubts whether the cost of this would exceed the amount now spent on special training centres. The L.C.C., on the other hand, is thinking of providing a combined reablement unit and sheltered workshop for the physically disabled, to be linked if possible with a placement service and an arrangement for including outworkers. Clearly there is room for useful discussion here. Both methods of training have their advocates, and it will be helpful to know the advantages and drawbacks of each, as seen through the impartial eyes of the Piercy Committee. The system of sheltered workshops provided by Remploy is criticised by the B.R.A. because it caters for only some 6000 disabled workers (albeit these are the most severely disabled, being judged unfit for open industry, anyhow at the time of their engagement), and because it makes no deliberate attempt at medico-industrial reablement. The C.C.C.C., however, holds that the value of Remploy factories to those for whom they are intended would be greatly increased if more hostels were available, and more transport provided, for disabled people who live too far away to seek work in them.

The disabled, like the rest of us, need incentives to bring out their best work. The experience of the Michael Works⁷—that "Men who had been listlessly and unenthusiastically doing their jobs, sprang to life when they knew that additional effort would mean a larger pay packet"—deserves to be kept in mind. Indeed, it is a weakness of many sheltered workshops that they do not take this very human quality into account. The C.C.C.C., regretting the heavy Remploy subsidy (£7 6s. weekly to each factory worker, after crediting sums obtained by the sale of products), suggests that a wise policy would be to

give pensions on assessment of disability, and thereafter—as an incentive to the fullest possible production—the rate for the job. It has to be borne in mind, of course, that an ambitious worker may be led in this way to drive himself too hard; but the factory doctor should be able to guard him against this risk.

The disabled, it seems clear, are not only being given care of a patchwork and piecemeal kind: they are also being hindered in doing as much towards their share of the country's work as they might. It is widely held that part of the trouble comes from their being under the care of so many departments—the Ministries of Labour and of Pensions and National Insurance, the National Assistance Board, and the local authorities. The C.C.C.C. recommends setting up a co-ordinating committee, representing all the departments concerned; and the B.R.A. goes further and asks for a public corporation (on the lines of the British Broadcasting Corporation), under the aegis of the Government but independent of it, represented in Parliament by a Minister without portfolio, and financed—to the amount already spent on the disabled—by Government funds. This policy-making body would be responsible for the welfare of all the handicapped, from school-leaving age onwards. There seems a risk that so large a body, paid for out of public funds, might in time develop into yet another Government department, with all the weaknesses, as well as the delights, attendant on such things. The interests of the disabled might be more successfully—and certainly more flexibly—safeguarded by a co-ordinating committee; or even by a little coöordination.

Annotations

FETAL HEPATITIS

JAUNDICE in the neonatal period is extremely common, and it may be difficult to establish its cause. The mild transient form usually described as physiological is undoubtedly the most usual; but syphilis, umbilical sepsis, erythroblastosis, and congenital atresia of the bile-ducts should all be excluded before this diagnosis is confidently accepted. Infective hepatitis, the commonest cause of jaundice in adults, has usually been disregarded because of its long incubation period; but it now seems that the foetus may be infected in utero. Dible and his associates¹ describe 4 cases of infants, including 1 with severe jaundice, who died in the first two days of life. At necropsy there was moderately severe hepatitis which was so far advanced that the lesions must have begun in utero. In all 4 there were the usual histological features of hepatitis: necrosis of liver-cells, bile-duct proliferation, histiocyte reaction, fibrosis, and liver-cell regeneration. Multinuclear giant-cells, apparently derived from parenchymal cells, and iron-containing pigment granules in liver-cells and histiocytes, were also conspicuous. Since the amount of iron, determined chemically, was not increased, Dible takes this finding as evidence of impaired capacity of the damaged liver-cells to incorporate iron in its usual organically bound form. Another notable difference from the picture in adults was the presence of foci of active haemopoiesis. Such foci are an important feature of the liver in erythroblastosis, and the possibility that haemolytic disease underlay the hepatic lesions was carefully excluded. Haemopoiesis in the liver is normal up to the time of birth, and foci are usually recognisable up to about twenty-four hours

⁷. Arthur, J. Through Movement to Life. London, 1952; see *Lancet*, 1953, i, 1054.

1. Dible, J. H., Hunt, W. E., Fugh, V. W., Steingold, L., Wood, J. H. F. *J. Path. Bact.* 1954, 67, 195.

postnatally; and their presence in these cases represents only some delay in the normal maturation process of the liver—which is scarcely surprising when that organ is grossly abnormal in other respects. Dible and his colleagues justifiably conclude that the pathological findings in these infants were attributable to their stage of development and were in no way incompatible with viral hepatitis.

The relationship of this neonatal hepatitis, apparently contracted in utero, to juvenile cirrhosis is next considered by Dible and his associates. In 2 infants who developed jaundice within a few days of birth and died after three and seven weeks, necropsy showed distinct diffuse hepatic fibrosis such as occasionally follows infective hepatitis in adults. In the absence of any other aetiological factor Dible et al. conclude that these 2 cases may represent the sequelae to the acute type of disease seen in the 4 previous cases.

It seems unlikely that the virus of ordinary infective hepatitis is responsible for in-utero infection, for there is no evidence that infective hepatitis in the mother is transmitted to the foetus. On the other hand, Stokes et al.² have reported the case of a woman, subsequently shown to be a carrier of an icterogenic virus, whose infant developed jaundice at four months and died with hepatic cirrhosis at eighteen months. In view of the frequency of icterogenic virus in blood-plasma, the rarity of in-utero infection implies either a considerable resistance to transplacental transmission of the virus or a simultaneous transmission of antibodies. Possibly neither type of infective-hepatitis virus is responsible, but some other agent such as herpes virus.³ Virological studies in further cases should answer this very important question.

VASCULAR INJURIES IN WAR

It has long been known that primary ligation of major peripheral arteries gives poor results. In the 1939-45 war the results were possibly worse than those previously reported,⁴ and DeBakey and Simeone⁵ found that of 2471 patients with arterial wounds only 135 had been treated by primary repair and reconstitution of the damaged artery. Since division of "critical" arteries (axillary, brachial, femoral, and popliteal) so often leads to loss of limb or life, it is understandable that a more active policy of arterial repair was initiated by the American medical services in the Korean conflict. Some encouraging preliminary reports are now appearing.

The interval between wounding and arrival at the surgical centre is vitally important; and in Korea evacuation by helicopter reduced the average interval below the critical level of ten hours. Ziperman⁶ notes a definite correlation between lack of vascular-surgical experience and amputation-rate; this was so evident that a special centre for the teaching and practice of vascular surgery was established in Korea. Ziperman reviews 218 peripheral vascular injuries, of which 162 involved "critical" arteries. In 132 cases the arterial wounds were repaired by end-to-end anastomosis, arteriorrhaphy, and vein grafting. The outstanding feature is the proportion of extremities lost—20% in the whole Korean series, compared with 40% in a 1939-45 series.⁵ Results were especially impressive in partial arterial tears which after debridement can be repaired by eversion sutures. Longitudinal closure of a defect may be followed by such narrowing of the lumen that thrombosis ensues.⁷ Moore et al.⁸ emphasise that damage of the intima always much exceeds that of the adventitia, and conclude that resection of the entire length of the injured vessel followed

by end-to-end anastomosis gives the most satisfactory results with the least disturbance of blood-flow. Where the severed ends of the artery cannot be safely approximated a free vein graft seems to be the best method; the place of preserved arterial grafts has not been fully determined. The use of 'Vitallium' tubes and other prostheses has apparently been abandoned. Ziperman strongly advises against ligation of the concomitant undamaged vein—a point which most surgeons would endorse.

LUPUS FROM B.C.G.

LUPUS vulgaris usually starts with the implantation of tubercle bacilli from an external source. In children it may develop from a primary tuberculous sore. In adults, who have probably already done battle with the tubercle bacillus in the lungs or bowel, bacilli implanted in the skin more commonly give rise to a different kind of lesion—verrucous skin tuberculosis. This suggests to Dowling and Wetherley-Mein¹ that the type of immunity derived from primary infection of the skin differs from that derived from extracutaneous foci. The bacillus recovered from the lesion of lupus is of low virulence, and such strains are rarely found in tuberculosis in other systems,² so it seems probable that the organism is attenuated in the skin itself; once lupus is initiated, the attenuated strain is of sufficient virulence to maintain the characteristically chronic process.

Jensen³ predicted the production of lupus vulgaris by the intentional inoculation of artificially attenuated tubercle bacilli—i.e., B.C.G. Lomholt⁴ first reported such a case. Ustvedt⁵ thought that the lupus must have arisen through superinfection, but Tolderlund⁶ considered that the bacillus recovered from this case was indistinguishable from B.C.G. 2 further cases of lupus following B.C.G. vaccination were reported^{7,8} but without bacteriological proof of the causal organism. Marcussen⁹ has now described 3 cases, in 2 of which there was good clinical and bacteriological evidence that the lupus was not due to superinfection. In all 3 cases the lesion spread from the site of B.C.G. vaccination, and in 1 it had persisted for three years. All 3 patients were tuberculin-negative before vaccination. 2 had no known tuberculous contact, and a tubercle bacillus recovered from their lesions proved identical with B.C.G. in cultural behaviour and pathogenicity.

In B.C.G.-vaccinated patients who subsequently develop tuberculosis of organs other than the skin, it is usual to find tubercle bacilli of high virulence; and such cases are attributed to fresh infection. The close similarity of the bacillus of lupus to B.C.G. makes this attribution less convincing in cases of skin tubercle. If, however, the laboratory criteria for their separation are valid, B.C.G. vaccination can probably give rise to progressive infection of the skin for at least several years. It has long been known that B.C.G. can survive in the tissues for up to eighteen months, and a case of tuberculous lymphadenitis attributed to B.C.G. was diagnosed three years after vaccination.

Marcussen raises the question of variation in the potency of the vaccine. If this were a material factor, one might have expected many more cases of lupus. Also, the accidental injection of enormous doses of B.C.G. has not provoked long-standing local infection. Variation in the host's response is a more probable explanation of these rare cases. It may be significant that one of Marcussen's cases was inoculated four times before

2. Stokes, J. jun., Wolman, I. J., Blanchard, M. C., Farquhar, J. D. *Amer. J. Dis. Child.* 1951, 82, 213.
3. France, N. E., Wilmers, M. J. *Lancet*, 1953, i, 1181.
4. Browne, J. J. M. *Brit. J. Surg.* war suppl. no. 2, 1948, p. 354.
5. DeBakey, M. E., Simeone, F. A. *Ann. Surg.* 1946, 123, 534.
6. Ziperman, H. H. *Ibid.* 1954, 139, 1.
7. Maybury, B. C. *Brit. med. Bull.* 1944, 2, 142.
8. Moore, H. G. jun., Nyhus, L. M., Kanar, E. A., Harkins, H. N. *Surg. Gynec. Obstet.* 1954, 98, 129.
1. Dowling, G. B., Wetherley-Mein, G. In *Modern Trends in Dermatology*. Edited by R. M. B. MacKenna. London, 1954.
2. Griffith, A. S. *Lancet*, 1916, i, 721.
3. Jensen, K. A. Cited by Marcussen (footnote 9).
4. Lomholt, S. *Acta tuberc scand.* 1946, 20, 136.
5. Ustvedt, H. J. In *Modern Practice in Tuberculosis*. Edited by T. Holmes Sellors and J. L. Livingstone. London, 1952.
6. Tolderlund, K. Cited by Marcussen (footnote 9).
7. Kalkhoff, K. W. *Hautarzt*, 1950, 1, 366.
8. Gilje, O. *Acta derm.-venereol.*, Stockholm, 1952, 32, 51.
9. Marcussen, P. V. *Brit. J. Derm.* 1954, 66, 121.

lasting skin positivity was obtained. Marcusen points out that these exceptional cases, which readily respond to treatment, do not affect the value of B.C.G. as a prophylactic measure.

PULMONARY TUBEROUS SCLEROSIS

PATIENTS with tuberous sclerosis usually come under medical care because of mental defect or epileptic fits resulting from cerebral damage. These symptoms generally appear in infancy, and the diagnosis can be made with confidence if the characteristic skin lesions—adenoma sebaceum or *peau chagrinée*—are present. Subungual fibromas are also peculiar to tuberous sclerosis,¹ and may be accompanied by brittleness and longitudinal ridging of the nails. Sometimes retinal tumours (phakomas) may be observed,² and tumours of the kidneys are not uncommon.³ These features are well recognised, and the hereditary nature of the disease was established by Kirpicznik⁴ as long ago as 1910. Much less is known about the pulmonary manifestations. Berg and Vejlens⁵ first described these in 1939; but only a few examples have since come to light, and it was not until 1949 that a case in this country was first reported.⁶ Dawson⁷ has now added 4 cases to the 9 previously recorded.

The presenting symptom of pulmonary tuberous sclerosis is usually breathlessness due to pulmonary insufficiency or to spontaneous pneumothorax—a common complication. Haemoptysis may occur, but cough and sputum are usually absent since infection of the lungs is only an occasional terminal event. Respiratory symptoms do not usually appear until the third decade, but they may be the cause of the patient seeking medical advice. In tuberous sclerosis sex-distribution is equal, but the pulmonary form affects women more commonly than men. Unless spontaneous pneumothorax is present, physical examination of the chest is not informative. Clubbing of the fingers has not been observed—a negative finding that may be of some diagnostic help. The typical radiographic appearance is of a network of lines throughout both lung fields, giving a miliary, reticular, or honeycomb effect. Death, from pulmonary insufficiency, spontaneous pneumothorax, or congestive heart-failure, ensues on an average about five years after the onset of symptoms. Typically, the lungs are riddled with cysts varying in size from a pinhead to a pea, and those lying just under the pleura produce small elevations of its surface. Vejlens⁸ found no special relationship between the cysts and the bronchial tree, although some communicated with the finer bronchi. The cysts are set in a firm matrix of new tissue which more or less replaces the normal lung and is composed of smooth-muscle fibres, fibrous tissue, and blood-vessels. The smooth-muscle fibres are usually the predominant element—and a feature of so few other conditions that their presence strongly suggests the diagnosis. The vascularity of the new tissue may help to account for the large amount of iron pigment commonly found in the lungs, and for the small haemoptyses which sometimes occur. The stimulus causing the normal lung elements to hypertrophy in this way is unknown.

Confronted with a clinical and radiographic picture which suggests pulmonary tuberous sclerosis, the clinician will seek confirmation of the diagnosis in other systems. Curiously, gross mental defect and epileptic fits are seldom associated with lung involvement; Dawson, for example, discovered only 1 instance of the pulmonary form in 64 fully investigated cases with

mental symptoms. The presence of adenoma sebaceum, *peau chagrinée*, subungual fibromas, or retinal phakomas may give a clue to the diagnosis; and physical examination or excretion urography may disclose irregularities in the shape of the kidneys suggesting renal tumours. Rhabdomyomas of the heart are sometimes associated with tuberous sclerosis.⁹ Radiography of the skull may reveal thickening of the bones or areas of increased density,¹⁰ and calcification of patches of "sclerosis" in the brain may show as "cotton balls."¹¹ Nodular periosteal thickening and cyst-like spaces may be seen in radiographs of the limb bones.¹² Rarely only the respiratory system may be obviously affected; Licht¹³ and Borberg¹⁴ have each reported 1 such case, and Dawson⁷ considers that 6 reported cases of diffuse cystic lung disease may also have been of this nature. Here a family history of tuberous sclerosis, the clinical features, and possibly lung biopsy may aid differentiation from other conditions with a similar radiographic picture, such as inhalation fibrosis, miliary tuberculosis, sarcoidosis, lymphangitis carcinomatosa, scleroderma, cystic bronchiectasis, bronchiolectasis, chronic bronchiolitis, diffuse pulmonary fibrosis of unknown origin, and the group of diseases described by Thannhauser¹⁵ as the "generalised eosinophilic granulomas."

A further possible diagnostic difficulty has been uncovered by Dawson,⁷ who has shown that abnormalities in the chest radiograph may be localised as well as generalised. In one of his cases with various stigmata of tuberous sclerosis chest films showed only a lobulated opacity which was found from a biopsy specimen to be a mucin-secreting adenoma; as there were numerous tumours elsewhere in the body the lung lesion was regarded, like these, as an expression of the underlying disease. The first radiographs of another case showed only infiltration in the left upper lobe, although the typical generalised pattern appeared in subsequent films; and Dawson points out that Paliard et al.¹⁶ previously reported a case in which radiography showed opacities confined to the upper lobes.

More information about pulmonary tuberous sclerosis would be welcome, and the interest aroused by Dawson's paper may result in the recognition of more examples of the condition.

PENICILLIN IN DIPHTHERIA

DIPHTHERIA has become uncommon in this country and in the U.S.A., so experience of treatment with penicillin is very limited. It has been used only in combination with antitoxin, and this combination has been found to have little if any advantage over antitoxin alone in saving life and reducing complications.¹⁷⁻²⁰ Cruickshank et al.²¹ found that a dosage of 40,000 units of penicillin four-hourly, combined with antitoxin, shortened the duration of carriage of *Corynebacterium diphtheriae* in acute faecal diphtheria, but they did not comment on the influence of penicillin on the clinical course of the disease. There are likely to be few opportunities in this country of confirming or refuting the finding, by Calvet and Herrera,²² that penicillin alone in large dosage (500,000 units six-hourly) is superior to antitoxin alone in the treatment of faecal and laryngeal

1. Kothe, R. *Arch. Derm. Syph.*, Wien. 1904, 68, 33, 359.
2. van den Hoeve, J. v. Graefes Arch. Ophthalmol. 1921, 105, 880.
3. Bielschowsky, M., Gallus. *J. Psychol. Neurol.*, Lpz. 1913, 20; Ergänz. 1, 1.
4. Kirpicznik. *J. Virchows Arch.* 1910, 202, 358.
5. Berg, G., Vejlens, G. *Acta paediat.*, Stockh. 1939, 26, 16.
6. Oswald, N., Parkinson, T. *Quart. J. Med.* 1949, 18, 1.
7. Dawson, J. *Ibid.* 1954, 23, 113.
8. Vejlens, G. *Acta path. microbiol. scand.* 1941, 18, 317.
9. Farber, S. *Amer. J. Path.* 1931, 7, 105.
10. Dalsgaard-Nielsen, T. *Nord. med. Tidskr.* 1935, 10, 1541.
11. Marcus, H. *Svenska Läk. Sällsk. Förs.* 1924, 358.
12. Gottlieb, J. S., Lavine, G. R. *Arch. Neurol. Psychiat.*, Chicago, 1935, 33, 379.
13. Licht, E. de F. *Acta radiol.*, Stockh. 1942, 23, 151.
14. Borberg, A. *Clinical and Genetic Investigations into Tuberous Sclerosis and Recklinghausen's Neurofibromatosis.* Copenhagen, 1951.
15. Thannhauser, S. J. *Lipidoses*. New York, 1950.
16. Paliard, Plauchu, Galy, and Papillon. *Pournon*, 1946, 2, 205.
17. Dodds, R. J. *Brit. med. J.* 1946, ii, 8.
18. Karelitz, S., Wassermann, L. R., Moloshok, R. *J. Pediat.* 1947, 30, 18.
19. Weinstein, L. *Amer. J. med. Sci.* 1947, 213, 318.
20. Bruyn, H. B., Brainerd, H., Leppila, B. W. *Ibid.* 1950, 219, 408.
21. *Lancet*, 1948, ii, 517.
22. Calvet, J. R., Herrera, R. G. *Bol. Coll. mdd. Habana*, 1953, 4, 501.

diphtheria and decidedly superior to the combination of large doses of penicillin with antitoxin. Several workers were surprised to find that the combination of sulphonamides and serum in the treatment of meningo-coccal infections was less satisfactory than sulphonamides alone.^{23 24} But in a disease such as diphtheria, where the severest complications and deaths are believed to be due mainly to a well-defined exotoxin, it is difficult to understand why antitoxin should have an unfavourable effect when combined with penicillin in the treatment of the acute phase.

CONVALESCENT HOMES

THE almoners, to whom falls the unenviable task of finding appropriate quarters for those needing either a restful convalescence or a recuperative holiday, have drawn up, for the Ministry of Health, a short report on the difficulties they encounter. Most of the difficulties, the almoners think, are new ones. Before the war the needs of patients convalescent from illness were supplied by the existing convalescent homes, some of which were run as private enterprises while others were sponsored by benevolent or contributory societies. Though some of these offered accommodation which by present standards was rather poor, most of them had a kindly matron, and supplied a moderate degree of comfort. Since the end of the war, the almoners find, the situation has altered radically. For one thing, thanks to modern chemotherapy, patients are nowadays usually ready for discharge from hospital much earlier in convalescence than they used to be : but the shortening of their illnesses is not necessarily matched by a shortening of the recovery period. Thus patients discharged from hospital may need more care than most convalescent homes are equipped to give, or than they can receive in their own homes. Discharge is also expedited by the pressure on hospital beds. Moreover, the improvement in hospital standards has led patients discharged to convalescent homes to expect the beds and food there to be at least as good as those they have just left ; and sometimes they are disappointed. Homes taking patients from London hospitals largely escape this last criticism—thanks to the contributions King Edward's Hospital Fund have made towards raising standards in them.

In one respect the situation is better than it was before the war : there are now some "rehabilitation homes" which aim at getting the patient fit and back to work by means of a planned convalescence. These homes are few, however, and severely restrict the types of patient they admit. Thus the Newcastle region has two rehabilitation centres for miners, the Manchester region has one centre for miners and another for dockers, and the Liverpool region has a centre for merchant seamen. While these groups are relatively favoured, there are others for whom it is difficult to get any convalescent care at all: for, though most of the homes in the National Health Service give simple treatments, most of them are not willing to accept heart cases, colostomy cases, cases requiring special diets (such as diabetic and gastric cases), tiresome skin cases, cases of non-infectious tuberculosis complicated by other diseases, severe rheumatic cases, and even mothers with babies. Yet these are the very people most likely to find the return home difficult.

Another complication derives from the laudable intention of the National Health Service to provide recuperative holidays for those who need them. The Act makes the provision of such holidays permissive, not obligatory ; and some local authorities have not so far used their powers to provide them. The line between patients needing convalescence and those needing recuperative holidays is by no means always clear, and the almoners say that where local authorities do not provide recuperative holidays "a large number of patients

join the queue for convalescence." In other areas the borderline patient is classed as "convalescent" or "recuperative" according to the state of the waiting-lists. Moreover, there is often nothing to mark the difference between a home taking convalescents, paid for by the regional hospital board, and a home taking recuperative-holiday-makers sent by a local authority ; and many homes take both.

A small survey made by the Institute of Almoners, in 1952, showed that of 2377 patients sent, on a hospital's recommendation, either for convalescence or recuperation, 61% went to National Health Service beds or contractual beds in independent homes, 18% went to recuperative beds, and 16% to beds in private homes ; 5% did not report where they went. Nearly 45% were admitted to a home as soon as they were ready to go or within a week ; and nearly three-quarters were accommodated within a fortnight. When a patient had to wait longer than this it was usually because he had some condition which made it important that he should go to a particular place. Reports from almoners working in the various regions show that "a surprisingly high proportion" of patients are admitted to homes within a few days of being regarded as fit to leave the hospital ward : "What the returns do not show, however, is the amount this has cost in almoners' time and in telephone calls." An absurd hindrance is created by the custom, current in most convalescent homes, of admitting patients on one day of the week only. If a patient's progress in the ward is not as good as might be expected, a booking may have to be cancelled at the last moment, which is annoying for those running the homes. A second admission day in the week would get over this difficulty in many cases.

Some evidence collected from almoners in the regions, set out in the report, suggests that patients living in country districts usually pursue their convalescence in their own homes. Patients from industrial areas are those who particularly need a change of scene. There should be no need, however, for them to travel great distances. At the moment convalescent patients, and particularly children, are apt to shoot about the island in an unsettling general post. Moreover, the idea that children need to be visited has not yet penetrated to convalescent homes : it is sometimes not the distance which keeps a mother away from the convalescent child, but the matron. The almoners say that more facilities for treatment are needed in convalescent homes for children, and more homes are needed for particular groups of children ; but they also think we should have a more accurate idea of the number of convalescent beds required—both for children and adults. They suggest that the homes should be classified more sensibly, so that patients having a difficult convalescence would be in a different place from people who need only a change of air before going back to work. There are enough convalescent beds in the country, they believe, to make this possible. Meanwhile, we might aim at higher standards of care in many of the existing homes. The almoners do not suggest that kindly matrons are getting scarcer ; but the comments of patients suggest that there are at least some tartars about nowadays.

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Special Articles

PREOPERATIVE ANÆSTHETIC OUTPATIENT CLINIC ANALYSIS OF 500 CASES

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A PREOPERATIVE anæsthetic outpatient clinic was first suggested by Lee (1949), and such a clinic has been held in this hospital since 1950.

The clinic has been held one afternoon a week except when annual leave or illness has prevented it. The patients seen were all the patients on the surgical waiting-lists and aged more than 40, all those who were to undergo major surgery irrespective of their age, and all those referred to us by the surgeons before they were placed on a waiting-list.

Routine

The surgical notes are read and a history is taken from the patient, who is already undressed to the waist and in a dressing-gown. The history includes present and past health, previous operations and anæsthetics, and previous blood-transfusions. While this is being written down on a form, suitably headed and divided to prevent too much writing, the clinic nurse weighs the patient, estimates his vital capacity, measures his ability to hold his breath by Sebranez's test, and measures his chest expansion. The patient is then examined, reassured, given advice on smoking, dieting, &c., and, if necessary, referred to other departments in the hospital. After all this has been noted, a prognosis, which may only be preliminary, is made, and the anæsthetic form is put into the surgical notes and shown to the surgeon concerned at his next visit to the hospital.

Analysis

Of the 500 patients included in this analysis 226 were males and 274 were females. In 8 cases an operation proved unnecessary; these were all orthopaedic cases—e.g., bursæ which had disappeared. In 10 cases the patient refused operation and examination; the suggested operations were all relatively minor—e.g., for tonsils in adults, hernia, and hallux valgus. The patients were referred back to their surgeons.

Age-groups

The numbers of cases in the different decades were as follows:

Years	20-29	30-39	40-49	50-59	60-69	70-79	80 or more
Cases	4	50	168	162	75	20	3

Proposed Operations

General surgical operations numbered 177, including total gastrectomy (3), partial gastrectomy (54), cholecystectomy (16), and prostatectomy (17).

Ear, nose, and throat operations numbered 122, including radical mastoidectomy (11), and submucous resection of nasal septum (65).

Gynaecological operations numbered 124, including total hysterectomy (19), vaginal hysterectomy (8), Mayo's vaginal hysterectomy (9), and repair of pelvic floor (69).

Orthopaedic operations numbered 59, including laminectomy (1), and Judet's arthroplasty (1).

Results of Examination

318 patients were considered fit for anæsthesia for the proposed operation, 22 were considered unfit for any form of anæsthesia for the proposed operation, and 142 were considered fit for some suitable form of anæsthesia following investigation and treatment.

The 22 patients considered unfit are analysed as follows:

For *prostatectomy*: 4 patients, of whom 2 had right-sided heart-failure (1 was immediately admitted to hospital), 1 was in uremia (arrived in the clinic on a stretcher and was immediately admitted to hospital), and 1 had just recovered from severe coronary thrombosis. These 4 patients underwent suprapubic cystotomy under local anaesthesia.

For *repair of the pelvic floor*: 6 women, all with various types of heart-failure. They were treated by the gynaecologist satisfactorily by the use of a ring pessary.

For *total hysterectomy*: 2 women, both with failing hearts. An artificial menopause was induced with radium.

For *vaginal hysterectomy*: 1 woman, with severe bronchiectasis. Her menorrhagia was stopped by dilating and curetting.

For *repair of hernia*: 3 cases (2 epigastric, 1 inguinal). These patients had such severe chronic bronchitis that a post-operative chest complication with breaking down of repair seemed almost inevitable. They were treated by the use of a suitable belt or truss.

For *minor orthopaedic operations*: 5 patients, 4 with mild heart-failure, and 1 with frequent anginal attacks. They were referred to the surgeon, who considered that operation was not vital.

For *partial gastrectomy*: 1 patient, aged 69, with chronic bronchitis and emphysema, and a duodenal ulcer. This patient was transferred to a physician for treatment.

Preoperative Investigation and Treatment and Type of Anæsthesia

13 patients (9 with cardiac lesions, 2 diabetics, and 2 with neurological disorders) were referred to physicians.

8 patients (6 with bronchiectasis, and 2 with pulmonary tuberculosis) were referred to the chest physician.

29 patients with dental sepsis were referred to the dental surgeon, and 10 edentulous patients for dentures.

4 patients with gross upper respiratory infection were referred to the ear, nose, and throat surgeon.

2 patients with thoracic-inlet syndromes needing urgent treatment were referred to the orthopaedic surgeon.

22 patients were treated for anaemia (1 with Hb 40% was admitted immediately).

11 patients were treated for mild heart-failure: 1 was immediately admitted to hospital, and all the rest were advised to have at least a week's rest in bed before operation.

In the case of 2 pregnant women coming for tonsillectomy, operation was postponed until after delivery.

35 patients were referred to the physiotherapist for special breathing-exercises, and 7 for postural drainage for at least three days preoperatively.

In 22 cases the operation was postponed until the summer.

9 patients were considered fit for local anaesthesia alone.

A patient who refused to submit to general anaesthesia had a submucous resection done under local anaesthesia.

In 9 cases spinal anaesthesia was advised.

8 patients were considered unfit for a relaxant drug if general anaesthesia was given: 6 of them had asthma, and 2 were thought to have myasthenia gravis.

Medical Conditions Found

Cardiovascular disorders included the following:

(1) Hypertension: raised diastolic blood-pressure was found in 106 cases. The range of diastolic pressures was as follows:

mm. Hg	100-109	110-119	120-129	130-139	140-149	150 or more
No. of cases	59	27	14	2	3	1

Of these patients 49 had no referable signs or symptoms save for, possibly, loud second aortic sounds; 47 had referable signs and symptoms; and 10 were in actual heart-failure.

(2) Previous coronary thrombosis: 3 cases were proved by electrocardiography, and 1 case was indefinite.

(3) Angina of effort: 4 cases.

(4) Mitral stenosis: 10 cases, of which 5 were well compensated, 4 were in early failure, and 1 was in definite failure.

(5) Heart-failure from other causes: 3 cases.

Respiratory disorders were present in many patients, especially in winter, as follows:

- (1) Chronic bronchitis was diagnosed in 42 cases.
- (2) Bronchiectasis was present in 7 (already seen by or verified by the chest physician).
- (3) Old quiescent pulmonary tuberculosis was present in 3 (verified by radiography and by the chest physician).
- (4) Finger-clubbing was observed to be gross in 6 cases and early in 4.
- (5) Calcified old pleural effusion was found in 1 case.
- (6) True asthmatics numbered 6.

Other conditions included the following:

- (1) Carcinoma of breast: 1 case (proposed operation cholecystectomy).
- (2) Thoracic inlet syndrome: 2 cases.
- (3) Suspected myasthenia gravis: 2 cases.
- (4) Superficial radial arteries in position likely to be mistaken for a vein: 2 cases.
- (5) Pregnancy: 2 cases.

Results of Investigations

Although *breath-holding and vital-capacity* tests were done on most of the patients the results were very often at complete variance with the patient's clinical condition, as in the following cases:

Case 1.—Proposed operation vaginal hysterectomy. Breath-holding more than 30 seconds, vital capacity 2300 c.cm., and Hb only 43%.

Case 2.—Proposed operation partial gastrectomy. Breath-holding 13 seconds and vital capacity 1900 c.cm. The operation was done with complete success.

Hæmoglobin was estimated in 67 cases. The estimation of Hb was asked for in all cases in which the patient was considered anaemic, and latterly, together with blood-groupings in all cases likely to need blood-transfusion owing to the severity of the operation. The range was as follows:

Hb %	40-49	50-59	60-69	70-79	80-89	90-99
No. of cases ..	3	5	7	17	21	14

Investigation for prolonged bleeding was undertaken in 3 cases where prolonged bleeding had followed extraction of teeth. The bleeding-times, coagulation-times, and blood-prothrombin level were normal. 2 of these patients had their operations satisfactorily. The 3rd patient underwent tonsillectomy and bled severely during the operation, but immediate stitching together of the anterior and posterior tonsillar pillars produced permanent haemostasis.

Chest radiography was done in 54 cases, with the following results:

	No. of cases
Nothing abnormal detected	32
Bronchitic type of chest (5)	Considered to be within normal limits
Bronchitic type of chest with emphysema (2)	8
Increased lung markings (1)	..
Bronchiectasis suspected	2
Enlarged heart	3
Enlarged heart with unfolding of aorta	3
Unfolding of aorta	2
Tuberculosis (considered quiescent)	3
Calcified pleural effusion	1

Comment

Many suitable patients were not seen in the clinic, because of the difficulty of giving them an appointment. For instance, nearly all patients with carcinoma were admitted as semi-emergencies, and there was no time for them to be seen in the clinic between their being seen by the surgeon and being admitted to the ward.

The full co-operation of the other departments of the hospital was obtained so that any investigations could be done the same afternoon and the patient need not come up to the hospital again.

Estimation of the respiratory and cardiac efficiency may well be more in correlation with the clinical condition if the machine described by Gaensler (1951) is

used instead of measuring the vital capacity and breath-holding. This machine measures not only the vital capacity but also the volume of air exhaled in a specified time.

ADVANTAGES OF THE CLINIC

To the Patient

To our surprise a great many patients are more frightened of the anaesthetic than of the operation. They are all greatly reassured at being examined, and investigated if necessary, and being passed fit before they come into hospital. In addition many have asked questions about the operation and its effects, and about the length of time they will be in hospital—questions which they have not had the opportunity of asking anyone else and have been worrying about. It has also been possible to comply with requests for admission on dates which suited the patient's domestic arrangements.

To the Surgeon

No criticism of the surgeons is implied by the number of patients found to be unfit for operation. In provincial hospitals, where junior medical staffing is difficult and surgical outpatient departments are crowded, the surgical teams cannot be expected to examine completely every patient put on the waiting-list. It is very pleasing for the surgeon to know that a patient coming to hospital for major surgery is considered fit to have the operation almost at once. This enables him to plan his beds and operating-lists with greater certainty.

To the Hospital

The number of beds available is increased by having the investigations and some of the treatment done in the outpatient department.

To the Anaesthetist

Simpson (1949) has stated that it is the anaesthetist's duty to examine personally each patient to whom he is going to give an anaesthetic. It is very convenient to examine the more serious cases on an afternoon set aside for this purpose, and not to have to rush into a ward at the end of a busy day. It is easier to discuss a case with the surgeon while the case is on the waiting-list than to inform him that some patients on his operating-list of the following day are unfit to have an anaesthetic.

DISADVANTAGES OF THE CLINIC

If a patient remains on the waiting-list for a long time after having been seen in the pre-anæsthetic clinic, he must be completely examined again on admission because, especially in old people, the general health may have rapidly deteriorated.

We wish to acknowledge the great help we have received in running this clinic from all the medical, technical, and clerical staff at Peterborough Memorial Hospital.

REFERENCES

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JOINT CONSULTANTS COMMITTEE

At a meeting of this committee held on May 11 with Sir Russell Brain in the chair, much of its time was given to the problems of hospital junior staffing. The committee received representatives of the Hospital Junior Staffing Subcommittee of the Central Consultants and Specialists Committee which had studied a great deal of statistical information bearing on the subject furnished by the Ministry, and in the light of which it had prepared a comprehensive report. The subcommittee commented upon the weaknesses of the existing staffing structure, drawing particular attention to the fact that the development of the hospital services in recent years called for a demand upon medical man-power which could not easily be met solely by the system of short-term appointments.

Other factors suggested by the subcommittee as contributing towards the problem were compulsory National Service, the widening gulf between hospital work and other forms of medical practice, the lack of security, and the deterioration of promotion prospects in the non-teaching hospitals.

The proposals formulated by the subcommittee to meet the situation included the abandonment of the present rigid registrar training ladder, and the appointment of all hospital staff below the consultant, according to the needs of the hospital, within two broad salary ranges, rising to—or even overlapping—the lower end of the consultant scale. At the upper levels the subcommittee envisaged that there would be scope for part-time appointments, which could be combined with other work—e.g., general practice. The subcommittee also laid stress on the need to provide greater security for hospital staff below the level of consultant, including the prospect of a permanent career, and an improvement of the prospects of promotion through the non-teaching hospitals. After a lengthy discussion the proposals were referred to a subcommittee of the Joint Consultants Committee for further examination.

A report was also placed before the committee regarding the use of the S.H.M.O. grade in obstetrics and gynaecology. In 1950 the committee had agreed with the Ministry that this grade might be appropriate for certain appointments where obstetrics was practised alone. In the light of experience, however, the Royal College of Obstetricians and Gynaecologists now felt that at this level of responsibility, obstetrics and gynaecology should invariably be practised together, and accordingly it urged that the use of the grade should be discontinued in this specialty. The committee endorsed this view and decided to make representations to the Ministry accordingly.

Consideration was again given to questions affecting the retiring age and superannuation rights of psychiatrists classified as mental health officers, and the committee decided to seek further advice from the professional bodies representing these officers before discussing the matter with the Ministry.

During the course of the meeting a number of points arose which again emphasised the need to improve the medical advisory machinery of regional hospital boards, and the committee agreed once more to urge upon the Ministry the desirability of giving advice to regional boards on this subject as it had done in the case of boards of governors and hospital management committees.

Other subjects dealt with in a lengthy agenda included matters relating to the interpretation of the pay-bed regulations, study leave, the employment of hospital staff on pneumoconiosis panels, the loan of hospital records, and the investigation of complaints involving members of hospital medical staffs.

CENTRAL HEALTH SERVICES COUNCIL

The Minister of Health has appointed or reappointed the following doctors to the Central Health Services Council and standing advisory committees for the period ending March 31, 1957 :

Central Health Services Council.

Prof. R. V. Bradlaw, * O. M. Duthie, W. G. Masefield, * F. M. Rose, Sir Harry Platt, * J. G. Scadding.

Standing Advisory Committees

Medical.—K. Cowan, Sir William Gilliatt, H. Joules, W. G. Masefield, Sir Harry Platt; three vacancies.

Dental.—Prof. R. V. Bradlaw, J. A. Moody, T. G. Ward.

Ophthalmic.—* J. H. Doggart, R. A. Greeves.

Nursing.—A. Elliott.

Maternity and Midwifery.—Arnold Walker.

Mental Health.—E. J. M. Bowby, W. G. Masefield.

Tuberculosis.—Sir Harry Platt, * F. Ridehalgh, * G. W. H. Townsend.

Cancer and Radiotherapy.—Sir Harold Boldero, Sir Stanford Cade, C. E. Dukes, J. A. Stallworthy, C. J. L. Thurgar, Prof. R. M. Walker.

* New member.

SCOTTISH ADVISORY COMMITTEE ON MEDICAL RESEARCH

The Secretary of State for Scotland has made the following new appointments of doctors to his Advisory Committee on Medical Research :

Prof. R. W. B. Ellis, Prof. R. J. Kellar, Prof. R. B. Hunter, and Prof. W. M. Millar.

The chairman of the advisory committee is Sir Edward Appleton, F.R.S. Members are normally appointed for a term of four years.

GENERAL MEDICAL COUNCIL

SESSION MAY 25-26

The General Medical Council met on May 25 and 26, and its session was followed by the sittings of the Medical Disciplinary Committee.

Dr. H. GUY DAIN moved the adoption of the report of the Pharmacopoeia Committee, which was approved. Sales of the *British Pharmacopœia* 1953 totalled (at April 30) 28,980. The report from the British Pharmacopœia Commission, 1953-58, recommended that new monographs on important drugs and preparations for which official standards are not provided, together with additions and amendments to existing monographs, should be published towards the end of 1955 as an *Addendum*.

The council received the annual examination returns for 1953. Dr. R. M. F. PICKEN contrasted the custom in different medical schools regarding exemption from the premedical course and examination. The preclinical and premedical teachers in his school were against such exemptions. Their view was that it was a good thing for students to have a year at the university before beginning the vocational side of their studies. The PRESIDENT remarked that the number exempted from the premedical course by the Scottish universities was very small indeed. He drew attention to the percentages of passes in the final examinations in the University of Cambridge in 1953: medicine 74%, surgery 64%, midwifery 60%; and in the final examination as a whole 39%. The representative of Cambridge University said that students were now required to pass all parts at the same time. "It is a pretty high 'plough,'" the President remarked.

Prof. R. J. BROCKLEHURST introduced the report of the Special Committee on Visitation of Medical Schools and Examinations. This committee felt that it was desirable that a smaller body than the whole council should consider the reports on visits. Such a committee could also deal with the annual returns of examinations. This recommendation was agreed to and a committee was appointed.

Medical Disciplinary Committee

The committee began its session on May 26, under the chairmanship of the President. Several cases were postponed to a special extra session in July.

RESTORATIONS

The Registrar was directed to restore to the Register the names of Charles Locksley Bikitsha, Ram Kissoon Nandlal, and Jeremiah Joseph O'Sullivan. These applications for restoration were made under section 21 of the Medical Act, 1950, after disciplinary erasure.

CASES POSTPONED

Herbert Albert Kenneth Rowland, registered as of The Vicarage, Cleator, Cumberland, B.M. Oxfd (1945), was summoned on a charge of infamous conduct in a professional respect for obtaining payment in respect of prescriptions improperly and dishonestly and with intent to defraud the Cumberland Executive Council. Mr. E. B. McLellan, instructed by Messrs. Le Brasseur and Oakley, solicitors to the Medical Protection Society, sought an adjournment because Dr. Rowland was in the Transvaal and had only recently received the charges, which he wished to defend. The committee postponed consideration until July.

Mr. Leslie Scarman applied for a postponement in the case of *Arthur Wright Scott Webster*, registered as of Fair View, Marston Road, Nottingham, M.R.C.S. (1949), who was charged with having behaved improperly to, and committed adultery with, a married woman with whom he stood in professional relationship. Mr. Scarman explained that Dr. Webster had been represented by another firm of solicitors until May 24, when they withdrew from the case. Counsel had only received his own instructions that morning. The committee stood the case over until its session in July.

Archibald Luke Basham, registered as of 11, Trinity Road, Rayleigh, Essex, M.R.C.S. (1928), did not appear and was not represented. He was in February of this year sentenced to twelve months' imprisonment at Chelmsford Assizes for defrauding the Essex Executive Council over prescriptions. After letters from him to the council's solicitors had been read the Chairman said that to give Dr. Basham an opportunity to appear they would postpone consideration of the case until July.

The committee postponed judgment for one year last May in the case of *Thomas Leven*, registered as of 2, Beech Avenue, Irvine, Ayrshire, L.R.C.P.E. (1945), who had been admonished at Ayr Sheriff Court for procuring 567 grains of morphine sulphate. A letter was received from the physician-superintendent of Hawkhead Hospital, Glasgow, where Dr. Leven is now a patient, saying that it would be in his own best interest for the case to be postponed for the present, because of his condition. The committee postponed consideration until the November session.

Robert John Gordon Williams, registered as of Rockdale, Abersooch, Caernarvonshire, M.R.C.S. (1941), did not appear to answer a charge of having been convicted at Pwllheli in 1948 of driving a motor vehicle when under the influence of drink, and of another conviction at Pwllheli in 1953 for being in charge of a motor-car when under the influence of drink. Mr. G. J. K. Widgery, solicitor to the council, read a letter from the practitioner saying that he could not possibly arrange to be present and he could only beg the committee for their forgiveness. When the Chairman asked if the committee would proceed with the case, members said that it should be made clear to Dr. Williams that he must be present. The case was postponed until the sitting in July.

In November, 1952, judgment was postponed for one year on *Jonathan Shutt*, registered as of 230, Lower Deptford, London, S.E.8, M.R.C.S. (1925), who had been convicted of unlawfully taking and driving away a motor-car at Kingston on Hull in 1951. Dr. Shutt was not present in November, 1953, when the solicitor to the council stated that notice of inquiry addressed to his last known address had been returned with a statement that the practitioner's present whereabouts were unknown. The committee postponed their judgment until May, 1954. The practitioner was again not present, and Mr. Widgery said that they had been unable to serve him with the notice of inquiry. The committee agreed to postpone the case.

FORGED CERTIFICATES

Moreen Catherine O'Brien, registered as of Endfield Woodhouse, Sheffield, M.B. Sheff. (1950), was charged with infamous conduct in a professional respect in forging 17 medical certificates for National Insurance purposes which purported to relate to her and to have been issued by other registered medical practitioners and by means of the certificates improperly obtaining £20 10s. 5d.

Mr. Widgery explained that Dr. O'Brien had married and was now Dr. Willis, but her name remained on the Register as O'Brien. She had been charged at London Sessions in November, 1953, with forging 4 medical certificates. She pleaded guilty and asked for 13 other cases to be taken into consideration. She was discharged conditionally for twelve months and ordered to pay 30 guineas' cost.

The Chairman announced that the facts alleged had been proved to their satisfaction and were not insufficient to support a finding of infamous conduct in a professional respect. They regarded the facts with the gravest concern. They were unable to regard statements made on Dr. O'Brien's behalf as providing the slightest justification, but they had determined to postpone judgment for one year, until their meeting in May, 1955.

JUDGMENT FURTHER POSTPONED

Patrick Kennedy, registered as of 2A, Kingswood Road, Gillingham, Kent, L.R.C.P.I. (1926), appeared. Judgment against him was originally postponed for one year in 1951 after

convictions for drunkenness in 1949 and 1951. The Chairman announced that to give him a further opportunity of providing satisfactory evidence as to his conduct, judgment had been postponed until November.

JUDGMENT POSTPONED

Judgment was postponed for one year in the case of *Herbert Trevor Duke*, registered as of 7, Manchester Street, London, W.1, M.B. Lond. (1952).

ABORTION

William Arthur Chanmugan Nason, registered as of 75, Tottenham Lane, Hornsey, London, N.8, L.R.C.P.E. (1925), L.M.S. Ceylon M. Coll. (1918), admitted a conviction at the Central Criminal Court in November, 1953, of unlawfully using an instrument on four women with intent to procure their miscarriage. The Registrar was directed to erase from the Medical Register the name of William Arthur Chanmugan Nason. This is subject to an appeal being lodged within twenty-eight days.

NEGLECT OF DUTIES

William Frank Cruickshank, registered as of Westwood, Brechin, M.B. Glasg. (1935), appeared on a charge of infamous conduct in a professional respect in failing to attend at his surgery, failing to visit or treat certain patients, and neglecting for a considerable period his duties as a medical practitioner under the National Health Service and disregarding his personal responsibilities to patients whom he had accepted on his list. Dr. Cruickshank was also charged with having been convicted at Coventry on March 13, 1954, of being drunk and disorderly. Mr. John Hobson, instructed by the solicitor to the council, said that in 1948 Dr. Cruickshank applied to the Angus Executive Council for inclusion on the list of medical practitioners and was accepted. Between December, 1952, and February, 1953, Dr. Cruickshank's surgery was not being properly attended to. Patients were finding it impossible to obtain treatment there. They waited and nothing happened, or they found a notice on the door with the words "No Surgery" written on it. Mr. James Ritchie, clerk to the executive council, said that copies of letters of complaint received by the council had been sent to Dr. Cruickshank for his observations. He had never replied. The National Health Service, Scotland, Tribunal had ordered the removal of Dr. Cruickshank's name from the list of the executive council of the county of Angus and the lists of neighbouring councils.

The committee found the facts alleged against Dr. Cruickshank in regard to National Health Service patients proved to their satisfaction, and that the facts were not insufficient to support a finding of infamous conduct in a professional respect. The Chairman announced that the committee regarded with grave concern the facts and the conviction. After careful consideration of the evidence they had decided to postpone judgment for one year.

UNLAWFULLY PROCURING DRUGS

Ralph Martin Case, registered as of 71, Gillott Road, Edgbaston, Birmingham, 16, M.R.C.S. (1934), M.B. Birm. (1934), had been fined £50 and in default of payment ordered to be imprisoned for three months at Grantham on October 30, 1953, after pleading guilty to unlawfully procuring dangerous drugs. Dr. Case previously appeared before the General Medical Council in November, 1947, for two convictions under the Dangerous Drugs Acts in that year. He voluntarily undertook hospital treatment in 1953 and was receiving intensive psychiatric treatment.

The Chairman said that in the light of Dr. Case's previous record the committee regarded with the utmost concern his further conviction. To give him one further opportunity of overcoming his tendency to abuse of dangerous drugs, they had decided to postpone judgment for one year.

JUDGMENT FURTHER POSTPONED

Judgment had been postponed for one year, until the present session, in the case of *Patrick Aloysius Gallen*, M.B. Glasg. (1929), registered as of 355, Garscube Road, Glasgow, who had had convictions in 1940, 1946, and 1952 of driving while under the influence of drink and of driving without due care and attention. The committee determined to postpone judgment for a further period of one year.

NAME NOT ERASED

Patrick Laurence Lyons, registered as of Highland Lodge, Kilkelly, co. Mayo, L.A.H. Dubl. (1948), L.R.F.P.S. Glasg. (1948), appeared in May, 1953, after convictions in 1951 and 1952 involving drunkenness. Judgment was then postponed for one year. In view of testimony to his conduct, the Registrar was not directed to erase his name.

MOTORING OFFENCES

Graham George Robertson, registered as of 22, North Ridge, Bedlington, Northumberland, M.B. Edin. (1934), appeared on a charge of having been convicted at the magistrates' court, Whitley Bay, on March 4, 1954, of driving a motor-car while under the influence of drink and driving in a manner dangerous to the public. In May, 1946, his name was erased from the Register. It was restored in November, 1948. The committee postponed judgment for one year.

NAME ERASED

Hugh Ley Puxon Peregrine, registered as of The Orchards, Twyford, Winchester, M.R.C.S. (1915), admitted being fined £10 at Winchester magistrates' court after pleading guilty to sending an indecent written communication through the post.

Mr. N. Leigh Taylor, solicitor, of Messrs. Hemsons, who represented Dr. Peregrine in his private capacity, asked for his evidence to be taken in camera. He wished to call a doctor and read the report of another psychiatrist. Both had said that as part of the information on which their evidence was based was obtained from persons other than Dr. Peregrine, under the seal of professional confidence, they felt unable to give that evidence other than in camera. The Legal Assessor said that he proposed to advise the committee that if they thought it right there was no reason why the public should not be excluded. The press and members of the public, by direction of the committee, withdrew.

The committee directed that, by reason of the conviction, the Registrar should be directed to erase from the Register the name of *Hugh Ley Puxon Peregrine*. When Mr. Widgery said that the police had asked for the return of the letters put in as exhibits, the chairman pointed out that Dr. Peregrine had twenty-eight days in which to lodge an appeal against the committee's decision. The letters must remain during that period.

POSTPONED JUDGMENTS

Florence Joseph O'Driscoll, registered as of 8, Moss Lane, Orrell Park, Liverpool, 9, M.B. N.U.I. (1928), had had judgment postponed for one year in May, 1953, to give him one further opportunity of overcoming his tendency to drink to excess. The Registrar was not directed to erase his name.

Judgment had been postponed for one year in the case of *Joseph Henry Bentley*, registered as of Littlewick, Limpsfield, Surrey, I.M.S.S.A. Lond. (1935), following convictions under the Dangerous Drugs Regulations, 1937, and the Dangerous Drugs Act, 1951. The Registrar was not directed to erase Dr. Bentley's name.

DRUG OFFENCES

James Ross, registered as of the Public Health Department, Town Hall, Barnsley, M.B. Edin. (1943), admitted eight convictions at Southend-on-Sea magistrates' court on Oct. 23, 1953, for offences concerning dangerous drugs. The committee postponed judgment for one year.

JUDGMENT POSTPONED

Patrick Stephen Gerrard Cameron, registered as of 14, Kirton Park Terrace, North Shields, Northumberland, M.B. Aberd. (1918), appeared in respect of five convictions. The first was in 1929, when he was convicted of being drunk in charge of a motor-car; the last was in 1953, for driving when under the influence of drink and in a manner dangerous to the public. Judgment was postponed for one year.

Parliament

Shortage of House-officers

IN the House of Commons on May 28, Dr. A. D. D. BROUGHTON called attention to the shortage of resident medical staff in the smaller hospitals in remote areas and industrial districts. Applicants preferred posts in larger hospitals, where they gained a wider clinical experience. They were attracted to hospitals situated in the more pleasant parts of the country. Salaries for these appointments ranged from £425 to £525 a year from which £125 was deducted for residence. The work of these doctors was thus less profitable to them than that of a medical officer on National Service in the R.A.M.C., while an assistant in general practice might be paid £1000 a year or more.

He also believed that the increase in the actions for negligence brought against junior hospital staff was deterring newly qualified men and women from exposing themselves to the danger of such charges. In larger hospitals, where responsibility was shared and the work supervised by senior medical staff, the danger of legal action was considerably less. Was the Minister, he asked, prepared to allow the hospitals which had difficulty in obtaining junior medical staff to offer a higher rate of salary, as was done by the smaller hospitals before the flat rate of pay was introduced under the health service? Or would the Minister allow hospital beds to be used for patients under the care of general practitioners?

Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the over-all shortage of junior hospital staff had been reduced from 15% at December 31, 1952, to less than 10% at December 31, 1953. Thus in 1952 there were 7212 officers of the various grades, and in 1953 the number had risen to 7815. The establishment was 8499. But much of this improvement might be due to the pre-registration year. Universities selected the hospitals where this year should be taken, and in the main they included only the large regional hospitals and the teaching hospitals. The shortage was particularly felt at the smaller peripheral hospitals, especially those dealing with a narrow range of work such as infectious disease, tuberculosis, and mental

and orthopaedic work. The substantial increase in demand in the last few years was often due to the up-grading of the smaller local peripheral hospitals with additional specialties. Compulsory military service took away doctors who when they came back were married and not prepared to take resident hospital appointments. The Ministry, she continued, had no evidence that claims for damages arose more particularly in the peripheral hospitals than elsewhere.

The earlier grades of pay might compare less favourably with those in other spheres, or elsewhere in medicine, but it must be remembered that the houseman's first year particularly was a continuation of his training as a qualified doctor. The Ministry did not believe that it was practicable to increase the number of qualified doctors. At present about 2000 a year qualified. Medicine had to compete with the demands of other professions, and the capital cost of increasing the medical schools would be a real deterrent and cause delay. At present the number of probable vacancies in "career" posts appeared to be fairly well balanced in relation to the intake, which a little while ago was a source of great concern. It would be wrong to turn out qualified doctors in excess of those who could have a reasonable prospect of a satisfactory and secure career. The number of doctors called up could not be reduced.

The most hopeful line of dealing with the shortage, she suggested, was to encourage general practitioners to share in hospital work and to encourage men returning from National Service to work in hospitals for a period rather than to go straight into general practice.

At the start of the health service it was open to the Ministry to approve an additional payment of £50 a year for house-officer posts which were difficult to fill. But the method had not been found efficacious, since it tended to blacklist a hospital. The Ministry looked with considerable reserve on the idea of incentive pay for what should be a comparable job and also on any suggestion that posts should be graded above their true worth—for example, that house-officer posts should be treated as senior house-officer posts solely because they were difficult to fill.

The problem was difficult, but direction was an impossible solution. Doctors must have freedom of choice, within limits, of jobs offered to them. Yet the

Ministry must see that these difficult and in some ways less attractive hospitals were adequately staffed. The Minister would be only too happy to support anything which could be done to facilitate negotiations to meet the shortage either by the extended use of general-practitioner services or by other means.

Pharmacy Bill

In the House of Lords on May 25 the Pharmacy Bill, a consolidation measure, was read a second time.

QUESTION TIME

Diesel-engine Fumes and Cancer

Mr. L. W. B. TEELING asked the Minister of Transport and Civil Aviation if he was aware that there was evidence to suggest that diesel-oil fumes might be a cause of cancer, and that research into this problem was being conducted by the Medical Research Council; and if he would give a general direction to the British Transport Commission to defer the substitution of all their trolley-buses by diesel buses until such time as the M.R.C. had made their report.—Mr. A. T. LENNOX-BOYD replied: I am not prepared to interfere in the commission's commercial decisions except for reasons of overriding national importance. So far as I am aware, no such reasons exist in this case.

Evaporated Milk

Replying to Mr. SOMERVILLE HASTINGS, Major GWILYM LLOYD GEORGE, Minister of Food, said he understood that there was no loss of vitamin A or riboflavin in evaporated milk stored at room-temperature; and (as judged by investigations on sweetened condensed milk) no change in biological value of the proteins after one year and only very slight changes after two to five years.

Reablement of Epileptics

Replying to Mr. W. L. WYATT, Sir WALTER MONCKTON, Minister of Labour, said that epileptics were admitted in appropriate cases to the Ministry's industrial rehabilitation and vocational training courses and special efforts were made to find them employment. A leaflet (D.P.L.5) has been issued to facilitate their acceptance by employers and fellow-workers. Remploy Limited were employing over 400 epileptics.

Mr. HASTINGS: Will the Minister consult the Minister of Health to see if many of these epileptics can be employed in connection with hospital work, where people with whom they come in contact will be much less likely to be frightened by these comparatively harmless fits?—Sir WALTER MONCKTON: I will certainly bear that suggestion in mind.

Cost of Medical Education

Replying to Dr. A. D. D. BROUGHTON, Miss FLORENCE HORSBRUGH, Minister of Education, said that the number of students taking medical courses in the current academic year with Ministry of Education grants was 1948, of whom 1121 held State scholarships and 827 held awards under the further-education and training scheme. She estimated the cost in fees and maintenance for the year at approximately £574,000. In addition, the Ministry admitted for grant the expenditure of local education authorities on making awards to students taking medical courses.

Hospital Pay-beds in Scotland

Replying to Mr. WILLIAM HANNAN, Commander T. D. GALBRAITH said that in Scotland during the year ended March 31, 1953, the proportion of section-5 pay-beds that were unoccupied averaged less than a quarter of the total. There were 913 such beds— $1\frac{1}{2}$ % of all staffed beds.

National Service Medical Officers

Replying to Dr. BROUGHTON, Mr. ANTHONY HEAD, Secretary of State for War, said that a doctor joining the R.A.M.C. for the period of National Service was commissioned in the rank of lieutenant and got basic pay of £401 a year. After one year he was promoted captain and got £511 a year, and after a further six months £593 a year. He might get temporary promotion to the rank of major, and there were at present 20 National Service officers holding this rank. For this rank basic pay was £785 a year in the first eighteen months' service, and £912 a year in the last six months. In addition to basic pay, marriage allowance of £117 a year for an officer under 25 and of £228 a year if he was older, and specialist pay of £73 a year, were paid where appropriate.

Advertising for Applicants for R.A.M.C. Commissions

Replying further to Dr. BROUGHTON, Mr. HEAD said that up to last year advertising to invite applications for R.A.M.C. commissions was mainly for specialists, and the yearly cost was under £300. Last year just under £1000 was spent on special publicity for the new terms of service of officers of this corps.

Resident Medical Staff in Hospitals

Dr. BROUGHTON asked the Minister of Health the total number of resident medical officers in hospitals in England and Wales; and how far below the establishment figure this number had fallen.—Mr. IAIN MACLEOD replied: I regret that information in this form is not available; but at Dec. 31, 1953, there were in hospitals in England and Wales the whole-time equivalent of 7815 medical officers other than specialists and senior registrars, compared with an establishment on Dec. 5, 1952, of 8499.

Deaths of Disablement Pensioners

Replying to Mr. A. J. MCKIBBIN, Mr. OSBERT PEAKE, Minister of Pensions and National Insurance, said that the numbers of deaths for each year since 1945 of disablement pensioners of the first and second world wars, were as follows:

Year	1914 war	1939 war
1945	9026	3158
1946	9130	3769
1947	10,311	4524
1948	9519	4556
1949	10,471	4430
1950	10,388	3836
1951	12,280	3810
1952	10,766	3205
1953	12,084	3311

Medical Officers in Northern Nigeria

Replying to Mr. JOHN TILNEY, Mr. OLIVER LYTTELTON, Secretary of State for the Colonies, said that the establishment of medical officers for the Northern Region of Nigeria was 91 and there were at present 25 vacancies.

Mr. TILNEY: Will the Minister bear in mind the importance of seconding not only specialists but also general practitioners, and look into the matter of their salaries as compared with those paid in this country?—Mr. LYTTELTON: We regard this matter as one of considerable concern, and we are doing our very best to get these vacancies filled.

Public Health

The Minister on Health and Welfare Services

ADDRESSING the County Councils' Association in London on May 26, Mr. Iain Macleod, the Minister of Health, made a plea for the better use of the domiciliary services, to relieve pressure on hospitals. It was, he said, not only a question of cost. Many types of patient were better cared for in their own homes than in hospital—this applied particularly to many children and old people and to most maternity cases. Local health authorities should make sure that there were enough home nurses and home helps for all patients whose condition did not necessitate admission to hospital. He would like authorities to consult general practitioners in their areas, to find out the extent to which doctors felt compelled by the shortage of home nurses and home helps to send patients to hospital who might otherwise stay at home. No old person—no patient of any age—should be removed to a hospital or institution solely for lack of such care as a home help could give. Here, too, was a great field for voluntary work.

Turning to the prevention of illness, the Minister said that at present less than 31% of children under 1 year of age were being immunised against diphtheria, compared with a target of 75%. A slightly greater proportion of newborn infants were vaccinated against smallpox, but the target should be the vaccination of every healthy infant.

Mr. Macleod concluded: "The aim is to place at the disposal of the patient nursed at home the same kind of co-ordinated team working under unified medical direction as would care for him in hospital." Without encroaching on the administrative responsibilities of the medical officer of health or other local-authority officers, the clinical responsibilities of the general practitioner

should be recognised by all domiciliary workers, who should ascertain his views and be ready to work under his general clinical direction. It seemed that general practitioners as a whole knew hardly anything about the health visitor or about what she was capable of. The fault could not be all on one side. Not all social workers were yet ready to work with general practitioners, but it would be most valuable if in suitable areas trials could be made in linking specially selected social workers with local doctors.

Segregation of Poliomyelitis Contacts

In accordance with suggestions contained in the report of the W.H.O. Expert Committee on Poliomyelitis,¹ Dr. Hugh Morrison and Dr. Leo Fay, medical officers of health for Taunton rural district and borough, have put forward to their respective councils a scheme for strict quarantine measures to be applied to household contacts of the first one or two cases of poliomyelitis in their areas after a period of freedom from the disease. The basis for this scheme is that transmission is largely faecal, and that in the early stages of an epidemic infection is not widespread among the community, as was formerly believed, but is mainly limited to the patient and those in intimate contact with him. These close associates will be confined to their own house and garden, where this is found to be practicable, for three weeks, and arrangements will be made to carry out shopping and other routine domestic tasks on their behalf.

The population—mixed urban and rural—numbers about 60,000, and the medical officers of health feel that this is a suitable and reasonably large area in which to test the effectiveness of these measures. While realising that positive results may be difficult to demonstrate, they hope that in their districts there may be some decrease in the prevalence of poliomyelitis, which has been high in recent epidemics.

One of the councils has already agreed to this scheme. Participation will be voluntary, and loss of wages will be made good.²

A Mass-radiography Drive

Between Sept. 15 and Oct. 3, 1953, two mass miniature radiography (M.M.R.) units from the Scottish Western Regional Hospital Board took radiographs of 13,537 people in Greenock, representing about one-fifth of the city's population. The best response in any age-group was among young adult females, of whom 2445 (two-fifths) attended. A diagnosis of active pulmonary tuberculosis was made in 70 cases of all ages, and 93 more were thought to need further observation.

The response of the public was extremely satisfactory and one of the M.M.R. units, sited at the town hall, dealt with an average of 675 persons daily, and on two separate days with more than 1000 persons. Far more people would have been radiographed if the units had not had to leave to fulfil previous commitments.

The campaign was preceded and accompanied by publicity in the local press, by posters, cinema-shows, lectures and announcements in schools, churches, and public meetings. The Scottish Council for Health Education, the Scottish Information Office, the National Association for the Prevention of Tuberculosis, and the Corporation of Greenock actively coöperated in the campaign, which was launched at the suggestion of the Department of Health for Scotland.

The numbers radiographed by the M.M.R. units per working day were more than twice the normal average, and the results of the Greenock experiment are held to show that campaigns of this kind reach a larger proportion of the population than visits of M.M.R. units to factories, offices, and institutions. The decision to launch a national publicity campaign against tuberculosis in Scotland and to inaugurate a series of mass-radiography drives in selected areas has been reached largely as a result of the Greenock pilot experiment. According to a memorandum from the Department of Health for Scotland, six such drives, accompanied by intensive publicity, have been inaugurated this year in areas where the incidence of tuberculosis has been high or where the local health authority has shown a special interest.

1. See *Lancet*, May 29, 1954, p. 1121.

2. *Somerset County Herald*, May 22, 1954.

In England Now

A Running Commentary by Peripatetic Correspondents

WE leave Chelsea about 5.30 on the last afternoon, exultant, like an army with banners. From foolish virgins who have bought armfuls of wonderful but overblown tulips that will lose half their petals on the way home, to the cactus enthusiast clutching his grisly but genuine prize, none is empty-handed. Streaming up towards Sloane Square, we know that we are the salt of the earth: truly we think, as we envy this fat Cockney dame her spiraea, and that ex-R.A.F. type his clematis, all good men are gardeners, and all good gardeners buy things on the last day at Chelsea if they can.

On Sloane Square platform, diluted by the rush-hour crowd, a little of the afflatus ebbs, and as we manoeuvre our awkward burdens into full carriages we begin to fear that we are mere eccentric nuisances. I climb aboard my bus at Putney a last solitary straggler of that proud army. My fellow passengers try to avoid being caught staring at me. My adiantum has broken in the tube crush and, though the flowers of my dodecathlon still nod bravely over my shoulder, the wet wrapping of its roots is beginning to fall apart and leafmould is dribbling over my clean trousers. Long before I reach home I decide that the green bug that bites man is as destructive as the green fly that bites his roses. But most of the things I bought last year are still alive, and some even flowering. Next Friday-a-twelfemonth will certainly see me playing hookey from my microscope again.

* * *

It was the eleventh day. The whole hospital brooded under a pall of gloom: every man jack of us hung hourly upon the orifices of Mrs. S.'s ureters. Lunch in the mess was no exception: most of us were bravely concealing our burden behind a thin façade of badinage, though the registrar (he is married but it was a Monday) was rehearsing the details to a visitor. ". . . We decided to start her on a Bull (1949)¹ and things were going reasonably well until the seventh day when she began to vomit and we could not keep the tube down. As it happened that was the very day that that article on the infusion of 40% dextrose into the inferior vena cava came out in *The Lancet*.² So we thought we'd try that. But the blood urea went on rising and yesterday . . ."

Just at that moment the house-surgeon made his entry. Trying to appear calm, he took his seat. All eyes were fixed on him as he lifted his soup spoon. He addressed the ceiling: "Eleven ounces," he said. An electric silence. And almost before the storm of incredulous expletives had burst, the phone rang for the house-surgeon. After a moment he returned and resumed his seat, again the cynosure of all eyes. "That was Sister," he said, "Wants to know whether Mrs. S. is to go on ordinary or light diet."

* * *

She lived alone and had done so for three years since the death of her husband. She had one son but he did not live with her. She did all her own housework—baking, washing of clothes, cleaning—and it was not surprising that she had housewife's dermatitis, which is why I saw her. She was an enthusiastic gardener and grew all her own vegetables; she had cabbages, parsnips, beetroot, celery, parsley, and leeks; and of flowers she had carnations, gladioli, sweet-peas, nasturtiums, and roses. She did all her own digging in the garden, made the drills and the plots, and kept it free of weeds. She was indeed a remarkable woman, for she had been completely blind for eleven years.

* * *

"Worse than the membership," muttered the pale man next to me, puffing nervously at his third cigarette. A tubby, red-faced chap grinned reassuringly. "Never mind," he said, "Once you've been up for the fifteenth time, you'll take it all in your stride"; and he gave a great whoop of recognition as some old cronies came into the room. Two hours later, I was led to my first interview for a senior appointment. They were having their tea, and my tongue stuck enviously to the roof of

1. Bull, G. M., Joeckes, A. M., Lowe, K. G. *Lancet*, 1949, ii, 229.

2. Russell, C. S., Dewhurst, C. J., Brace, J. C. *Ibid*, May 1, 1954, p. 902.

my mouth. I smiled wanly, but the glum, detached faces did not flicker. No glittering prizes (raised eyebrows); no dazzling contributions to research (sidelong glances of disapproval); no feats of athletic prowess, no artistic or musical accomplishments (shaking of heads). The final blow was muffed by a mouthful of bun: "Then, what do you do at the weekends?" I blushed scarlet. And that was that.

It was almost worth it all to see the joy of the new consultant as he rushed off to telephone the little woman. The rest of us waited on. Perhaps someone would come and say "Thanks for coming so far; I wish we could have given you all the job," or something like that. But they must have forgotten. It was getting dark in the cold side-streets as we walked slowly to the station.

* * *

Why do ward sisters delight in transposing all the beds like a shuffled pack of cards? In the good old days it was enough for beds to be in geometrically straight lines with bed tables and lockers at right angles, wheels retracted through 180°, and flowers trimmed to a uniform height. Thus they remained, apart from placing the garrulous near the door with deaf or non-English-speaking neighbours. Now, however, patients have become pieces of furniture—to be rubbed, dusted, and moved around the ward. I believe this is all part of an organised conspiracy to undermine our conditioned reflexes—a mischievous plot to throw the ranks of the medical profession into Pavlovian confusion. No sooner do I begin to recognise Mrs. A in the third bed, with obesity and chronic bronchitis, than she is replaced by Mrs. B who has ulcerated legs but bears a striking resemblance to her predecessor. Any fresh acquaintance is doomed to short life because there is always a Mrs. C with gall-bladder trouble and like ample features to add to the confusion, and there are times when I suspect I have seen the same patient twice on one round. Then, adding insult to injury, the house-physician is blamed for getting the notes out of order.

* * *

I am condemned by my years and a heart that has lost much of its vigour to walk with shortened steps, to be careful not to slip or be bumped, and never to get out of breath. When there is the slightest suspicion of pain in my chest, I stop for a few moments, lean on my stick, and survey my somewhat compulsory surroundings. And I am continually seeing something new—something I must have passed scores of times without noticing. In a suburban stroll I watch the birds—starlings on their chimney pots, a kestrel hovering over the allotments, a group of sparrows squabbling on the road over a crust. I see that many houses are badly in need of paint, or that the curtains in some are overdue for washing or a visit to the cleaners. I notice, too, that older men and women have increased in numbers since my interest was aroused in this age-group—old women with tired legs and old men with wrinkled faces. When I pay a visit to the town, however, it is easier to halt and look around. As an excuse for standing, there are always shop windows with their displays of furniture, tobacco, fish, groceries, and all the countless other things in the romantic list of human needs. But I cannot always pick and choose where I stop, and the other day an old friend was surprised to find me gazing with rapt attention at a window of diaphanous nylons.

* * *

Indirect Nidoscopy.—Some weeks ago a kindly patient gave me three nesting-boxes which I carefully placed in what I considered strategic positions in the garden. They remained unoccupied, and hope had almost died when last evening I chanced to see a bluish-white flash near one of them. The problem was to confirm the diagnosis of blue-tit tenancy; for the box was solidly made, without hinge or opening other than a circular aperture of less than an inch diameter.—A hurried visit to the surgery, and there appeared in the laryngeal mirror, not the cords, but a tiny nest with eight eggs. Some time later another inspection revealed the inverted and surprised face of mother blue-tit, who hissed her disapproval of the encroachment of electric light into her comfortable home.

I think I shall ask a surgical friend to come ferreting, with his gastroscope. The home life of rabbits might be interesting.

Letters to the Editor

DAMAGES AND REFUSAL OF TREATMENT

SIR.—On May 21 the Court of Appeal dismissed an appeal for increased damages on the ground that the plaintiff had refused medical treatment. The *Times* report (May 22) states:

"On July 16, 1952, he fell into the hold of the ship and suffered only very minor physical injuries, but afterwards he developed a serious anxiety state from which he had not recovered.... When the nervous symptoms developed he was recommended to have treatment in the Rainhill Mental Hospital, Liverpool. He had then and subsequently refused to go into that hospital for electrical shock treatment. Mr. Justice Jones awarded damages based on the view that if it was the right thing for the plaintiff to have gone into the hospital and have the treatment recommended by all the medical opinion he must suffer the consequences of not having gone."

The *Times* reports the judgement on appeal as follows:

"Lord Justice Singleton said that . . . it was the duty of the court to say that if a man was recommended by his own medical advisors and others to undergo a course of treatment, he ought to undergo it, if he was advised there was a reasonable chance of recovery and the treatment was reasonable. He would dismiss the appeal."

"Lord Justice Denning said that viewed subjectively the man's attitude was quite understandable. He was an uneducated, ignorant man, who did not realise that a mental hospital nowadays was very different from what it was 30 or 40 years ago, and owing to his anxiety neurosis he was not in a fit state to make a reasonable decision. The difficult question was whether the Court was to admit that subjective condition of his as a reason for refusing medical treatment. He (his Lordship) thought not."

This judgment must give rise to serious doubts in the medical profession, particularly among those responsible for dealing with this sort of case.

Was the suggested treatment reasonable, and did it offer the patient the best chance of recovery?

The indications for E.C.T. are not generally agreed. Most authorities would regard it as a satisfactory and even life-saving procedure in severe endogenous depression, well worth the risk it entails. In anxiety states following an industrial accident, on the other hand, many, like ourselves, would regard it as definitely contra-indicated in favour of industrial rehabilitation, following an early settlement of the claim. From this standpoint, therefore, either the rejection of the appeal should have been based on a diagnosis of a depression, or (as is our opinion) the plaintiff was correct on strictly medical grounds in rejecting the treatment offered.

Is it expedient for clinical judgment to receive such strong backing from the law?

This question raises wider and more serious issues. E.C.T. requires the signature of a statutory consent form by the patient or his relatives. The consent form implies dangers, which have to be accepted by the patient or his relatives. The less widely known dangers of E.C.T. were referred to by Harvey Jackson,¹ writing on his experiences of leucotomy in patients suffering from long-term mental illness:

"Working on such material meant that one encountered some patients with quite gross atrophic changes in the brain. As no such shrinkage was related to mental disease, on the submission of the psychiatrists of the institution, it led me to seek an explanation in treatment. The more experience one has gained, the more does one feel that electro-convulsive therapy has been responsible for much atrophic change, possibly arising out of repeated diffuse petechial haemorrhages."

In future the acceptance of these and similar dangers will not be based on clinical considerations alone, but also on the knowledge that the law may penalise the

1. J. ment. Sci. 1954, 100, 62.

patient by withholding compensation, regardless of whether there is a general consensus of medical opinion as to the correctness of the treatment.

If this ruling were generally applied it could spread to other fields of medicine and seriously affect clinical practice. For instance, can a medical practitioner be found negligent, or as having shown inadequate professional skill, for having withheld a treatment such as this, which at least in theory can now be responsible for a patient losing a claim for compensation?

G. D. MORGAN
ELIZABETH TYLDEN.

London, W.2.

TEACHING-BEDS AT A REGIONAL HOSPITAL

SIR.—Last week you noted that King's College Hospital Medical School has agreed with the South East Metropolitan Regional Hospital Board to make use of clinical facilities at Dulwich Hospital for undergraduate teaching; and that the Minister of Health has agreed to a special grant for this purpose. This is good news.

Since the war it has been obvious to some of us who have been teachers at one or other of the medical schools and examiners at one or more of the finals that there are far too many medical students. In spite of planning, it would seem that this particular problem can only be adjusted by supply and demand.

On the other hand, since the introduction of the National Health Service the bulk of the good clinical material has been referred to the regional hospitals rather than to the teaching centres: some of the latter are comparatively starved in this respect. We cannot possibly object to this trend. A good doctor who has a good case at his disposal nowadays knows that the local hospital is well staffed by competent consultants; so he naturally sends his patient there instead of incurring a much longer journey to the Metropolis (under which heading I include the large provincial cities and university centres). In fact the patient may be seen and treated by the same consultant in either case.

It has become painfully obvious to many examiners in the final examinations that most candidates are almost entirely lacking in personal clinical experience, however good their book and blackboard teaching may have been.

Apart from the fact that I have worked in a regional hospital concurrently with teaching-hospital practice, it now falls to my lot to visit hospitals over a large area. There one finds, as a rule, unlimited clinical material well accommodated on the whole, good facilities, in being or pending, and a competent staff: but no students.

Lest my teaching-hospital friends and colleagues should think that I am underestimating their capabilities and their excellent influence, may I explain that I consider the patient to be almost as important as the teacher in clinical instruction!

This major problem will have to be tackled sooner or later: it will not solve itself; pre-registration house-appointments afford merely a partial solution. Undergraduate students will have to be farmed out. It means a lot of work for the deans and their staffs; but it is gratifying to know that a start has been made—although I have in view hospitals farther afield than Dulwich.

London, W.1.

FRANK COOK.

REMUNERATION OF HOSPITAL MEDICAL STAFF

SIR.—I have the greatest admiration for Sir Russell Brain and would hate him to think that the rank and file of consultants are not grateful to him for all his efforts on our behalf.

To my mind the great obstacle to his obtaining a satisfactory agreement with the Government has been their right to refuse arbitration. Here is another principle which would close the county courts and all others. Such an injustice must be removed, and that must be Sir Russell's next task if he will lead us again. On this

occasion he must be armed with greater power than before. The present dissatisfaction of the profession must be exploited to unite it (we could scarcely be less united than at present) and to place behind Sir Russell an organisation capable of threatening the resignation of all consultants unless justice is done and Spens implemented.

J. S. MAXWELL.
Hull.

SURGICAL TREATMENT OF ACUTE OSTEITIS IN CHILDHOOD

SIR.—The article by Mr. Bremner, Dr. Neligan, and Dr. Warrick (May 8) makes good reading. While I agree with the writers that their figures are too small to settle the question whether in the treatment of acute osteomyelitis the administration of penicillin should be accompanied by surgery or not, I consider theirs an excellent contribution both for the meticulous presentation of their work and the modesty of their claims. It is interesting that they end their report with a few words of caution for those who would follow their method, particularly as to the high standard of medical judgment required and the necessity of a daily reassessment of the problem. I think the whole question has been well summarised in your annotation of May 8 where our study¹ of the late results in a hundred cases of osteomyelitis treated surgically is favourably reviewed.

I prefer to avoid entering into a new dispute with Mr. Browne and Dr. Bodian (May 22). I am interested in their statement that they had never used early surgery because "it was hardly fair to the patients to use on them a method that we [the authors] were convinced was not the best available." For some of us to be convinced we must wait for the time when Mr. Browne and Dr. Bodian publish an objective analysis of their late results in a way similar to that followed by Mr. Bremner and his colleagues, and also by us. I have no courage to disillusion Mr. Browne and Dr. Bodian as to the reasons which made us terminate our discussion in 1947. I am pleased to read that Mr. Browne has for some years abandoned the repeated ordinary aspiration he recommended so strongly in 1947 and is now performing a thorough lavage under general anaesthesia with the use of several needles and the help of another surgeon. It is also reassuring that firm pressure over the part after lavage is now advised. Finally, I cannot but state my satisfaction on reading that the dosage of penicillin advised by the authors in 1947 (50,000 units daily for an average child of 7 years) is no longer recommended. What then would have been the purpose of continuing the discussion in 1947?

Nuffield Orthopaedic Centre,
Oxford.

J. TRUETA.

PERIPATETIC PRACTITIONERS

SIR.—The council of the Medical Defence Union is seriously disturbed at the number of its members—mainly recently qualified or temporarily registered practitioners—who fail to furnish an address at which they can be reached by postal communications.

This operates to their disadvantage in two ways: (1) they do not receive a copy of the annual report, containing useful advice on procedure to be followed in threatened or actual litigation associated with allegations of negligence; and (2) they do not receive communications advising them that they are in arrear with their subscriptions, whereby they cease to be entitled to the benefits of membership until payment of the arrears is made good.

With the present tidal wave of medical litigation, it behoves every practitioner to satisfy himself that he is not only a member of a reputable defence organisation, but a member "in benefit." That may be ensured by paying the annual subscription through a banker's order and checking by reference to his bank or bank statement that payment has been made at the due date. There is nothing more unfortunate

1. Trueta, J., Morgan, J. D. *Brit. J. Surg.* 1954, 41, 449.

than for a member to seek advice and legal representation, only to find that, through failure to pay his subscription, he is not entitled to any assistance.

On a further matter which has, perhaps, a similar cause: the attention of the council has been drawn to numerous members whose names have been deleted from the Medical Register owing to their failure to reply to communications addressed to them by the Registrar of the General Medical Council. It is of paramount importance that practitioners should give an address at or through which they can always be reached by telephone or letter.

Medical Defence Union,
Tavistock House South,
Tavistock Square, London, W.C.1.

ROBERT FORBES
Secretary.

DO REDHEADS BLEED EASILY ?

SIR.—I was interested and instructed by the report in your issue of May 22 (p. 1061) of Mr. Walker Ashcroft's paper to the Royal Society of Medicine. I should like to ask what is the evidence that red-haired females tend to bleed easily. It is a claim often made but I have been unable to find factual corroboration in the literature. Redheads are also alleged to be more susceptible to rheumatic fever.

A shock of red hair is remarkable and easily remembered, and I suspect it is this selective memory that has biased clinical observations. In a series of 98 normal individuals,¹ 14 of whom had red hair, I estimated the bleeding-time by the Ivy technique (3 incisions on two different days). In conformity with other workers,² I found that females on average had longer bleeding-times than males, but there was no statistical difference between the groups arranged by hair colour. The striking feature of this normal series, with a technique as carefully standardised as possible, was the extreme variations both between individuals and even in one individual. But the bleeding-time does not necessarily measure a "tendency to bleed."

Portsmouth.

J. R. O'BRIEN.

SAFER HYPOTENSION

SIR.—There are several ways in which chlorpromazine could contribute to safer hypotension for cerebral surgery without resorting to the active cooling described by Dr. Dundee and his colleagues in their letter of April 24.

The narcobiotic property of chlorpromazine described by Decourt³ causes a reversible depression of activity of all cellular life. It could, therefore, conceivably reduce the activity of the cells of the brain, rendering them more resistant to aggressions, including anoxia. Admittedly, a similar effect can be produced by cooling, but the necessity for duplication of the process is open to question.

The specific action of chlorpromazine in abolishing central autonomic activity^{4,5} might be of assistance in preventing the cardiovascular emergencies that arise during neurosurgery, following transmission of retractor pressure to the mid-brain, or active surgical intervention at the base of the brain. Finally, chlorpromazine itself possesses peripheral ganglion-blocking properties and it is not surprising therefore that smaller doses of 'Afonad' are required to produce hypotension.

These remarks are not made in criticism of the method described. They are made because hypothermia is given the credit which is probably due to chlorpromazine. Equally good results might well be obtained without the additional complication of hypothermia.

Lambeth Hospital,
London, S.E.11.

D. A. B. HOPKIN.

1. O'Brien, J. R. *J. clin. Path.* 1951, 4, 272.
2. Pauwen, L. J., Roskam, J., Derouaux, G., Puissant, A. *Arch. int. Pharmacodyn.* 1942, 67, 390.
3. Decourt, P. *C.R. Acad. Sci., Paris*, 1953, 236, 1195.
4. Pocidalo, J. J., Cathala, H. P., Humbert, J., Tardieu, Mme. *C.R. Soc. Biol. Paris*, 1953, 146, 368.
5. Cathala, H. P., Pocidalo, J. J. *Ibid.* p. 1709.

EGGS AND RHEUMATIC FEVER

SIR.—We would like to comment on several statements in your annotation of April 17.

It is true that streptolysin S has not been shown capable of producing lesions of rheumatic type; but in the reference you cited in support of this point none of the animals survived more than 48 hours, which is scarcely long enough. The statement that choline deficiency may be associated with a rise in plasma-phospholipid is contrary both to current concepts and to the intent of the sources cited. As a determining factor in rheumatic-fever susceptibility we do not envision a choline deficiency severe enough to cause fat accumulation in the liver but merely one which is capable of producing a relative lack in certain individuals who may have an unusually high choline requirement. We regard the relation of choline intake to the synthesis of plasma-phospholipid as enabling or permissive rather than stimulating. Evaluation of methionine as a substitute for choline is complicated by species differences and by the influence of other dietary factors such as protein and vitamin B₁₂. In any event, it seems significant that the greatest incidence of subjects with a below-average plasma-phospholipid or childhood egg intake was found in patients with the more severe grades of heart-disease or multiple episodes of acute rheumatic fever.

ALLAN D. WALLIS

Epicopal Hospital,
Philadelphia, Pennsylvania.

ELLENMAE VIERGIVER.

SEX AND SOCIETY

SIR.—Dr. Sherriff's letter last week perhaps deserves some analysis:

"Those of us who hoped for a lead from the *Practitioner* in its symposium on Sex and its Problems must have been sadly disappointed."

By what right does Dr. Sherriff speak for this putative group and why expect a lead from a symposium, which is "a collection of views on one topic"?

"Nowhere is a radically new approach to sex suggested."

Dr. Sherriff's new approach is a policy of licence which is older than some hills.

"If our criminal law on male homosexuality were to be civilised as in France, Scandinavia, Switzerland, and most socially advanced European countries, many of these problems would simply fade away."

"Civilised" begs the whole question. The implication of "most socially advanced" is that the countries named and unnamed are more socially advanced than we are. But are they? "...many of the problems would simply fade away": of course they would, but they would be replaced by many more.

"Fifty years ago the most frantic rubbish was uttered about the deadly evils of masturbation."

It still is, and among the rubbish is the statement that masturbation is of no importance.

"In another fifty years posterity will likewise marvel that we could make such a mountain out of the molehill of homosexuality."

This is the kernel of the letter. Dr. Sherriff thinks that homosexuality is a mere molehill. I do not; it often ruins lives and is contagious.

"Let us hope that a kindly and earthy sexual common sense will then prevail, which would minimise homosexuality and other sexual disabilities more than anything else."

But why "let us hope" when in the preceding sentence he has said it will? I deny that such a view could be "kindly," but am inclined to agree with "earthy." The last part of the sentence is obscure: "Let us hope that a... sexual common sense will then prevail, which would minimise homosexuality... more than anything else." Minimise the quantity of it or the importance of it?

What does "anything else" refer to? Make it less culpable than kissing or courting?

"Meanwhile, let us do all we can to urge overdue reforms in law and opinion."

"Overdue" is another question-begging word. Certainly there is nothing in Dr. Sheriff's letter which should make us want to do anything of the sort.

Beckley, Sussex.

C. G. LEAROYD.

HEPARIN IN ANGINA PECTORIS

SIR.—It has been claimed that heparin, in addition to its effect on blood-coagulation and plasma lipids, may also relieve the effort pain of ischaemic heart-disease. This claim was recently put to the test in 14 patients (13 men and 1 woman) with effort angina due to coronary-artery disease, and although the numbers are small the results may be of interest to anyone contemplating using heparin in this manner. The patients were selected only for their ability to attend hospital for intravenous injection twice weekly for six months; even so, 2 did not complete the course.

The heparin was kindly supplied by Messrs. Evans (Liverpool), and a control solution of saline was used, made up in ampoules indistinguishable from the heparin.

The patients were divided into two groups of 7: one group was given heparin, 10,000 units intravenously twice weekly; and the other group had saline in the same way. At the end of three months both groups were interrogated and, unknown to the patients, the treatment was then switched over; those who had previously received heparin were given saline and vice versa. The results showed that after three months 3 patients had improved on saline and 4 on heparin. At the end of the second three months 6 claimed improvement on saline and 4 on heparin.

In this small series, therefore, intravenous heparin was no better than saline in relieving the numbers of attacks of angina of effort.

D. H. DAVIES
Bristol Royal Infirmary.
D. W. BARRITT.

ELECTROCARDIOGRAPHIC CHANGES IN THE DUMPING SYNDROME

SIR.—I would point out to Dr. Gardberg (May 22) that my article (Feb. 13) included an example of electrocardiographic changes in a normal person after a meal. Reference was also made to the fact that these changes do occur without clinical symptoms.

If one accepts the view that the vasomotor symptoms, as distinct from the other aspects of the dumping syndrome, are merely an exaggeration of normal physiology, it follows that a proportion of normal people are likely to show a similar type of response after meals. The extent to which these changes are affected by gastrectomy is under investigation.

County Hospital, York.

C. N. PULVERTAFT.

HOSPITAL, DOCTOR, AND PATIENT

SIR.—Before replying to Dr. Naish's questions (May 8) may I emphasise my complete agreement and sympathy with her views.

My reply to the letter from Parent (April 3) was not intended to contradict, but rather to show that this regrettable state of affairs was by no means universal and was largely avoidable if hospitals and doctors were more humane and less pompous and detached from their true responsibilities.

This hospital has a visiting period every evening of the week for both adult and children's wards. The sister normally alternates with her staff nurse for duty during this time. I consider it an essential part of the sister's duty to meet and talk to the relatives of every patient in her ward. She can and does suggest an interview with the surgeon to any relative who is worried, or has queries with which she cannot herself deal. Often the surgeon

himself takes the initiative in asking relatives to meet him when complications in a patient's illness have arisen or if the diagnosis of some dangerous, crippling, or mysterious disease has been made.

The sister or her deputy normally talk to the relatives of every patient due for an operation (however trivial) on the following day, and a special pass is given permitting visiting during that and the succeeding two days (outside the normal visiting-hours).

This is a large hospital of 750 beds, serving one of the most thickly populated areas in the country, showing that such methods can be made to succeed in the "big" hospital and not merely in cottage hospitals or nursing-homes.

Oldchurch Hospital, Romford, Essex.

R. A. KING.

PORPHYRIA TREATED WITH NEOSTIGMINE

SIR.—In your issue of May 1 Dr. Gillhespy and Mr. Smith report a case of porphyria combining, it is said, clinical and biochemical features not hitherto described. The unusual features are listed in their summary as paralysis of the left recurrent laryngeal nerve (stated in the text to be the *right* recurrent laryngeal nerve), deterioration in the clinical condition following electroconvulsion therapy, hirsuties, lymphocytic infiltration of the muscles, and the presence of uroporphyrin I and porphobilinogen in the urine (presumably porphobilinogen). None of these features can be considered unusual, with the possible exception of lymphocytic infiltration of the muscles. The presence of porphobilinogen in the urine is a constant and characteristic feature of acute porphyria. The identification of the urinary uroporphyrin as the type-I isomer "from its behaviour in ethyl acetate solution" (not further amplified) is unsatisfactory, and in any case it is well recognised that both uroporphyrins I and III, at least, are obtainable from acute porphyria urines. Clinical features such as paralysis of the vocal cords, hirsuties, &c., have frequently been described.^{1,2}

It is hard to understand several other points in this article. It is stated that the faeces contained a "decarboxylic" porphyrin: perhaps this should be dicarboxylic.

The presence of macronormoblasts in the marrow was thought possibly to indicate subnormal amounts of liver factor, so 'Anahæmin' was given with a return to a normoblastic marrow in a few weeks. The value of this is vitiated by the absence of any peripheral blood studies.

With regard to the exhibition of neostigmine and its beneficial effect in this one case, such a satisfactory response is to be welcomed. One should note, however, that this drug has been given before for acute porphyria with good effect³⁻⁶ but in other instances without benefit.^{7,8} The efficacy of any treatment is notoriously difficult to assess in acute porphyria, in which spontaneous remission and rapid improvement are so often encountered.

A myasthenia-gravis-like picture has been described previously in acute porphyria (compare Denny-Brown and Sciarra⁹ on this point). The marked improvement described by Dr. Gillhespy and Mr. Smith, when neostigmine was administered and the return of symptoms when it was discontinued are compatible, as they suggest, with the coexistence of acute porphyria and myasthenia gravis, although they add that "the absence of other signs and symptoms of myasthenia gravis make this argument unlikely." This point could be more clearly

1. Waldenström, J. *Acta med. scand.* 1937, suppl. 82.
2. Vannotti, A. *Porphyry und Porphyriekrankheiten.* Berlin, 1937.
3. Waldenström, J. *Nord. med.* 1944, 23, 1562.
4. Gordin, R. *Ibid.* 1948, 37, 480.
5. Veflingstad, H. *Ibid.* 1949, 42, 1432.
6. Olggaard, H., Roos, B. E. *Ibid.* 1953, 49, 411.
7. Ashby, D. W., Bulmer, E. *Brit. med. J.* 1950, ii, 248.
8. Fawcett, J. W. *Lancet*, May 22, 1954, p. 1079.
9. Denny-Brown, D., Sciarra, D. *Brain*, 1945, 68, 1.

assessed if it had been stated whether the expression "fully recovered" indicates, as it implies, that the patient is now no longer dependent on neostigmine.

Neostigmine may possibly have some place in the treatment of acute porphyria, and certainly any rational form of treatment should be considered in this disease which is so difficult to control. It seems to us doubtful, however, whether the authors have presented a sufficiently convincing argument for its trial in every case "when porphyria has been diagnosed."

Department of Chemical Pathology
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School, London, W.C.1.

C. RIMINGTON
A. GOLDBERG.

NURSING BY THE MOTHER

SIR.—No doubt Miss Schoo is right when she says, in her letter last week, that children at her hospital are quieter without their mothers; but there are many reasons for being quiet—confidence is not the only one.

Any normal mother is very anxious if her child is ill enough to attend hospital, especially if she does not know what is going on. Naturally, this anxiety in the mother upsets the child. There are two ways of dealing with this. You can remove the mother, thus making both of them more anxious, though they are prevented from showing it. This may keep the hospital quiet, but it is not so conducive to "normal emotional development" as Miss Schoo thinks. The alternative is to relieve both of them; the mother, as well as the child, wants to be reassured that he is no worse off than his fellow-patients. Of course, having the mother in the hospital, and then treating her as an ignorant and unreasonable interloper, ensures the worst of both worlds: it upsets everybody.

Maudsley Hospital,
London, S.E.5.

JOHN RICH.

CONTROL OF CANCER MORTALITY

SIR.—Dr. Malcolm Donaldson (April 17) says that I "believe" certain things about cancer. It is true that I believe certain conclusions are valid when, so far as I have been able to find, they are compatible with all the accumulated evidence to date; when they are the only conclusions which that evidence, abundant from all angles, consistently allows and, indeed, demands; and when they are at the same time not opposed by any conclusive evidence to the contrary—the contrary evidence being found ambiguous, inconclusive, or patently fallacious. Dr. Donaldson will allow, I am sure, that such belief is different from that which dictated bleeding as a standard treatment for many ailments not so long ago—different from that, too, on which the great programmes for control of cancer mortality were formulated and, unfortunately, have since been sustained in some instances in spite of the exposure meanwhile of their false basis. He can enlarge the field of evidence by including the age-specific breast-cancer mortality-rates from Denmark, the State of Missouri, the State of Minnesota, and the State of New York in addition to all the areas previously mentioned, but he will not find in them any consistent or assured indication of decline. And he would find that the rates for all cancer (combined) in Sweden in recent years are practically identical with those in Ontario and the other provinces of Canada. (Data for earlier years or for breast cancer separately are not at hand.)

The limitations of microscopy and histopathology and, too, of large numbers in providing comparability of two or more series, and also the imperative need for reasonable comparability for drawing valid deductions from a difference between survival-rates, are demonstrated further by the fully 60% over-all five-year survival-rate in 2727 cases of breast cancer in the years 1935–44 in one clinic and 43% in 952 cases in the years

1933–41 in another clinic. If difference in selection of cases can be disregarded and comparability thus assumed, then treatment in one clinic was obviously greatly superior to treatment in the other, and, in fairness to the patients, those treated at the inferior clinic should have been sent to the superior one. However, such a contention of superiority of one clinic over the other would be as embarrassing, it is thought, to the individual clinicians of one as the other, and, fortunately, no such contention need be entertained because the difference is largely accounted for by the difference in the proportions of "stage I" cases in the two clinics. Approximately 50% of the patients in the clinic obtaining the 60% five-year survival-rate and only 16% in the clinic obtaining the 43% survival-rate were "stage I." In cases with axillary involvement the former clinic had a five-year survival-rate of about 40%, the latter clinic 36.3%. The small difference could be due to the vagary of such figures whether or not it is "statistically significant" but it may indicate that difference in selection of cases is not entirely confined to those without axillary involvement. As pointed out previously (Jan. 30), the only reasonable explanation for the great difference between the "stage I" proportions of 50% and 16% is a difference in selection of cases, the former including as cancer some types excluded from the latter. Such a difference in selection cannot be eliminated with any assurance even by maintaining the same personnel or by their attempting over the years to apply the same criteria and techniques. The material submitted changes and this changes the results despite the application of the same criteria and techniques.

The evidence reviewed shows clearly, I think, that the number, if any, of breast cancers in which early treatment might obviate the lethal remote spread is so small in relation to those in which earlier treatment does not obviate the spread that treatment of them makes no decisive impression on the mortality-rates. As noted (Jan. 30), no more precise estimate of that small proportion, if any, is available today. That possible proportion, determined by the evidence, does not compare at all with the high proportion of cures previously considered possible and on which control programmes were based, nor does it compare with the proportion of cures to be inferred from persisting propaganda.

The overwhelming approval of the public for lectures on cancer is hardly convincing evidence of either their value or their lack of any harm. A lecture on any medical subject almost always attracts a large and attentive audience. The danger of such propaganda may have to be reckoned from another angle. Here is a case in point:

A prairie farmer of over 200 lb. with a thoroughly hearty appetite suffered some slight abdominal distress for about ten days. He consulted his physician who could find no cause for the distress but, fearful of any delay, ordered an X-ray examination. The radiologist reported "suspicious of gastric cancer." In spite of the fact that his wheat was just ready to cut, the patient was sent immediately by air nearly 2000 miles for expert attention. A laparotomy failed to reveal any cancer, but when the stomach was opened a small ulcer, said to be about 5 mm. in diameter and without any induration, was found. A partial gastrectomy was then performed. In spite of his five hours in the operating-room, the patient did well with the assistance of transfusions and other supporting therapy. In two weeks he flew back to his frozen harvest with some feeling of assurance that he would not die from gastric cancer.

This case is perhaps extreme in the flight of nearly 2000 miles, in the five hours in the operating-room, and in the gastric resection; but, along with the thousand women on the waiting-list at one cancer detection clinic in Ontario,¹ it reflects fairly well the state of mind of both the public and the profession. Some day an

1. Previously cited: *Canad. J. Publ. Hlth*, 1949, 39, 343.

accounting may be required of the number and total cost of all examinations made on the false premise that a reasonable delay will greatly jeopardise the patient's chance of survival.

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N. E. MCKINNON.

MENTAL CARE

SIR.—Your leading article last week and Dr. Ling's interesting report on the mental-health services in Amsterdam raise some provocative suggestions. It would seem that Dr. Ling's article the Prevention of Mental Illness might more aptly be entitled the Prevention of Mental-hospital Admissions, since it is considered that there may be too many mental-hospital beds in this country.

The conclusion that mental-hospital admissions and readmissions could be reduced if a domiciliary psychiatric supervisory service were actively pursued as in Amsterdam is backed up by a comparison of hospital statistics. If these figures are to form a basis of discussion, then I must beg to submit the claims of Sheffield in the competition for fewer beds.

The Middlewood Mental Hospital has 2089 beds (1815 authorised) for the thickly populated area of Sheffield, Rotherham, Doncaster, and adjacent urban districts comprising a total population of 1,025,667 (i.e., 1 bed per 490 of the population, not 276 as in Greater London). The annual admission-rate over the past four years has averaged 790 (685 in 1953). It would seem, therefore, that a comparison of Amsterdam with London is not valid for the rest of this country :

	London	Amsterdam	Sheffield
Number of people per 100,000 in mental hospital in 1950	412	330	300
Annual admission-rate (% of population)	0.32	0.1	0.09

I am unable to cite the suicide-rate for the Sheffield area ; but if the mental-hospital figures provide an index of mental health in the community, then Sheffield may rank as mentally healthier even than Amsterdam. On the financial side Sheffield, too, is saving a considerable sum of money in its mental-health services, and I must here pay tribute to the local health authorities who persevere have to cope with domiciliary psychiatric problems, perhaps not with the facility of the Dutch but to the best of their resources.

If it is, indeed, a good policy to regard admission to mental hospital as the last resort, then Sheffield has already obtained a start in the direction of the Dutch system.

Middlewood Hospital,
Sheffield.

F. T. THORPE
Medical superintendent.

"THE DANGER OF MACHINES"

SIR.—As the author of the *Daily Express* article referred to by Dr. Organe last week, I should like to say how much I regret any trouble which my report has caused, either to Mr. Dickson Wright or to the anaesthetists.

I must point out, however, that I attended the meeting by invitation along with several other newspaper reporters, including at least one representative of the American press, and that in my account Mr. Dickson Wright was accurately reported.

It seemed to me and to some of my colleagues that Mr. Dickson Wright's statements were not mere lighthearted asides but that he was airing a serious grievance. This was also the view of two surgeons with whom I discussed Mr. Dickson Wright's speech. I have since learned from Mr. Dickson Wright that his comments were not intended to be taken so seriously and that he was unaware that reporters were present.

I went to much trouble to give Dr. Organe the opportunity of commenting on the speech so that his views on behalf of the Association of Anaesthetists could be given similar

prominence to those of Mr. Dickson Wright. Dr. Organe could not be contacted but I left messages for him.

My statement that Dr. Organe and other anaesthetists demonstrated their machines to the visiting American surgeons was not intended to suggest that Dr. Organe was present when Mr. Dickson Wright made his remarks. I do not believe that it did, in fact, give this impression to our readers.

Daily Express,
Fleet Street,
London, E.C.4.

CHAPMAN PINCHER
Medical correspondent.

MALARIA AND MILK

SIR.—With reference to your leading article of May 1, I doubt whether milk prevents or reduces the severity of malaria in adults or babies. In my experience babies are often infected under the age of 2, and they may die suddenly from a severe infection or from convulsions. This sudden disaster is rare in babies over 2, but I have often seen it in younger infants on breast-milk. At El Kharza oases in 1943 and 1944, when malaria occurred in epidemics, I succeeded in stopping these sudden deaths in infants by giving them prophylactic 'Eeuquamine.'

ATTIA TAWFIC.
Suez, Egypt.

DIET AND CORONARY DISEASE

SIR.—May I express a few remarks on the thoughtful paper by Professor Duguid in your issue of May 1.

The artery is often narrowed when degenerated, but not always from inside ; it may be narrowed by the degeneration of the perivascular—i.e., by pressure from outside. The red-free ophthalmoscope may show it quite clearly.

Professor Wenckebach, of Vienna, cited the results of necropsies in 5000 cases from Viennese hospitals ; half of the patients died from coronary thrombosis with pretty good coronary arteries and half died from other diseases with badly sclerotic coronary arteries, but not even a history of angina.

The spasm of the artery would easily explain many puzzles, as a badly degenerated muscle will obviously be unable to produce an intense spasm.

Winternitz showed in anatomical specimens the peculiarities of vasa vasorum and the dependence of the intima on them for its nutrition.

N. PINES.
London, E.1.

SIR.—Statistical graphs are always arresting, but I do not think your readers should allow themselves to be too much impressed by those appearing in the letters from Dr. Leitner and Mr. Daw in your issue of May 22.

Dr. Leitner has reproduced a graph illustrating the coincidence of high-fat-calorie diets with high death-rates from degenerative heart-disease in certain nations ; and a very handy graph it is for those who would argue that fat causes coronary disease. But it is the kind of thing that can be turned out to support almost any notion. Probably one could draw very similar curves if instead of fat-calorie percentages one took motor-car sales or, for that matter, anything else that goes with national prosperity.

Mr. Daw's mortality curves suggest to me that the fat restriction, which made itself felt chiefly in the later years of the war, could not have been the factor responsible for the discontinuity in recorded death-rates beginning to appear as early as 1940. Almost anything but diet might have been responsible, even the laying up of motor-cars at the outbreak of war, for instance. Which reminds me : did not Morris and his colleagues¹ find that bus-drivers had more coronary disease than bus-conductors (double-deck vehicles) ? Have we stumbled on something ?

Department of Pathology,
Royal Victoria Infirmary,
Newcastle upon Tyne, I.

J. B. DUGUID.

1. Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts C. G., Parks, J. W. *Lancet*, 1953, ii, 1111.

Obituary

JAMES CALVERT SPENCE

Kt., M.C., M.D., LL.D. Durh., Hon. D.Sc., F.R.C.P.

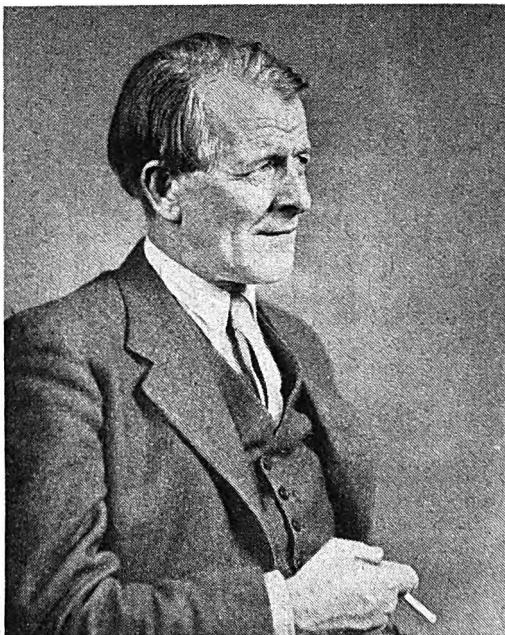
The death of Sir James Spence will be deeply regretted by many different kinds of people, and it is a measure of his achievement that they will go on thinking and talking about him and his ideas for many years to come. He had the perception and the zest of an artist, joined to an uncommon power of analysis, high courage, and a strong will. Unlike most men of 62, he had much still to give, and the loss is great not only to his friends but to his profession—which has few such prophets.

Born in 1892, the son of Magnus Spence and Isabella Turnbull, he was educated at Elmfield School, York, and at his native Newcastle upon Tyne. As a medical student he was gay, versatile, and athletic, but he was not among the recognised contestants for prizes and scholarships, and it was a general surprise when he gained honours in his final M.B. Then as later, his strength of character and intellect were commonly underestimated by casual and even quite familiar acquaintances.

War broke out soon after he qualified in 1914, and Spence, whose grandfather had been a sea-captain and shipbuilder on the Northumbrian coast, decided to be a doctor in the Navy. But this proved impossible: though he had the fitness of a footballer and mountaineer, he had lost one more molar tooth than the regulations permitted. So he entered the Army, and saw service at Gallipoli, in Egypt, and in France, with a field ambulance of the 11th Division. He won the Military Cross and bar.

In 1919 he became casualty officer at Great Ormond Street Hospital, thus entering paediatrics. But his next appointment was as John and Temple research fellow at St. Thomas's Hospital, where his work was in the borderland between medicine and biochemistry, and it was as chemical pathologist and medical registrar at the Royal Victoria Infirmary that he returned to Newcastle. Nevertheless his interests were really clinical, and it was not long before he began the association with the Newcastle city health department which he maintained for thirty years. The then medical officer of health, Prof. Harold Kerr, wanted to use active clinicians in the work of the child-welfare centre, and Spence, with his Great Ormond Street background, was one of the first to be so employed. This may not have been his introduction to the social and preventive aspects of medicine, but it was certainly one of his earliest expeditions into the territory which he did so much to open up. It was, too, during these years between 1924 and 1931 that he came into close association with the man who more than any other influenced his philosophical outlook on medicine and broadened his understanding of the basic needs of medical education. This man was "Jim" Bernard Shaw, with whom he spent, in 1927, a happy year as a Rockefeller research fellow at Baltimore.

On his return to England began the venture of the



Babies' Hospital, in which the ordinary nursing care of the children was undertaken by the mother—not in a ward, with its risks of cross-infection, but in a home-like single room. Even yet the lessons of this enterprise are not applied as they should be; but many visitors to Newcastle have been persuaded that it is safer and more convenient, as well as more sensible and kinder, not to separate mother and child if this can be avoided. They have also seen that medicine, and medical research, can be practised on a high level in simple surroundings. In the Babies' Hospital he found willing collaborators in

Lady Ridley, in Dr. Gavin Muir, and in Mr. William Wardill, now of Bagdad; and their combination of enthusiasm, careful house-keeping, intense social and clinical interest, and surgical skill was to give their small hospital a large place on the medical map. Later, in the second world war, Spence was to demonstrate that, given leadership, really bad buildings could be turned into a positive asset. Transferred to an orphanage, the Princess Mary Maternity Hospital found itself working under almost every possible inconvenience; but the staff, put on their mettle by this challenge, set out to show that what matters to the mother and child is care and skill, not chromium plate. A high and rising standard of practice was maintained, and an example was set. In this humane if unprepossessing institution, newborn infants were not (as so often) removed to another ward. Mothers, said Spence,

have been "mystified by an arrangement under which their babies have been taken away from them at the time when, at the end of nine months' waiting, they had expected to possess them."

In the early 1930s, being now on the clinical staff of the Royal Victoria Infirmary and of the Newcastle General Hospital, he began the series of therapeutic trials of which a notable example was his report in 1933 to the Medical Research Council on the antirachitic activity of calciferol. By this time he had also been brought more deliberately into the affairs of the city health department. In 1933, at the request of the Ministry of Health, he carried out a small but classical "investigation into the health and nutrition of certain of the children of Newcastle upon Tyne between the ages of one and five years." Thereafter his help was often in request by the city, and Sir John Charles, then the M.O.H., recalls "long summer afternoons spent in the front garden of his house, while the plans of a proposed new children's department of the Newcastle General Hospital were subjected to that painstaking, practically-minded scrutiny which was the secret of Spence's success as an administrator." This association, evident again in the investigation into the causes of infant mortality in 1939, published jointly by the Babies' Hospital and the child-welfare department of the city, developed further after Spence's appointment in 1942 as the first Nuffield professor of child health in the University of Durham. 1947 saw the beginning of the "1000 families survey" which is a study, jointly undertaken by Spence's department and that of the present M.O.H., Dr. Stanley Walton, into the health and illness of the Newcastle

children born in May and June of that year. Thus this medical link between university and city has become very strong, and visitors are often surprised to learn that a teaching unit can be so close to the people of the area it serves. These visitors have been numerous, for Spence's department is regarded as one of the most fruitful experiments in social medicine in this country if not in the world. To many coming from countries where the care of children presents appalling problems it has seemed that Spence and his young colleagues gave them something they could not find elsewhere. Newcastle was dealing with what mattered.

Listening to Spence—and when in the mood he talked a great deal—was an invigorating exercise. He tried his effervescent thoughts on anyone handy, and they were all uttered so persuasively that it was hard to tell what was wisdom and what was not. Yet from all the complexity he came to conclusions that had some of the simplicity of genius. His conclusion about the practice of medicine was this :

"The real work of a doctor is not an affair of health centres, or public clinics, or operating-theatres, or laboratories, or hospital beds. Techniques have their place in medicine, but they are not medicine. The essential unit of medical practice is the occasion when, in the intimacy of the consulting-room or sick-room, a person who is ill, or believes himself to be ill, seeks the advice of a doctor whom he trusts. This is a consultation, and all else in the practice of medicine derives from it."

To students the art of consultation is best taught in the outpatient department, though the two or three students who are allowed to attend must listen unobtrusively till the patient has gone; and both student and doctor may learn much from the mother, who is commonly a good observer of her own child. In the training of students he set little store by examination or by lectures. He had a deep faith in universities, in the ready interchange of thoughts between their members and their faculties; and (as a means of securing this) in the collegiate system of Oxford and Cambridge. His presidential address last autumn to the Newcastle medical society was notable for an attack on the introduction into medicine of the concept of *services*—by which a member of "the consultant and specialist service," for example, may be appointed to a hospital and work in it, but thinks of himself less as part of the hospital than as part of the service. What is needed for group work in medicine, he believed, is not services but *institutions* (large or small) whose members form a functional whole.

By 1938 his influence had begun to spread, and to many national bodies he gave of himself prodigally and without thought of any personal benefit except that participation in them would make him more useful to his own faculty in Newcastle. In these fifteen years English medicine has changed its orientation; and those who have been close to any of the many-sided developments in education, in hospital policy, in paediatrics, or in the integration of the social sciences into medicine, know how much the present pattern owes to Spence. He served on policy-making committees at the Royal College of Physicians; he gave evidence to the Goodenough Committee; he was an early member of the advisory council of the Nuffield Provincial Hospitals Trust, and he belonged to the Medical Research Council and the University Grants Committee. One who worked with him on the U.G.C. writes :

"When he joined the committee in 1943 it had important work to do. The Government had realised from its war experience the unique importance of the universities to the country in its time of need. The Goodenough report was on its way, and a comprehensive health service was being mooted. When the war ended, the universities were faced with sudden and enormous expansion in staff, facilities, and students. Later the work of the medical faculties had to be co-ordinated with that of the National Health Service. This was the perfect milieu for Spence's genius. He brought to all those

problems a vivid imagination and a warm humanity, and an unshakeable belief in the integrity of his fellow men and their capacity to do the right thing, once they had realised what that was. He was impatient of the small mind, and the myopic vision; and he grew very restless when he saw that large and important views were being evaded because of tradition or detail. In the best sense he was at heart a revolutionary. He would repeatedly urge that a problem should be considered in its broadest aspects, and the decision based on principle and the future, rather than on expedience and the past."

In council or committee, a discussion proceeding on praiseworthy but pedestrian lines would be brought up short by two sentences from James Spence that made his startled hearers begin to think afresh. Someone once described him as the Puck of English medicine; and certainly, when he shyly materialised at some conventional gathering, he carried a faint suggestion of belonging to the Wild. A faun perhaps!—but who ever heard of a faun being re-appointed to the M.R.C.!

Vivid, elusive, and occasionally perverse, he was not always a comfortable person. Though profoundly compassionate he was not incapable of giving pain, and though he believed in everybody he did not get on easily with everybody. So strong a personality sometimes demanded its own way, and for all his sympathy and tolerance he might be hard to cross. Yet he will be remembered by thousands chiefly for his kindness, and by his friends for the strength of his affection and his support. The hospitality of his heart was evident in the home which he and his wife made so understandingly together.

When he knew that he could not live long he wrote : "My serenity surprises me. Never before in any circumstance of a very varied life have I felt such calmness. An unexpected contentment has settled on me." He always felt that, however far a man wandered, he should have roots in one place to which he would return. For him Newcastle was that place, and at the end of his life his chief hope was that he had done something that would really help the ordinary people of Northumbria among whom he had worked and whom he so much admired and loved.

Sir James Spence married Kathleen, daughter of R. Downie Leslie of Aberdeen. They have a son, who is an architect, and four daughters, of whom one is a nurse and one a medical student. His published lectures in this country include the Bradshaw lecture (1940) and the Charles West lecture (1946) at the Royal College of Physicians, and the Linacre lecture at Cambridge (1951). He was Cutler lecturer at Harvard in 1949 and Blackader lecturer in Canada in 1949, and in 1948 he visited Australia, where he received an honorary degree from the University of Western Australia. He was knighted in 1950 and was president of the British Paediatric Association in 1951.

RECOLLECTIONS

James Spence was perhaps the most attractive personality I have ever met. I never climbed with him, but I have often thought that mountaineering expressed most clearly, perhaps, his personality. His gaze always seemed to seek the distant peaks and his mind delighted in the problem of how to achieve the difficult or seemingly impossible; nothing thrilled him so much as a new journey over difficult and often unknown ground. It was his zest for life and his capacity for regarding every phase and every incident in life as an exciting adventure that made him so enchanting a companion. This quality did not leave him, even in the later days of his illness; what would have been to most a depressing experience was transmuted by his spirit into yet another new adventure, that was to be savoured to the full, for it could only happen once.

His spirit was infectious and few of those who knew him were unaffected by it. To work with him was a thrilling experience. Ideas and values had a way of being taken out of the dusty recesses of the mind and after being turned upside down and viewed carefully

from every angle put back in a different and more seemly place. But he was a practical reformer and no romantic visionary. He knew his fellow-creatures too well for that. And his knowledge was of the deepest and most intimate kind based on a long experience of the practice of medicine, the kindest of hearts, and the most sensitive of minds. Herein lay his value as a counsellor, for he combined an imaginative and revolutionary approach with sympathetic understanding of the common man and what he could do. There is, unfortunately, no-one quite like him, but the ideas for which he worked so selflessly must prevail.

G. W. P.

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The name of James Spence will always be connected with the Newcastle Babies' Hospital, since it was the essence of his achievement; but it is perhaps not so generally known that the idea of it originated in the mind of an old friend of his who started it after the 1914-18 war.

Miss Greta Rowell had spent her early life in Florence where she had run a small school for young children. At the beginning of the war she returned to her home in Newcastle and became immediately concerned by the number of children roaming the streets while their mothers were making munitions in the nearby factories, and she founded one of the very earliest day nurseries in England. After the war was over and the nursery was no longer needed, Miss Rowell became interested in the ideas of Truby King, and while having dinner with her father and an old friend of his one night, she said to this friend (who always wanted to remain anonymous): "What this city really needs is a Babies' Hospital and if you were decent enough you would buy me a house for it." The next day he bought her 33, West Parade, and she set about collecting a committee to raise enough money to equip it. There was room in it for six babies and two mothers and its purpose was to be largely for the instruction of mothers in the care and feeding of their babies.

As honorary physician Miss Rowell appointed a young doctor who had recently returned from the war to practise in his native city. His name was Dr. Spence. Being a young man of vision and imagination, he recognised the opportunity that this afforded him to carry the work of this mothercraft centre further—into the field of sickness and disease in infants. The risk of admitting babies to the wards of a children's hospital was great in those days, and Dr. Spence further maintained that it was impossible to study the nature of disease in babies except under the most natural conditions, which were in their mothers' arms.

I first joined the committee in 1925 and became its chairman in 1929. A new matron, Elizabeth Cummings, had been appointed in 1928 and she proved to be exactly the right woman to help Dr. Spence in the creation of his life's work. He always said that the best and happiest years of his professional life were spent in that little hospital. He was certainly the centre and inspiration and leader of a most harmonious team; and the hospital grew, by first buying the house next door, and then a few years later, the house next door to that, so that there was finally accommodation for 36 babies and 8 mothers. They were exciting times. Money was short and the matron had to wash the walls and paint the furniture; but the committee never hesitated to give Dr. Spence what he wanted when he asked for it, and raise the money for it later.

One of the chief features of the clinical work in those early days was William Wardill's development of his technique for the repair of hare-lip and cleft palate. He and Dr. Spence worked so happily together that their relationship resulted in the perfect example of a combined clinical unit, with none of what Dr. Spence always held to be the artificial segregation of children into medical and surgical cases.

In the 1930s moves were made to amalgamate with the Royal Victoria Infirmary and to build a Children's Hospital on the Castle Leazes site incorporating the

Babies' Hospital and the children's wards of the infirmary. But protracted negotiations prevented this scheme from being realised before the outbreak of war in 1939. As the Babies' Hospital was situated so near to the Elswick works of Vickers Armstrong, it was decided that it should be moved to my house ten miles out of the town. Blagdon was ideally suited to the purpose, for there was a large nursery wing which had been added to the house in 1820 by the Lady Ridley of the day who had twelve children, with twelve little rooms, six each side of a long corridor, with a large day nursery at the end.

The hospital remained at Blagdon until 1944. Those members of the honorary medical staff who had not been called up took a weekly rota of duty, coming out to Blagdon each day. There was no resident house-physician. Dr. Spence continued of course to be the central pivot round whom everyone turned and on whom everyone depended. As the matron, Miss Cummings, wrote to me last week: "He was always ready to listen, nothing was too trivial for him to take notice of, he never put you off and said he hadn't time." He was a marvellous man to work for, he got the very best out of all the staff, they would have done anything for him."

The hospital flourished and grew and gradually encroached into more and more of the house until it regained the 36 beds it had had at West Parade, while more than 300 mothers were admitted during the five years. On Aug. 22, 1944, at 7 p.m. our part of the house was found to be on fire. As great good fortune had it, Dr. Spence happened to be doing a round at the time, and, with the help of two R.A.F. men who had seen the smoke from the Great North Road, he organised the removal of the children with complete calmness and resource. Later he returned to help to fight the fire and it was characteristic of him that he was one of the last people to leave the building and indeed he was almost overcome by the smoke before he could be persuaded to go.

In 1946 the hospital began again, very much as it had in the beginning, in two converted houses in Leazes Terrace.

It was his ambition to plan and build a Children's Hospital incorporating all the knowledge and experience he had gained at West Parade, Blagdon, and the Newcastle General Hospital. That this ambition was never realised is one of the many tragic aspects of his early death; and for those of us who could have furthered the building of such a hospital, our remorse is great.

As the days and years go by we shall miss him more, and the world will become darker when we no longer see it through his eager eyes and quick interpreting mind. He loved courage and integrity and courtesy. His only fear in dying was for the suffering he knew he must inflict upon his family and friends.

U. R.

* * *

Every university lives by the moral drive of a few of its members; a good university is one that is fortunate enough to find both moral and intellectual leadership in the same person. That, I think, is what the Newcastle division of the University of Durham chiefly owes to James Spence. His favourite test of university teaching and research was "excellence." His idea of excellence was best displayed in the surroundings which he himself devised for its practice: in his Babies' Hospital; in his outpatient clinic and research laboratories at the main teaching hospital, the gift of the Nuffield Provincial Hospitals Trust; and, perhaps best of all, in the babies' department of the Maternity Hospital. There, throughout the war years, he had to bring excellence out of the really atrocious physical conditions of a makeshift "evacuation" building, until he shamed the university and the Ministry of Health into an inspired scheme of conversion which, beyond all expectation, almost succeeded in

translating even his ideas of excellence into what was, in effect, a new maternity hospital of a hundred beds built for little more than £60,000. Indeed, his chosen field of excellence was so utterly the intimate one of the consulting-room and the bedside, that laymen bred to the habits of a megaphonic age found it difficult sometimes to account for his national and international reputation. In the most public of his lectures he used the same conversational tones as to his half-dozen students at a clinical consultation. There could be no clearer proof that knowledge, humanity, and moral purpose are their own advertisement, and hardly need to speak above a whisper. In his later years he showed the same intimate clinical approach to the problems of social medicine, as, for example, in his "thousand children" survey on Tyneside. In those years, he was much occupied in national committee work on problems of administration, planning, and policy; but he found his happiness in the hope that he had founded a teaching school after his own image in the northern university where his heart was. And that hope was surely not in vain.

P.

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The influence of James Spence was so largely personal that it is difficult to pay tribute to it so that future generations will understand the esteem in which he was held by his contemporaries. There are some men—the majority—who achieve eminence by building some part of the factual structure of knowledge. There are others—the architects of knowledge—who give shape to particular concepts. Both leave contributions which are evident, not only to their contemporaries, but to their successors. But there are yet others—a few—whose contributions lie in appreciating needs and creating the climate of opinion in which these can be translated into realisable concepts. Their influence is to be measured, not in terms of the factual contributions which survive them, but in the value that was placed on their advice during their lifetime.

To a certain extent no man can achieve eminence in his profession without contributing in each of these ways. James Spence made his own contributions to factual knowledge. In his work for child health he developed his concept of the particular field of medicine in which he was interested. But it is probable that it was in his contribution to professional thought, of the form and shape which medicine should take to meet the needs of its own development and the society which it serves, that his influence was most pervasive and profound.

At the time of his death James Spence was serving for a second period on the Medical Research Council. That in itself was an indication of the regard in which his advice was held. He attended his last council meeting on April 23. His advice on detail was as valuable as ever; but it was typical of him that, ill as he was, his main concern was to ventilate a problem broader even than medicine itself. He was concerned with the whole question of the relationship of scientific knowledge to the intellectual development of our society, not in any vague or sentimental sense, but as it expressed itself in the concrete problem of integrating the effort of the scientific organisations of government with that of the universities. It was this ability to appreciate the larger significance of the drift of events, and to arrest the attention of those who might influence them, that gave his advice its peculiar value. Not that he was proved always to be right. No man who attempted to foresee distant developments could hope to be. But his opinions were never negligible and, more often than not, showed a grasp that seemed almost inspired.

Foresight of this range is a talent which, in general, men appreciate only in retrospect. At the time it is

seldom welcome. Perhaps the greatest tribute that can be paid to Spence as a man is that his contemporaries were prepared to heed him and yet still held him in affection. If his character had been different, he might so easily have followed the commoner lot of the imaginative and become a mere rebel. He had, however, a fundamental generosity of temperament which conditioned his attitude to others and their response to him. This, combined with a very characteristic whimsical charm, endeared him even to those with whom he was in most disagreement. To juniors he was an inspiration. His curiosity was ever alive and he retained the capacity to see the fascination of the ordinary. But he never forgot the man behind the work; and there must be many who remember the appreciative aside which showed that the true measure of their achievement had not been overlooked. To contemporaries and juniors alike, he was a very stimulating, very human, and most engaging colleague.

H. P. H.

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Who shall replace him, in casual conversation, in sober committee, in exultant planning, in trying to solve human problems? Sometimes his talk seemed perversely alien to a subject under discussion, but patience, out would come the illuminating phrase. The Goodenough Committee would not have been what it was without his sane and even his humorous suggestions. On the Medical Research Council there was always his imaginative attitude to put an almost magical touch on the solution of a difficult problem. On Nuffield advisory and steering committees his hard preparatory work and impromptu interjections helped everybody to keep a proper perspective.

Quite apart from his contribution to paediatrics, the diffusion of his influence over many fields of medical and social endeavour has had, and will long continue to exert, a fertilising and beneficent effect. A great figure passes.

E. R. C.

* * *

As long as he had the strength he insisted on living his usual life, a very brave decision reached after considering the problem as an abstract one. So not so long ago I watched him doing what I always thought he did best, of all the talents at his easy command—debating at a council table. On such occasions he rarely intervened early; and when he did speak, the relevance of what he was saying in his clear way might not always be at first apparent. But as discussion went on it would become evident that Spence had once again cast his mind more widely and further ahead than had anyone else. He had that rarest of gifts, the ability to be penetratingly wise about small matters as well as great, and all with the most unaffected simplicity. For he hated pomposity; and how often he checked it so disarmingly with that "Come now" spoken with his half-smile and the merest but still definitely visible lift of his eyebrows. It was easy for one so gifted to be an accomplished physician; his heart made him a good doctor. And what a joy it was to see him where he loved to be best, at work in his own unit. Always encouraging his utterly loyal team to fresh and greater efforts, whether in the wards or at the conference table, he still gave of his wisdom, but with a subtly different technique; now clarifying an issue in a pungent sentence or two, now braking an incorrect approach by an impish aside. The work he has begun will continue to modify human experience.

And, the day's work over and whatever might be toward, memory will hold him the gayest and best of good companions.

J. L.

One cannot pass in and out of a man's life without taking much for granted. There are few occasions for the high heroics or for the proclamations of loyalty and approval, or for the recording of dissent. Men work together, knowing how they will react to this or that, gently demurring or approving as the case may be. In their companionship they come to use a common currency, which is acceptable to all. And in these comings and goings there is usually no need for the specific recognition of those who lead and those who follow. Leadership, that intangible virtue, rests lightly on the shoulders of those whose fate it is to wear it. It rests unchallengeably on certain shoulders, and it rested indubitably on those of James Spence.

In his early years—and this manner of attack he never entirely abandoned—it was his practice to hatch some provocative idea, elaborate it with flourishes and extravagances, and then launch it and himself upon a series of specially selected auditors, all known to be prone to react promptly and surely. Account would be taken of their reactions; and the idea, trimmed here and there, the flowers and flounces suppressed, but still much the same in essence, would be officially paraded in appropriate quarters. James loved this gay challenging method of argument and formulation of opinion, and I can bear witness to its success both here and abroad. But despite its apparent "ingenuousness" it was a skilfully prepared tactic, and the process of chiselling, correction, and refinement added immeasurably, as he knew it would, to the persuasiveness of the basic idea.

In later years his earlier ebullience had abated to a considerable degree, and in all the affairs with which he was concerned—medical and clinical research, university education, the administration of the National Health Service, and the management of its hospitals, there was no shrewder or more practically minded counsellor than James Spence, and none who had a better idea of their fundamental economics. It is impossible in a few words to visualise one's loss, and the loss is greater indeed for those who were nearer to him. Charm, gaiety, frankness, versatility, liveliness of mind, readiness of tongue, all these were part of him. And in addition the deeper qualities of friendliness, courage, humanity, and the will and ability to understand the mind and motivations of others—these too were there. And behind that patience, and integrity, and a confidence and trust in the ultimate purpose of the universe and its Maker.

For anyone who knows the story of the final months of James Spence's life, and the courage which he manifested, in complete keeping with his character and history, there is a striking comparison to be drawn in the last chapter of *Marius the Epicurean*. And perhaps there is to be found his best epitaph. He was amongst those happy parents in the greater sense—"planting with a cheerful good humour the acorns they carry about with them, that their grandchildren may be shaded from the sun by the broad oak trees of the future."

J. A. C.

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His singleness of purpose and his patient thoroughness of application of that scientific method must have inspired many of us. But it was the man himself who was great, and mainly because of his humility.

At a small gathering where someone had lauded his position he turned to me and said, indicating his wife, "these are the truly great people." Spence tried to give every sick or well child what he knew his wife would like her children to have. I for one, would like to tell her that thousands of mothers are grateful to him and to her for his work.

F. C. N.

ARTHUR O'NEILL

O.B.E., M.R.C.S.

Dr. O'Neill, who was a former medical superintendent of Napsbury Hospital, died at Brighton on May 12 at the age of 76.

The son of an Army Officer, he was brought up in Devonshire and he studied medicine at St. Bartholomew's Hospital. He was a fine rugby forward who captained the Barts XV and played for England; in one international match he continued playing with a fractured clavicle. Later he played cricket for the Gentlemen of Hertfordshire.

After qualifying in 1907 he held house-appointments at Windsor and Eton Royal Infirmary and at the North-Western Hospital in London. In 1909 he was appointed to the staff of Middlesex County Mental Hospital at Napsbury, near St. Albans, and he spent the rest of his professional life there. He was appointed O.B.E. for his work as registrar when the hospital was a military unit in the first world war, and later he became its medical superintendent. He retired in 1942.

E. S. S. writes: "When I first knew O'Neill he was in the early fifties, erect, with a fine presence, very much one of the old school in appearance and manner. He bore a striking resemblance to C. Aubrey Smith, the cricketer and actor. In many ways he was a typical Irishman—a great raconteur with a colourful sense of humour, and a winning smile. He was an unrivalled teacher of hospital administration—five of the six medical officers then on his staff have since become medical superintendents. He was also a sound clinician, often affecting to despise modern advances, but in fact always seeing that his hospital was in the van of progress. He rarely, if ever, missed a hospital function, however unimportant it might seem to his juniors, and he took a special interest in the chronic and friendless patients, whom he knew intimately."

Dr. O'Neill leaves a widow and two daughters by a former marriage.

Appointments

East Anglian Regional Hospital Board:

- CRAWFORD, W. J., M.B. Belf.: anaesthetic registrar, East Suffolk and Ipswich Hospital.
 LEE, LUCY T., M.B., N.U.I.: anaesthetic registrar, United Norwich hospitals.
 LYON, J. B., M.B. Camb., M.R.C.P.: consultant dermatologist, venereal disease clinics, Ipswich hospitals area.
 McNAMARA, KATHLEEN, L.R.C.P.I.: anaesthetic registrar, Newmarket General Hospital.
 MORTON, MARGARET B., M.B. Edin., D.C.H.: paediatric registrar, Peterborough area.

Newcastle Regional Hospital Board:

- CHARLTON, AVRIL E. M., M.B. Durh., D.A.: asst. anaesthetist, Newcastle General Hospital and associated hospitals.
 GOODWIN, M. A., M.B. Leeds, F.R.C.S.E.: asst. orthopaedic surgeon, Sedgefield H.M.C.
 LIDGATE, M. M., M.B. Birm., D.P.M.: consultant psychiatrist, Winterton Hospital, Sedgefield.
 RAMSEY, T. A., M.B., B.Sc. Glasg., F.R.F.P.S.: senior casualty officer, Hartlepool H.M.O.

North East Metropolitan Regional Hospital Board:

- CARTER, P. J., F.R.C.S., D.L.O.: part-time consultant E.N.T. surgeon, Tilbury and Riverside Hospital.
 GARDNER, FRANCES, M.D. Lond., F.R.C.P.: part-time consultant physician, The Mothers (S.A.) Hospital and Thorpe Coombe Maternity Hospital.
 LARKIN, I. L. M., M.D. Lond.: full-time consultant pathologist, Oldchurch Hospital and other hospitals in the Romford group.
 LUTWYCHE, VIVIEN U., M.D. Camb., M.R.C.P.: full-time consultant chest physician, Epping and Buckhurst Hill chest clinics.
 McGOWAN, F. M., M.D. Camb., M.R.C.P.: full or maximum part-time consultant physician, Oldchurch Hospital and St. George's Hospital, Hornchurch.
 MAYER, HELEN M., M.R.C.S., M.R.C.O.G.: part-time consultant obstetrician and gynaecologist, Forest Gate Hospital.

Sheffield Regional Hospital Board:

- KWELLA, J. P., M.D. Warsaw: whole-time anaesthetist, Mansfield and Nottingham areas.
 MACGREGOR, D. F., B.M. Oxf., D.P.M.: whole-time consultant psychiatrist, Carlton Hayes Hospital, Narborough, Leics.
 McKEECHANIE, SAMUEL, M.B. Glasg., B.A.: whole-time consultant anaesthetist, City General Hospital and Barnsley hospitals.

Notes and News

MEN AT WORK

THE Joint Committee on Human Relations in Industry, appointed in April, 1953, by the Department of Scientific and Industrial Research and the Medical Research Council, has issued its first report,¹ which describes its policy and research projects. Five subcommittees have been set up, to deal with research on incentives, management organisation, technological change, promotion and training, and special groups in industry. Twelve research projects have been approved, at an estimated cost of £89,000; part of the cost is being met by United States Economic Aid under the Conditional Aid Programme.

The subject of incentives is being approached in several ways. The results of previous research are to be evaluated by the M.R.C. group for research in industrial psychology at University College, London. Birmingham University will carry out research in Midlands industry on the effect of incentive schemes on productivity. At Manchester University the effect of conventional output norms on output will be studied; and the team at University College, London, will also examine the effect of the worker's better understanding of the results of his efforts on morale and productivity. A further investigation on incentives for management is being carried out by the British Institute of Management.

Problems of management organisation featured frequently in the topics for investigation suggested to the committee. The M.R.C. team at University College, London, is carrying out research on communications in industry; and pilot research is being sponsored at South-east Essex Technical College on the relations between line management and functional specialists.

Research into factors impeding or facilitating change is being conducted at Liverpool University; and the Tavistock Institute of Human Relations is to clarify some principles of production in the coal industry—notably the relation of technological factors to social or work organisation. Technological changes in the electronics industry in several Scottish firms will be studied at Edinburgh University; and a pilot research on the human aspects of introducing automatic control techniques in industrial processes will be carried out at Cambridge University.

Political and Economic Planning are inquiring into factors affecting the utilisation of university graduates in industry; and the Acton Society Trust will study the effect on efficiency and morale of promotion policies and practices.

The effective employment of special groups in industry is an important problem as regards older workers, married women, and young people; a project for study of married women employed as part-time workers in a London factory has been approved.

The committee has as its main objective the establishment of a balanced and continuing programme of social-science research related to the needs of industry in this country, which will be financed from British Government funds as these become available. The need for trained research-workers is recognised by the committee as one of the chief factors affecting the realisation of its programme. It hopes to promote better liaison between research groups and national and industrial organisations, and would welcome suggestions from interested bodies.

WORLD HEALTH ORGANISATION

THE seventh World Health Assembly concluded its three-week session at Geneva on May 21. The general orientation of W.H.O.'s work was not changed by this assembly, but proposals were made for more intensive action in sanitation, dental hygiene, and poliomyelitis. Further steps were taken to meet the situation arising from the fact that the Regional Committee for the Eastern Mediterranean has been unable to meet since 1950, the Arab League having decided that its member countries would not send delegates to regional meetings attended by delegates from Israel. A procedure was unanimously adopted to enable the regional committee to meet in two separate subcommittees. The eighth assembly will be held in Mexico next spring.

The Executive Board began its 14th session on May 27, and elected as its chairman Dr. H. van Zile Hyde, chief of

1. Human Relations in Industry: Department of Scientific and Industrial Research and the Medical Research Council. H.M. Stationery Office. 1s.

the division of international health, U.S. Public Health Service. The board endorsed the choice of Copenhagen as the permanent site of the W.H.O. regional office for Europe.

INTRAMEDULLARY NAILING

THE second number—one might almost say volume—of the new journal, *Clinical Orthopaedics*,¹ devotes two-thirds of its space to the use and abuse of the intramedullary nail. The terrifying illustrations of the possible complications of this method of treating fractures may do something to discourage its use by the uninitiated, though Dr. D. M. Street, in the introductory chapter, does not appear very sanguine about this. In spite of the balanced outlook expressed in the early chapters (there is the revealing remark "It behoves us to become skilled in the neglected art of traction and casting"), later contributions leave an impression that the application of the method has been taken to rather fantastic lengths. An eminent surgeon once said: "Go to America to learn what can be done in the field of surgery and how to do it; but not whether to do it." This volume hints at the truth of this dictum; nevertheless there is much to be learnt from it, and the editors are to be congratulated on bringing so much information together under one cover.

BEDSIDE TELEPHONE FOR ALL

PATIENTS in Acton Hospital, London, can now telephone relations and friends from their beds. The instrument and coin-box are on a trolley; and, by an extension device, the instrument can be brought on to the patient's lap. A long length of flex from the trolley is plugged into one of several sockets in the ward. Volunteers take this trolley round the wards twice a day; and the rest of the time it is kept in the hall, where it is connected and can be used, and from which it can be fetched if need be. This system, believed to be the first of its sort in Great Britain, was inaugurated by the Postmaster General on May 13. So far patients seem to have used the telephone largely for long-distance calls—perhaps because friends who are nearer at hand will be visiting them.

University of London

At a recent examination for the academic postgraduate diploma in psychological medicine the following were successful:

J. E. A. Bartlet, J. L. J. Lumey, Mary M. McQuade, M. J. Rosenthal.

University of Sheffield

On July 3 the honorary degree of M.D. is to be conferred on Dr. J. L. A. Grout.

University of Leeds

The first Matthew Stewart lecture will be given in the Littlewood Hall, Instructional Block, the General Infirmary, on Thursday, June 17, at 4 p.m., by Prof. G. R. Cameron, F.R.S., who is to speak on the Exploration of the Cell.

Royal College of Surgeons of Edinburgh

At a meeting on May 26, with Mr. R. Leslie Stewart in the chair, the following were admitted fellows of the college, having passed the requisite examinations:

M. Y. Alyan, George Choa, G. A. Clark, R. S. Cowie, J. A. Cunningham, W. B. L. Downing, E. R. Duchenne, Jack Fogel, P. J. F. Grant, M. E. Lake, T. G. Lorentz, J. B. Lowry, Patrick Madore, A. T. Matheson, V. S. Metgud, B. M. More, Patrick O'Brien, A. F. Rateb, A. N. Razdan, Isidore Robins, Michael Salvavis, R. T. Singh, C. D. Sinha, J. A. van der Merwe, R. I. H. Welsh.

British Association of Paediatric Surgeons

The inaugural meeting of this association is to be held from Wednesday, June 30, to Friday, July 2, in London. Morning lectures will be held at the Royal College of Surgeons, Lincoln's Inn Fields, W.C.2, and afternoon lectures at The Hospital for Sick Children, Great Ormond Street, W.C.1. The programme will include lectures and discussions on Congenital Malformations of the Rectum and Anus, Acute Intussusception, Cardio-oesophageal Syndrome, Hiatus Hernia, and Intestinal Obstruction and Peritonitis in the Neonatal Period. Prof. Ian Aird will also give a lecture and show a film on the Surgery of Conjoined Twins. Further particulars can be had from the secretary of the association, Mr. D. J. Waterston, The Hospital for Sick Children, Great Ormond Street, W.C.1.

1. *Clinical Orthopaedics*, no. 2. Editor-in-chief: Anthony DePalma. Philadelphia and London: J. B. Lippincott. 1954. Pp. 247. 48s.

Naval Doctor Honoured

Surgeon Lieutenant-Commander A. P. M. Nicol has been appointed a member of the Royal Victorian Order.

Institute of Dermatology, London

Two semi-permanent exhibitions are being shown at the institute during the summer course. The second, from June 7 to 26, by Dr. R. G. Cochrane, will be on Leprosy.

University College Hospital Medical School

Prof. Henry K. Beecher (Harvard) will deliver a Holme lecture at 4 p.m. today, Friday, June 4, on Drug-induced Changes in Sensation.

Faculty of Radiologists

The annual meeting is to be held in Dublin on June 18 and 19. Subjects to be discussed include pneumo-encephalography after head injury, placentography, moving-beam therapy, and carcinoma of the lung.

Colyer Medal

The Faculty of Dental Surgery of the Royal College of Surgeons of England has made the first award of this medal to Sir William Kelsey Fry, for his work on maxillofacial surgery.

West London Medico-Chirurgical Society

The annual banquet of this society will be held on Monday, June 28, at 8 p.m., at the Apothecaries' Hall, Black Friars Lane, E.C.4. Tickets (£2 2s.) can be obtained from the secretary of the society, Mr. K. G. Rotter, West London Hospital, W.6.

Institute of Child Health, London

Dr. Orvar Swenson (Boston) will deliver the Alex Simpson Smith lecture at The Hospital for Sick Children, Great Ormond Street, W.C.1, on Wednesday, June 30, at 5 p.m. Dr. Swenson is to speak on Congenital Defects in the Pelvic Parasympathetic System. Applications for tickets should be sent to the dean.

Prison Medical Services

The annual conference of prison medical officers and psychologists was held at the Home Office on May 28, with Dr. H. K. Snell, director of medical services, in the chair. Dr. D. S. Macphail and Dr. R. C. Simpson spoke on Psychotherapy in Prison and Advances made in Group Treatment, and Dr. A. A. S. McDonald and Dr. M. R. P. Williams on Medical Aspects of Long-term Imprisonment.

Glasgow Chemotherapeutic Research Unit

On May 28, at the Western Infirmary, Glasgow, Mr. James Stuart, secretary of State for Scotland, opened the new building of this unit for research into the treatment of acute rheumatism and blood diseases. The Western Regional Hospital Board has contributed £50,000 for the building, the Medical Research Council have provided the medical staff and the equipment, and the board of management for the Glasgow Western Hospitals have undertaken to provide the day-to-day services and nursing staff. Dr. James Reid is the director of the unit.

Westminster Hospital

Proposing The Guests at the old students' dinner on May 28, Dr. Gerald Garmany said that, as a psychiatrist, he felt hampered by an inadequate history : works of reference did not provide the information which was dynamically important in the subjects' lives. He asked Sir John Charles to deny that psychiatrists are paid special portage fees for taking examination couches on domiciliary visits : everyone knew that a folding camp-bed was quite sufficient. Sir John Charles, in reply, preferred to talk about performing dogs, and incidentally quoted a military preceptor of his who declared : "If I say a thing once it may be true ; if I say it twice it's probably true ; if I say it three times it is true ; but if I say it four times you've ruddy well got to believe it." Mr. A. C. H. Bell paid an impressive tribute to Mr. Aubrey Goodwin, adding, by way of relief, a terrifying account of The Chairman's exploits as big-game hunter, when he was last seen, with rifle raised, under the pubic arch of the largest elephant. Mr. Goodwin had intended to make a speech about women doctors, whom he would have compared to wines of various types. But (you see) the topic of his speech was irrelevant to the warmth of its reception.

Coloured Tablets

Branch representatives of the Pharmaceutical Society have asked the society's council to discourage manufacturers from producing gaily coloured tablets, because these attract children.

Nutrition Society

On Friday and Saturday, July 23 and 24, at the University College of North Wales, Bangor, this society is holding a symposium on the Efficiency of Food Conversion in Farm Animals. Further particulars may be had from Dr. R. J. L. Allen, c/o Monkhouse & Glasscock Ltd., Snows Fields, S.E.1.

New editions have been issued of *Appointments in Her Majesty's Colonial Service* (H.M. Stationery Office, 3s.) and of the Colonial Office publication *Appointments in Her Majesty's Colonial Research Service*.

Births, Marriages, and Deaths**BIRTHS**

MARTIN.—On May 27, at Sedan House, Chester, to Dr. Rosemary Martin (née Bolam), wife of Dr. Geoffrey Martin—a son.

Diary of the Week

JUNE 6 TO 12

Tuesday, 8th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 p.m. Prof. Arnold Sorsby : Nature of Refractive Errors.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2

5 p.m. Sir Edward Mellanby, F.R.S. : Actions of Vitamin A as a Controller of Structure and Function of Tissues.

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2

5.30 p.m. Dr. Brian Russell : Pyococcal Infections.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

3 p.m. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Prof. J. Louw (Cape Town) : Vesico-vaginal Fistulae.

Wednesday, 9th

UNIVERSITY OF LONDON

5 p.m. (University College, Gower Street, W.C.1.) Prof. John R. Pappenheimer (Harvard) : Theory for Renal Hemodynamics.

INSTITUTE OF DERMATOLOGY

5.30 p.m. Miss B. M. Partridge : Infections due to Yeast-like Organisms.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

3 p.m. (Hammersmith Hospital, Ducane Road, W.12.) Professor Louw : Indications for Caesarean Section.

UNIVERSITY OF OXFORD

5 p.m. (Radcliffe Infirmary.) Prof. A. D. Gardner : Bacteriological Episodes.

Thursday, 10th

ROYAL COLLEGE OF SURGEONS

5 p.m. Mr. H. S. Morton : Potentialities of the Electrogastrograph. (Hunterian lecture.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12

4 p.m. Dr. Edwin Clarke : Cervical Spondylosis with Cord Compression.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1

5 p.m. Section of Ophthalmology. Mr. A. G. Cross : Uveitis in Childhood.

INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children, Great Ormond Street, W.C.1

5 p.m. Dr. Lawson Wilkins (Baltimore) : Endocrine and Non-endocrine Causes of Stunted Growth.

INSTITUTE OF DERMATOLOGY

5.30 p.m. Dr. J. O. Oliver : Pyogenic Cocci in Skin Disease.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

NOON (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Professor Louw : Surgical Emergencies in Pregnancy.

ALFRED ADLER MEDICAL SOCIETY

8 p.m. (11, Chandos Street, W.1.) Dr. A. P. Cawadias : Psychological Factors in Graves's Disease.

UNIVERSITY OF ST. ANDREWS

5 p.m. (Medical School, Small's Wynd, Dundee.) Lord Boyd-Orr, F.R.S. : The Widening Field of Medicine.

Friday, 11th

POSTGRADUATE MEDICAL SCHOOL OF LONDON

2 p.m. Mr. J. K. Monro : Observations on Urinary Stone.

4 p.m. Prof. A. Bradford Hill, D.Sc., F.R.S. : The Clinical Trial.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2

5 p.m. Prof. W. C. W. Nixon : Inertia in Labour.

INSTITUTE OF DERMATOLOGY

5.30 p.m. Dr. A. D. Porter : Pyococcal Infections.

Saturday, 12th

NORTH EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY

10.30 a.m. (North Middlesex Hospital, Edmonton, N.18.) Mr. M. Bates : Thoracic Actinomycosis. Dr. J. V. Davies : Incidence of Tuberculosis in School-children and their Contacts.

SURGERY OF THE THYMUS GLAND *

SECOND (AND THIRD) THOUGHTS

GEOFFREY KEYNES

M.D. Camb., F.R.C.P., F.R.C.S., F.R.C.O.G.

CONSULTING SURGEON TO ST. BARTHolemew's HOSPITAL,
LONDON, AND TO THE NEW END THYROID CLINIC

The surgery of the thymus has really centred around its association with myasthenia gravis, and this began many years ago with the observation that tumours of the thymus were often accompanied by the symptoms of myasthenia. Removal of these tumours proved to be difficult, and it was not until 1936 that the celebrated American cardiac surgeon, Blalock, successfully removed a thymoma with alleviation of the associated myasthenia gravis. A few years later he took the further logical step of removing the apparently normal thymus gland from myasthenic patients, since most of them do not have a tumour to account for the disease, and in 1941 he reported favourably on the results obtained in 6 patients.

This report was noticed by Carmichael and Carson of the National Hospital, Queen Square, who then had under their care a young woman with severe myasthenia gravis. This patient, they judged, would soon die unless some active steps could be taken to help her. Until that date, February, 1942, patients with myasthenia gravis could be treated with neostigmine ('Prostigmin'); but though it often gave them great relief, this did not prevent the disease from getting worse when it was of a progressive type, and so could not always save their lives.

This patient at the National Hospital happened to have been operated on by me some years before for a nodular goitre, and so I was invited to do this new operation of thymectomy—partly, perhaps, because she happened still to have some signs of mild thyrotoxicosis. The operation was done, both thymus and part of the thyroid being removed; the patient, with a struggle, survived and soon began to lose her symptoms of myasthenia. In a few months these disappeared altogether and for eleven years or more she has been quite well; for a long time she was doing heavy work on the land.

The result provided encouragement for further operations of the same kind, and within the next three years over 50 thymectomies had provided a considerable body of experience on which to base some assessment of the results that were likely to be obtained. The mortality of the operation was at first rather alarmingly high, but the results seen in the survivors were such as to make it justifiable to proceed; and soon, with increased experience, the mortality fell to such a low level that it could be discounted.

In all this work I had the immense advantage of close association with J. E. Piercy and the staff at New End Hospital, and to them is due very much of the credit that accrues from any good results that we have obtained.

Successive Assessment of Results

In June, 1945, I first attempted to present the whole subject in a Hunterian lecture at the Royal College of Surgeons and was able to review the results obtained in 51 operations (Keynes 1946). From the beginning we found it difficult to classify the results, the manifestations of myasthenia being so exceedingly various. Eventually we decided to make it as simple as possible by recognising four categories as follows:

- A. Quite well. Normal life without neostigmine.
- B. Greatly improved, but needing some neostigmine.

- C. Somewhat improved, neostigmine less than before.
- D. No improvement.

At this time in 1945 there were 33 patients for assessment, and the results came out as follows in round figures:

A. Well	9	60 %
B. Greatly improved	11	
C. Somewhat improved	8	24 %
D. No better	5	15 %

Several of these results had persisted for over three years, so that it seemed that some degree of permanence had been achieved.

After the publication of this lecture an increased number of patients presented themselves for operation, and by July, 1949, there were 120 for assessment (Keynes 1949). The results of the follow-up were found to be:

A. Well	39	32.5 %	65.8 %
B. Greatly improved	40	33.3 %	
C. Somewhat improved	31	25.8 %	
D. No better	10	8.3 %	

It will be noticed that even with nearly four times as many patients the results were still very much the same as before. The good results at first were not merely beginner's luck; they were a true picture.

A sinister feature of the disease was the extremely bad results obtained by primary operation on the patients with thymic tumours. I soon came to recognise that the thymoma introduced a different clinical state demanding a different approach, and from the start these patients were excluded from the assessment of results. For many years now they have been treated first with high-voltage X-ray therapy and sometimes have not been operated on at all. By this method the results have greatly improved.

Since 1949, with more than 200 patients without thymomas to be assessed, the results have remained very much the same, though if anything slightly better. An independent investigation of 100 of my patients carried out by a young Canadian physician, Dr. R. T. Ross, in 1951-52 showed 41 of 93 patients to be in category A, with 26 in category B—i.e., an excellent result in 67, or nearly 70%. This was considerably better than anything I had ever claimed myself. The average period of follow-up was by this time four and a half years. The same patients have just been re-examined by another independent observer, Dr. J. A. Simpson, at Queen Square without any significant change in the assessment being found after the lapse of another two years.

Criticisms and Cold Water

Meanwhile another view was gaining ground on the other side of the Atlantic. A team of observers at the Mayo Clinic, Rochester, Minnesota—notably Dr. L. M. Eaton and Dr. O. T. Clagett—were performing thymectomies for myasthenia gravis, and in April, 1950, they published a paper in the *Journal of the American Medical Association* in which they reported the results of 72 operations comparing them with 142 control patients who had not been operated on. Their survey showed "that the favourable results occur more frequently among the surgical cases." But further analysis they believed to suggest "that factors having to do with selection of cases for surgery accounted for these better results." Their conclusion was that thymectomy did not influence beneficially the course of myasthenia gravis, and they only advised operation for the removal of tumours because of their potentially malignant character. This pronouncement received much publicity and was quoted on numerous occasions because it was supposed to have finally discredited the claims of anyone who held different views. Dr. Eaton and Dr. Clagett gave the figures relating to our patients, from which it was evident that we claimed a much larger proportion of complete remissions than they did; but they made no

* The Annual Oration, delivered before the Medical Society of London on May 10, 1954.

attempt to explain this discrepancy and in fact passed over the figures in silence.

Their method of assessment was, however, entirely different from ours, since they did not separate the tumour patients from the non-tumour patients, having apparently not appreciated that the disease in those two kinds of patients runs a different course and demands a different therapeutic approach. All outside critics quite failed to notice this important difference—that the Mayo Clinic selected their patients with the emphasis on thymomas and lumped all their results together, whereas we exclude the thymomas and assessed a far more homogeneous series of patients none of whom had tumours. There seemed to be a tendency among writers of leading articles in the journals of this country to try to discredit the surgical treatment of myasthenia gravis with douches of cold water drawn from the Mayo Clinic cistern without attempting any critical examination of the essential difference in our approach. A very recent leading article in *The Lancet* (1954) repeated all the old arguments yet again, with further doubts expressed by Dr. Grob (1953) from Baltimore; but once more there is no indication that any distinction was made between patients with thymomas and those without. As a result, the surgical results in Baltimore again appear inexplicably inferior to ours—8·1% complete remissions compared with 41%, according to Ross's figures. Again the conclusion is that "Keynes's good results from thymectomy will influence some physicians, while the findings at the Johns Hopkins Hospital and the Mayo Clinic will make others hesitate."

Ever since beginning this investigation I have noticed that physicians often approach the problem with the fixed idea that, because spontaneous remissions sometimes occur in myasthenia gravis, therefore all surgical claims to have produced remissions are to be distrusted or discounted. How often have I not heard physicians of experience begin saying: "Yes, but I can remember a patient who had a spontaneous remission which has lasted seven years . . ."? I have longed to break in rudely with the question "Yes, but can you remember 50 patients who have had complete remissions lasting many years?" And anyway what proportion of patients treated medically do in fact have remissions of long duration?" This second question is an embarrassing one, because no physician in this country has ever recorded the results in a series of medically treated patients at all comparable with the unusually extensive series that has now been submitted to surgery. R. T. Ross in his paper on 100 consecutive patients from my series tried to get some idea of the frequency with which significant remissions occurred spontaneously, and his conclusion was that in "three large series of patients (all from American sources) treated by medical means alone . . . the proportion of cured or greatly improved is smaller, and the proportion of deaths due to myasthenia gravis is much higher" than in the group of patients he had examined. Statistical analysis of our results had established that the patients who benefited least from the operation were those in whom the disease had lasted longest and had therefore had the greatest opportunity for developing spontaneous remissions. In fact, it has always seemed to me, in the course of examining some hundreds of patients, that spontaneous remissions of long duration are relatively uncommon, and that their number is far surpassed by the remissions occurring after surgery which have been proved by the lapse of time to be indeed permanent, so that we may almost begin, after periods of up to twelve years, to speak of "cure."

Second Thoughts?

I have referred in the title of this address to my having had second thoughts (or even third thoughts) on this most interesting subject. I can claim, however,

that my thought-processes have been pretty consistent and that I have found no strong reasons for making any startling change in my beliefs. I am not, however, the only party who has had second thoughts on this matter.

In December, 1952, there was a meeting of the Association for Research in Nervous and Mental Disease in New York. One of their discussions was contributed by Dr. Eaton, Dr. Clagett, and Dr. Bastron of the Mayo Clinic (1953), and the subject was: "The thymus and its relationship to diseases of the nervous system: study of 374 cases of myasthenia gravis and comparison of 87 patients undergoing thymectomy with 225 controls."

It is worth noting at this point that the Mayo Clinic had asserted a few years before that there was no convincing evidence that the thymus gland was in any way connected with myasthenia gravis. Nevertheless the first part of this paper was entirely concerned with the consideration of "the evidence for a relationship between the thymus and myasthenia gravis"—pathological, physiological, and clinical, including surgery. Attention was drawn to the work of A. B. Bratton (to which I had referred in 1945) in showing that the thymus was histologically abnormal in a large proportion of glands from myasthenic patients. Some account was then given of the thymoma in myasthenia, the relation between these tumours and the disease being clearly demonstrated. The physiological evidence was summarised and held to suggest that the thymus interferes with the synthesis of acetylcholine, but it was thought to be inconclusive. This was before the publication of the work by Andrew Wilson to which I shall refer later.

The clinical evidence was then considered. "It was admitted that it had been the thesis of these authors that since remissions in myasthenia gravis may occur with or without thymectomy, improvement which follows thymectomy cannot necessarily be attributed to removal of the thymus. Consequently the value of thymectomy could be determined best by a comparison of the course of the disease in a large group of patients treated surgically with its outcome in a large group treated non-surgically." No-one would quarrel with this; but exactly the same principle had led this same group to pronounce to the world only two years before that the operation of thymectomy had no influence on the course of the disease. This statement had gone the rounds, had been repeated in every article on myasthenia and thymectomy, and had led one writer to announce that "the wave of enthusiasm for thymectomy is now over," implying, I suppose, that it had only been performed because "enthusiasm" had exaggerated its claims. This implication ignored the fact that all our claims were based on evidence obtained under the close supervision of our medical colleagues, who might be assumed to be without surgical "enthusiasm." It is easy for a surgeon to be too pleased by his delight in his own skill, and many a time have we seen this happen. In fact the Mayo Clinic pronouncement, made with all the weight of the authority of that remarkable foundation, had unwittingly done incalculable harm to the cause of those unhappy people who had become the victims of myasthenia gravis. Neurologists and physicians had been discouraged from recommending thymectomy, because everyone, even junior students, thought that it was no longer regarded as of any value.

Yet in December, 1952, the same Mayo Clinic group stated: "It is our opinion that the inclusion of more cases, followed for a longer period of time and by somewhat stricter methods, allows us to reach more definitive conclusions than those given in the last study, published in 1950." The next revelation is in the sentence: "From a study of table 16 it is readily seen that patients who have thymomas do not get along as

well as those who do not have thymomas," and later, "consequently, the remainder of this study is devoted largely to a comparison of surgical and non-surgical patients who do not have thymomas." In the next sentence is the remarkable discovery that: "It is of interest to find that in a comparison of surgical and non-surgical patients who did not have thymomas the better results are found in the surgical group. In this latter group 45·8 per cent. of the patients obtained a result justifying the risk, discomfort and expense of surgical treatment; this is contrasted to an incidence of such results in only 16·2 per cent. of the patients in the non-surgical group. Furthermore, the percentage of those who were worse or who had died of myasthenia gravis was considerably greater in the non-surgical group." Further elaboration of the statistical evidence was all found to point in the same direction. Tribute is paid to the value of the guidance received from Dr. Berkson in the proper use of statistical methods—difficult, as he truly says, for non-statisticians to comprehend, but enabling the non-statisticians to arrive at the proper interpretation of their own results.

I suspect that an important factor in this complete volte-face by Dr. Eaton and Dr. Clagett was their decision to study their non-tumour patients apart from their thymoma patients. This may even have been more important than revising their statistics. Nevertheless they still had to include one pretty bit of qualification in their final sentence. "It is possible that the operation itself stimulates certain endocrine metabolic processes within the patient that account for the favourable result." They are nothing if not cautious and have supplied a wonderful example of the twisting of a plain fact into a complicated theory in order to suggest that the operation of thymectomy is not what it appears to be.

Dr. Henry Viets, of Boston, in the ensuing discussion played his gentle irony on Dr. Eaton. "It is not easy," he said, "to make a right-about face or even a partial right-about face. It takes courage and persistence in not stopping after you have made a decision but going ahead and working further on the material, until you can show to your own satisfaction and to the satisfaction of others that you have drawn the correct conclusion." This is all very true. Dr. Eaton said later that the speakers in the discussion had been unusually generous in their remarks, particularly in view of the fact that this study had forced him to make a complete reversal of his previous stand in regard to the virtues of thymectomy.

This "complete reversal" of opinion is to be found in a highly specialised volume published last year in Baltimore which will be read by no-one except a few neurological specialists. I am grateful to the Queen Square specialist, Dr. J. A. Simpson, who drew my attention to this paper which now confirms the results which I put forward seven years ago, but which have ever since been damned with fainter and fainter praise, even while the results as seen in the actual patients got better and better.

It will be a long time before the medical profession in general will have any inkling of this remarkable recantation that has taken place. The whole affair is an interesting study in the elusive subject of the formation of medical opinion. We do not often see so clearly the way in which truth gets overlaid by muddled thinking, or how exaggerated deference is paid to a given opinion because it emanates from a large American clinic rather than from a smaller London one.

This we must take philosophically since it is a tribute to the cool way in which we, as a profession, regard our novelties. We look at them very carefully all round before we admit them to the canon of accepted practice. This deliberation may be irksome to the individual

because life is short, but it is perhaps wholesome in the long run.

The Thymoma

I have already referred to the thymic tumour, or thymoma, as having been the foundation on which the surgical treatment of myasthenia gravis was based. It seems to be inescapable that the disordered neuromuscular mechanism known as myasthenia gravis is connected with the growth of an epithelial tumour of the thymus, just as metabolic disorder depends on epithelial hyperplasia of a tumour of the thyroid, or disorder of calcium metabolism depends on the growth of an epithelial tumour of the parathyroid. Not more than 15% of myasthenic patients are found to have thymic tumours, but it has become plain that these 15% are in a far more serious plight than the other 85% without tumours. So bad, in fact, were our initial results with primary removal of these tumours that I soon decided that a different plan must be adopted with this unfortunate minority. Second thoughts suggested the substitution of high-voltage X-ray therapy for primary operation, and in a Cecil Joll lecture given last November at the Royal College of Surgeons (but not yet published) I examined the results of this altered approach.

Thymic tumours are not common, but I have had the opportunity of studying 41 of them. Of these 41 patients all the earliest ones treated surgically are dead; but of the 26 treated first with deep X rays 20 have had a subsequent removal of the tumour, with the following results:

Quite well and symptomless	4
Considerably improved	8
Initial improvement, then relapse	3
No better	1
Died	4

A good result, then, has been obtained in 12 patients out of 21 (57%) and 4 of these are quite well (14%). 3 patients have had no operation at all after deep X rays and are also well. X rays cannot, however, be relied upon to extirpate all the cells of a thymoma unless a dangerously high dosage is given. Operation should therefore be done as well when circumstances allow.

The necessity for avoiding primary operation for tumours underlines the importance of carrying out a careful radiographic examination of every patient as a preliminary, and I believe that every one can be detected in this way. It depends on correct exposures in the correct position, the lateral ones being of much greater importance than the anteroposterior in which the shadow of the mediastinal tumour will be obscured by that of the great vessels. Tomography may occasionally be of value. In the Joll lecture I also examined the question of the malignancy of the tumours. It used to be thought that the so-called lympho-epithelioma was benign, and it is true that it seldom metastasises to neighbouring lymph-nodes; but second thoughts, in the light of this large series of tumours suggest that in fact it is malignant. It does sometimes metastasise to lymph-nodes, it spreads locally to neighbouring structures, it can give rise to widespread recurrences some years after removal, and it can infiltrate surrounding tissues.

Removal of a thyroid adenoma is often advised because of the possibility that it may become malignant. The same argument might be applied to the thymus in the absence of a tumour were it not that the onset of the disease with a tumour is normally rapid and the tumour is found to be there as soon as the disease is diagnosed. In one patient, however, this was not true. She had had symptoms of myasthenia for twelve years. Three years after they started, she was seen in our clinic but was sent away because the symptoms were so mild. Nine years later she had become much worse, and a small tumour was then diagnosed by radiography. There is the other possibility that the "silent thymomas"

known to thoracic surgeons are an inactive phase of the neoplasms producing myasthenia. It is more than probable that some of the myasthenic tumours had been present considerably longer than the symptoms of the disorder, and had the patients happened to have been radiographed, as in mass radiography which reveals most of the "silent thymomas," the tumours might have been detected and removed in their pre-myasthenic phase.

The Patient's Attitude

My second thoughts now lead me to a consideration of the psychological aspects of myasthenia gravis, for there is no doubt that psychology is important in this connection. I am afraid that the myasthenic patient is apt to acquire a neurotic outlook at an early stage of the disease. It is in fact an iatrogenic state, since a very large proportion of patients, if you take a careful history, will tell you that their doctors treated them for weeks, months, or even years, for "nerves," assuming that there was not really anything the matter. A young sailor of my acquaintance was treated as a malingerer because his complaint of muscular weakness was unassociated with any objective signs. The famous character in *Punch* who told his doctor "As soon as I sees a job of work I comes over all of a tremble," was probably suffering from myasthenia gravis. I have heard patients describe how they have tried desperately with tears and protestations to get someone to believe in the reality of their complaint, only to be sent from one practitioner to another until at last someone, more observant than the others, has diagnosed myasthenia at a glance and proved it in five minutes with a shot of neostigmine—again producing psychological frustration in the patient, because the immediate feeling of well-being produces an ecstasy of hope which is quickly dashed as the effect of the injection wears off.

On one occasion a young man arrived at Queen Square from Persia by aeroplane with a large number of relatives surrounding him. He was lying on a stretcher in full evening dress completely helpless, and had not stood up or walked for many weeks. He was given a rather large injection of neostigmine, and a few minutes later sprang from his stretcher and rushed to the basin to be sick, to the amazement of his entourage who thought a miracle had happened. This was perhaps not a good psychological beginning, as he was afterwards very unhappy in hospital. He was depressed and lonely owing to the language difficulty, and it was extremely difficult to know how much or how little he had in fact benefited from the operation.

So often myasthenic patients are very depressed people. Their feeling of helplessness is such that they have virtually abandoned hope before the operation is done, and they are unwilling to give up their dependence on the drug which they have found in the past to be the only thing between them and complete collapse. Again, the psychological overlay makes assessment of results difficult, and dependence on a drug almost amounting to an addiction is an added complication.

Many patients do, of course, escape all psychological abnormality. They have often told me that a myasthenic life, even with neostigmine, is a living death, and that they would face any risk if they could be offered a reasonable prospect of recovery. They are eager to get better and are encouraged by the slightest evidence that their symptoms are abating. Naturally these patients are the easiest to deal with and a source of great satisfaction to their doctors and nurses; but even this euphoristic attitude has its dangers. Patients are sometimes so determined to get well that they will pretend to be better every day and assert that the doses of neostigmine can be reduced, when observation makes it clear that they are no better at all. I have even known them make pseudo-recoveries in order not to "let the surgeon down"—a touching form of doctor-

patient relationship which it is hard, though necessary, to shatter.

Occasionally a disturbing force finds its way into the patient's consciousness through the medium of the press.

A girl of 16 $\frac{1}{2}$ was sent to St. Bartholomew's Hospital from Australia. Waiting for her was a cousin who happened to be a reporter on the staff of a daily paper. He obtained access to the patient as a relation, possessed himself of the medical details, and set to work. Before long the patient was known to the press all over the world as "the girl with the frozen smile," and her progress was followed by thousands of sympathetic readers. Fortunately, she was a tough character and kept her head. Her progress was slow, but recovery was ultimately complete. Her smile unfroze, and the young man who welcomed her home became her husband with the happiest result.

Fortunately most English people are too sensible to allow their minds to interfere with their bodies—their psychosomatic balance is good. But even the most seemingly balanced individuals sometimes suffer small lapses. I have known several young women who have completely recovered, and normally get through their work and ordinary life after operation without recourse to any drug. Yet they admit to sometimes taking a tablet of neostigmine on Saturday evenings, and further inquiry always elicits the admission that it is before they go to a dance. Their confidence and common sense demands just that additional support which their previous sufferings had forced into their consciousness.

Residual Symptoms and Irreversibility

Assessment of myasthenia gravis after operation also has to take account of another difficult feature of the disease which may be summed up by the term residual symptoms. Many patients classified in category A are completely symptom-free; but others might at first sight be regarded as still myasthenic, since there is a visible ptosis or on examination a demonstrable ophthalmoplegia. It is, however, notorious that some of the muscular weaknesses in myasthenia may become irreversible. This is seen in its extreme form in a patient dying of the disease when all the muscles, including the respiratory muscles, have become quite unresponsive to neostigmine. Death follows from respiratory paralysis. But long before this, quite early in the disease, it is not uncommon to find that one or more ocular muscles do not respond to the drug. When the thymectomy has been followed by disappearance of all the other symptoms, the ocular palsy will persist, will still be unaffected by the drug, and is presumably to be attributed to a permanent change in the muscles. A patient may thus be genuinely non-myasthenic, though still complaining of diplopia. Sometimes they are found to be still taking neostigmine because of this, but the drug can be discontinued without making any difference. Another patient may be perfectly well except that she is conscious of some fatigability at her monthly periods. To that extent she may be called, if you wish to be very strict, myasthenic. But this is using the term in an academic sense. Clinically the patient is perfectly well and needs no treatment. It might be objected that, if this slight susceptibility exists, the patient might relapse; but long experience has shown that, when patients have reached this stage of recovery, they do not in fact ever relapse. On the whole, as time passes, the patients tend to progress from category C to B and from B to A. A few have relapsed from C to D, and very occasionally from B to C, but never as yet from A to a lower category. The time factor in recovery is, therefore, very important. Sometimes recovery takes place very rapidly; at others it may start quickly and then slow down, the full result not becoming established for months or even years.

Residual symptoms and irreversibility may perhaps come to be explained on the basis of the changes in the muscles recently described by Prof. Dorothy Russell

(1953). Coagulative necrosis with phagocytosis she found to be sometimes widespread, with obvious diminution in the number of muscle-fibres.

There are so many things of this kind in myasthenia that are difficult to explain, that it is easy to conclude that the thymus gland does not provide the whole answer. That is obviously true, but at any rate it takes us far enough to leave us in no doubt that the thymus provides a clue to be followed as far as is humanly and scientifically possible.

Children

During the early part of the investigation I was assured by several physicians of whom I inquired that myasthenia gravis did not occur in children. In this connection one of our patients who came to us rather fortuitously is an interesting object lesson. He came to New End Hospital about something quite different but one glance told my colleague, J. E. Piercy, that he probably had myasthenia gravis. He was persuaded to submit to an injection of neostigmine with obvious improvement. He was a man of 42 and he now recalled that he had always rather crawled through life; he also bethought him that as a boy he had had the same appearance; and finally he produced his own portrait showing the same myasthenic facies, at the age of 2. He subsequently had a thymectomy, from which he greatly benefited. Better late than never!

Another unexpected experience was being called into Great Ormond Street Hospital to see a child of 4½ that had been brought in apparently moribund from dyspnoea and debility. Dr. Wyllie had never seen myasthenia at this age, but thought of trying an injection of neostigmine. The child immediately recovered, and was proved to have a severe degree of myasthenia. I performed a thymectomy, the symptoms quickly disappeared, and she has been quite well ever since, that is for nine years. Soon afterwards I was called again to Great Ormond Street to see a child of 2½ who was even worse than the first one. She was deeply cyanosed and only semi-conscious. She also responded to neostigmine, and a thymectomy was attempted. On this occasion I certainly failed to remove the whole thymus gland, for after initial improvement she relapsed and she died a few weeks later. A second lobe of the gland, as large as the one I had removed, was found post mortem.

I find that altogether I have now operated on 21 children from the ages of 2½ to 16 (see table). 2 of these patients died soon after operation—not, it appeared, from respiratory paralysis, but rather from cardiac failure. Nothing was found post mortem that could easily account for their deaths. These cardiac failures may perhaps be explained by the work of Burn (1953) who has shown that the rhythmic contractions of the heart muscle are due to the local production of acetylcholine; it seems that the supply of acetylcholine may sometimes be deficient here too. 2 other children, including the one already mentioned whose death was due to my failure to remove the whole gland, died after an interval.

Of these 4 children, 3 were extremely ill and would not have survived for long without surgical interference. One of them was so ill that we thought it best to give her a preliminary course of deep X-ray therapy to the thymus gland. X-ray treatment in general does not meet with much success in myasthenia gravis. For this child it was rather a last resort, and she did appear to improve considerably during a long course which was interrupted more than once because she seemed to be getting worse instead of better; but in the end she did improve enough to make us think the operation could be done with reasonable safety. In this we were disappointed. The 4th child, aged 6, who died more than a year after operation, was very mildly affected when it

THYMECTOMY FOR MYASTHENIA GRAVIS IN CHILDREN

Age	Severity	Date of operation	Result
16	+++	June, 1944	A
4½	++++	November, 1945	B
2½	++++	February, 1946	Died June, 1946
15	+++	August, 1946	C[fB]
14	++	July, 1947	A
16	++	January, 1948	A
16½	++	May, 1948	A
16	++++	December, 1948	Died postop.
16	+++	November, 1948	B
16	++	March, 1949	A
14	++	April, 1949	C
15	++	July, 1950	A
10	+	December, 1950	A
12½	+++	March, 1951	Died postop.
7	+	April, 1951	B
16	++	May, 1951	A
5	+	December, 1951	A
6	+	March, 1952	A
14	+	September, 1952	Died April, 1953
12	+++	September, 1952	B[A]

Summary of results: A, 11; B, 4; C, 2; died, 4.

was done, the symptoms being mainly ocular. In spite of this she became steadily worse and finally died of the disorder—a striking example of the vagaries of this extraordinary disease. An incident of this kind suggests that, even if it is true that the thymus gland is responsible for initiating the disease, the process can sometimes still go on, after the responsible agent has been removed, until the abnormality becomes irreversible.

The 17 children who survived fortunately present us with a very different picture. 11 of them are perfectly well (A) and 4 more have only minor residual signs (B). 2 have experienced definite though not striking improvement. Over two-thirds, therefore, of this special category of myasthenic patient have completely recovered or almost so, most of them being beforehand extremely ill or obviously deteriorating. 5 of them were only mildly affected, but were submitted to operation because the physicians in charge regarded the disease in children as being usually progressive.

It is now some years since we have seen any children in the very acute phase of the disease that I have described in the 2 seen at Great Ormond Street. It is certain, however, that others have died without being diagnosed as suffering from acute myasthenia gravis. A striking example was described by Dr. Alwyn Griffith (1949). From the details of the description it was clear to me that myasthenia was the cause of death, and Dr. Griffith fully agreed when I drew his attention to this probability.

I hope the facts that I have given about these children are enough to convince even the most sceptical observers that thymectomy does have some influence on the course of the disease. It is difficult, for me at any rate, to believe that 15 of these 21 children would have had spontaneous remissions permanently of such degree if they had been treated only with neostigmine.

Laboratory Findings

It is now a good many years since attempts were first made to prove by laboratory experiment that the thymus was indeed an endocrine gland and was producing an active secretion responsible for the interference with the production of acetylcholine. It is ten years since Andrew Wilson, now professor of pharmacology at Liverpool University, working with Stonor (1954), showed that the serum of a myasthenic patient, when added to muscle-nerve preparations of a frog, could produce a block in neuromuscular transmission. This effect was not produced by serum from a normal individual and is not obtained with serum taken from a myasthenic patient under the influence of neostigmine. The same results were obtained using the sciatic-nerve/gastrocnemius-muscle preparation of the cat, and similar

observations have been made by other workers in the same field.

If, however, laboratory evidence was to be obtained to support the rationale of the operation of thymectomy, it was necessary to subject the thymus gland itself to suitable experiments. Over a number of years therefore, I sent all the glands removed from myasthenic patients to Professor Wilson to use as he thought best. He first had to find a solvent which would extract the active principle, if it existed, from the gland without destroying it or altering its properties. This he achieved by having the fresh glands immersed in acetone during transit from the operating-theatre and for subsequent storage, and then by extracting them with acetone, the simplest and most innocuous solvent. By this means Wilson (1953) obtained an active extract which showed consistent evidence of a neuromuscular blocking action on a variety of biological preparations, including the phrenic-nerve/diaphragm of the rat, and the sciatic-nerve/gastrocnemius preparation of the cat and hen. The extracts have also been tested on small animals such as chickens and mice with a positive result. The activity of the extract he found to be closely connected with the clinical result of the operation—that is to say, the most potent extracts were obtained from the glands of those patients who had benefited most from the thymectomy.

Wilson was careful not to claim that the thymus was necessarily the primary source of the active substance, but admitted that it might be merely a storage organ for something produced elsewhere. This seems, however, to be unlikely in view of the great clinical activity associated with the epithelial tumour of the thymus, for in these patients the disease is usually particularly rapid in onset, severe in its manifestations, and fatal in its outcome. It is difficult to imagine an epithelial tumour acting in these circumstances merely as a reservoir.

Professor Wilson has just informed me that he is satisfied now that he can produce not only paralysis in the muscle/nerve preparation of the cat and other species, but also a paralysis in animals which lasts up to twenty minutes after the intravenous injection of one dose. He also finds that thymus extract makes the muscle more sensitive to the effects of tubocurarine. He has used for some time the foetal thymus of the whale, for he finds that effects resembling those produced by extracts from the thymus of myasthenic patients are also produced by extracts from the foetal and infantile organ, though not from the thymus glands of normal adults. A film which he has made demonstrates the effects of thymus extract on chicks and mice in comparison with those of an injection of tubocurarine and decamethonium.

Conclusion

There are so many peculiar features in myasthenia gravis, and the disease is so variable, that too many second thoughts can lead to endless speculations, so that the mind becomes bemused with theory at the expense of facts. Let us, therefore, keep our gaze firmly fixed on what is definite—the fact that epithelial tumours of the thymus are usually associated with a specially virulent form of neuromuscular failure; that a large proportion of myasthenic patients are permanently and often completely relieved of their symptoms following thymectomy; and that these thymus glands can be made to yield a potent extract which repeats on the laboratory bench the nerve-blocking effect ordinarily obtained with tubocurarine. Second thoughts, with these facts kept in view, have not persuaded me to doubt that the operation of thymectomy is indeed the best hope for the sufferers from one of the most distressing and humiliating diseases to which human flesh is heir.

References at foot of next column

POTASSIUM DEFICIENCY IN CONGESTIVE HEART-FAILURE

THREE CASES WITH HYponatraemia, INCLUDING RESULTS OF POTASSIUM REPLACEMENT IN ONE CASE

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REPORTS of a low serum-sodium level (hyponatraemia) and resistance to mercurial diuretics in chronic cardiac failure have been increasing in the last three years (Squires et al. 1951b). The syndrome develops from several months to several years after the start of continuous mercurial therapy, and is usually first noticed when the patient ceases to respond with a diuresis to the administration of mercurials. The blood-urea level often rises, the serum-sodium level is low (105–125 m.eq. per litre=240–290 mg. per 100 ml.), and the patients usually have hypochloræmic alkalosis. Squires et al. have explained the hyponatraemia as due to the excessive loss of chloride resulting from the administration of mercurials, but patients who have received ammonium chloride also have hyponatraemia. Edema and congestive failure can be severe despite the low serum-sodium level. There have not yet been any reports of the syndrome in patients not treated with mercurials.

Clinically the patients often become confused and drowsy and have muscular weakness and cramps. The development of hyponatraemia is thought to carry a serious prognosis.

Squires et al. (1951a) found by balance studies in oedematous patients with heart-failure that there was depletion of intracellular potassium and overhydration, and that diuresis led to a loss of cellular water and a gain of potassium by the cells. These patients were not hyponatraemic. Iseri et al. (1952) found by direct tissue analysis a low intracellular potassium in cardiac and skeletal muscle of chronic cardiac patients, but they used necropsy material, and potassium is known to leave cells very soon after the death of the tissues (Winfield et al. 1951). On the other hand, Stock et al. (1951), using direct tissue analysis, found depletion of intracellular potassium in only 1 of 11 patients, none of whom, however, was seriously hyponatraemic.

Materials and Methods

All the balance calculations were made as described by Gamble (1951) and Squires et al. (1951a). The techniques of tissue analysis and calculations were those described by Darrow (1946). The constant diet offered to all the patients contained adequate calories and nitrogen and about 30 m.eq. of sodium, 25 m.eq. of potassium, and

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TABLE I—BALANCE STUDIES IN CASES 1 AND 2

Day in hospital	Levels in serum (m.eq. per litre)				Balance (m.eq.)		Volume of extra-cellular fluid (ml.)	Composition of muscle				Normal composition of muscle						
								Per 100 g. of fat-free dry solids				Per litre of intracellular fluid		Per 100 g. of fat-free dry solids		Per litre of intracellular fluid		
	Na	K	Cl	HCO ₃	Na	K		Na (m.eq.)	Cl (m.eq.)	K (m.eq.)	H ₂ O (ml.)	Na (m.eq.)	K (m.eq.)	Na (m.eq.)	Cl (m.eq.)	K (m.eq.)	H ₂ O (ml.)	
Case 1:																		
44	106.1	4.1	73.2	27.3	+38.9	-31.2	+346											
45	107.3	4.6	78.6	23.6	+34.2	-28.7	+315											
46	104.5	4.2	74.3	24.9	+33.7	-20.3	+221											
47	106.2	4.0	78.3	22.1	+31.9	-11.9	+197	9.43	5.43	22.1	397*	6.39	66.6					
Case 2:																		
31	120.3	4.9	87.4	28.3	+29.7	-26.2	+184											
32	115.6	5.9	80.2	24.2	+30.2	-24.3	+203											
33	110.8	5.4	81.6	23.7	+28.4	-21.0	+228											
34	113.4	5.1	82.3	26.0	+27.9	-18.7	+141	14.32	6.12	26.9	391†	18.61	84.1					

* 327.7 intracellular +69.3 extracellular.

† 316.7 intracellular +74.3 extracellular

about 40 m.eq. of chloride daily. The patients took a constant diet for three days before the electrolytes were measured on four successive days. Muscle biopsy, if any, was done on the last day of the balance study.

Case-histories

Case 1.—A male machine operator, aged 33, had three months' progressive breathlessness, palpitations, loss of appetite, and muscular weakness, but no orthopnoea, history of rheumatism, venous congestion, oedema, or cardiac enlargement. His blood-pressure was 130/75 mm. Hg.

On admission he was in a state of digitalisation, having recently received both digitalis and mercurials.

Course.—Severe congestive failure with oedema had developed by the thirteenth day in hospital, and ascites and oliguria by the eighteenth. 'Thiomerin' and aminophylline reduced his ascites and oedema by the twenty-eighth day. Electrocardiography showed right ventricular preponderance, depressed RST segments, flat T waves, a normal R-R interval, and ventricular extrasystoles. Diuresis fell off rapidly by the thirty-second day, and the serum-sodium level fell from 136 m.eq. per litre a week earlier to 106 m.eq. per litre. The serum-potassium and serum-urea levels were normal, but the serum-chloride level fell to 75 m.eq. per litre. The blood-urea level rose from 25 to 38 mg. per 100 ml. On the forty-fourth day in hospital an electrolyte-balance study was started, with muscle biopsy on the forty-seventh day (table i). The patient became more confused and weak during this period, and oral potassium was started as soon as the biopsy was done. He died suddenly next day, having received only 1 g. of potassium citrate.

Necropsy revealed interstitial pneumonia and pulmonary fibrosis; and death was presumed to have resulted from right heart-failure.

Case 2.—A married woman, aged 47, had a year's history of epigastric and substernal pain, followed by angina and dyspnoea. Ankle oedema and ascites appeared nine months later, for which she was treated with bi-weekly injections of 'Neptal.' These continued until after admission to hospital.

On admission there was severe congestive heart-failure with oedema. The blood-pressure was 185/115 mm. Hg. Electrocardiography showed an old posterior myocardial infarct.

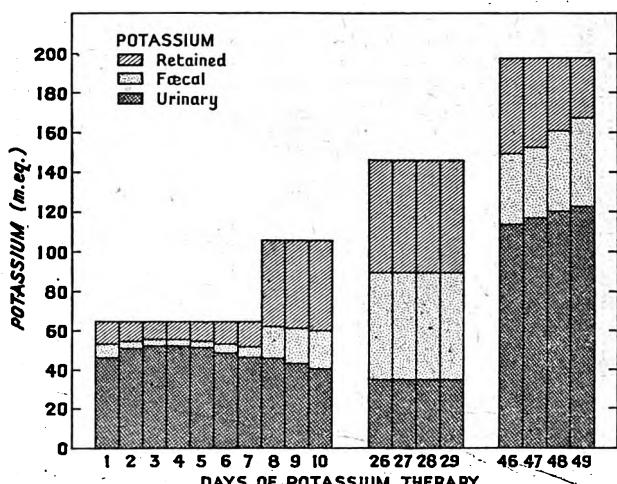
Course.—The patient's response to mercurials fell off within the first fortnight. By the fourteenth day in hospital her blood-urea level had risen from 41 to 64 mg. per 100 ml. and her serum-sodium level had dropped from 136 to 122 m.eq. per litre. The rest of the blood chemistry was normal except for hypochloraemia. Electrolyte-balance measurements were started on the thirty-first day, with muscle biopsy on the last balance day (table i), after which potassium therapy was started. The patient died quite suddenly and unexpectedly on the fourth day of potassium therapy, with a rapid feeble pulse and shock. Electrocardiography on the last day of life showed no change from before, her serum-potassium level was normal, and her pulse remained normal until several minutes

before death. She had received only 10 g. of potassium citrate in four days.

~ **Necropsy** revealed an enlarged heart and liver, with evidence of an old posterior myocardial infarct but no signs of fresh coronary thrombosis or pulmonary emboli.

Case 3.—A married woman, aged 38, had had "diphtheria" at the age of 8 years, but no history of rheumatic fever. She had had no disability until 1942, when dyspnoea with occasional swelling of her ankles developed. In 1948 ascites appeared and she was admitted to hospital where the diagnosis of congestive heart-failure with oedema and ascites was confirmed. She had the signs of mitral stenosis and aortic incompetence, with doubtful tricuspid stenosis, presumed to be of rheumatic origin. She had auricular fibrillation. At that time liver-function tests were normal, and the blood-urea level was 20 mg. per 100 ml. There was no evidence of renal impairment. The patient was digitalised and has so remained, and injections of neptal 2 ml. twice a week were started. Since 1948 she had been in and out of hospital for repeated aspirations of recurrent ascites. It is estimated that at least 1 litre of neptal had been given up to the end of 1953, during which time she had restricted her daily intake of fluids to two pints and had moderately restricted her intake of salt. On Oct. 29, 1953, she was readmitted to hospital in poor condition. By this time organic mercurial diuretics had ceased to be effective, despite the adjuvant use of ammonium-chloride.

On examination she had congestive heart-failure with gross ascites and a moderate right pleural effusion. There was auricular fibrillation with an apical rate of 76 a minute. The heart was enlarged. The blood-pressure was 115/60 mm. Hg. The patient was cyanosed and required oxygen.



Partition of administered potassium during the course of therapy in case 3: total height of each histogram represents total intake of potassium both as potassium citrate and potassium chloride and in the diet.

Investigations.—The urine contained no albumin or sugar, and its specific gravity was 1.026. Microscopy revealed occasional red blood-cells and epithelial cells. Liver-function tests were normal. The blood-urea level was 28 mg. per 100 ml. Electrocardiography showed auricular fibrillation, with RST depressions due to digitalis. Electrolyte balance-measurements were started on the twenty-eighth day, and muscle biopsy was done on the last balance day (table II) before potassium therapy began. A second muscle biopsy was done forty-nine days later at the end of another balance study. Potassium therapy was begun with potassium citrate 9 g. daily. Electrocardiograms were taken daily and the Q-T_c values calculated. The serum-potassium level was determined at intervals (table II). At no time was there any electrocardiographic evidence of potassium intoxication or

Progress.—The daily intake of potassium citrate was increased to 18 g. after eight days. The patient tolerated this higher intake of potassium without untoward effect. After twenty-three days she was changed to potassium chloride 9 g. daily; this was later increased to potassium chloride 12 g. daily. After about ten days' potassium therapy the patient greatly improved. She lost her orthopnoea and peripheral cyanosis, and she required fewer pillows and no longer any oxygen. She could get out of bed and be active about the ward during the day. Her peripheral oedema subsided, and her ascites accumulated less quickly. She was discharged on a maintenance dose of potassium citrate 2 g. daily.

Results

Table I shows the electrolyte balance and tissue analysis in cases 1 and 2. These patients were in consistent negative potassium balance and positive daily sodium balance. They had both recently finished mercurial diureses, and only case 2 had any peripheral oedema. The chloride space calculations showed that both patients were collecting extracellular fluid at the rate of 141–346 ml. a day despite their hyponatraemia. The serum showed a pronounced lowering of osmolarity (normal total base Na+K=150 m.eq. per litre) entirely because of low sodium and chloride levels. The serum-bicarbonate levels (expressed here as m.eq. per litre, the normal

range being 24–27) were normal. In the absence of accurate measurements of the pH of the serum an increased ratio of bicarbonate to chloride in the serum cannot be taken as indicating alkalosis. But, since the urine of these patients was more alkaline than usual (pH 6.9 to 7.4), with very little ammonia and titratable acidity, and since all the published cases of hyponatraemic heart-failure in which reliable measurements of the pH of the serum were made appeared to show alkalosis, it was assumed that our three patients were also alkalotic. This assumption was further supported by the finding of a gross deficiency of potassium in all three.

The composition of the biopsy specimen of striated muscle is expressed in tables I and II both as m.eq. per 100 g. of fat-free dry solids and per litre of intracellular fluid as indicated by chloride space calculations. The extracellular and intracellular water in the biopsy specimen is expressed as ml. of total water per 100 g. of fat-free dry solids. Our values for the composition of striated muscle (average of three healthy people) are shown in table I together with the values given by other workers. It can be seen that the biopsy specimens of muscle obtained from our patients showed extreme intracellular deficits of potassium and cellular overhydration, confirming the findings of Squires et al. (1951a). The amount of sodium per 100 g. of fat-free dry solids looks superficially normal; but, when correction is made for the hyponatraemia, it appears that intracellular concentration may be high normal (case 1) or abnormally high (case 2). Since various "normal" intracellular-sodium values have been published, and since neither case 1 nor case 2 could serve as their own controls, the question of changes in intracellular sodium will be considered in case 3, where there were two muscle biopsies, before and after potassium therapy.

The initial balance study in case 3 (table II) showed results similar to those obtained in cases 1 and 2. Case 3 was gaining about 30 m.eq. of sodium and losing

TABLE II—BALANCE STUDIES IN CASE 3

Day in hospital	Levels in serum (m.eq. per litre)				Balance (m.eq.)		Urine		Volume of extracellular fluid (ml.)	Composition of muscle						Remarks		
					Na	K	Na excreted	Volume (ml.)		Per 100 g. of fat-free dry solids				Per litre of intracellular fluid				
	Na	K	Cl	HCO ₃						Na (m. eq.)	K (m. eq.)	Cl (m. eq.)	H ₂ O (ml.)	Na (m. eq.)	K (m. eq.)			
27					+30.8	-36.7	-	497										
28					+30.7	-34.3	-	590										
29					+30.8	-28.6	-	583										
30	104.3	6.0	81.3	29.0	+31.0	-21.9	-	599	+212	16.71	18.78	6.05	457*	23.4	48.0	Failure, confined to bed		
31					+30.5	+10.1	-	594										
32					+30.6	+7.8	-	597										
33					+30.6	+6.5	-	601										
34					+30.6	+4.8	-	605										
35					+29.4	+7.9	-	709										
36					+28.7	+8.0	-	718										
37					+34.1	+40.3	-	720										
38					+16.6	+40.6	--	742										
39					+15.8	+41.9	-	752										
40	112.1	4.0	88.2	20.1	+17.1	+42.1	-	745	+104									
51	118.6	6.0	95.3	20.2												Potassium citrate 9 g.		
56					+18.7	+58.0	-	845										
57	120.2	6.0	98.5	19.9	+20.9	+57.4	-	863	+113.4									
58					+15.6	+59.3	-	880										
59					+12.4	+56.8	-	850										
65	140.3	6.7	106	28.6												Potassium chloride 9 g.		
71	142.5	5.8	113	26.7														
75	141.0	4.7	107	27.8												Potassium chloride 12 g.		
76					+10.8	+40.1	9.33	830										
77					+5.8	+36.1	13.42	1075										
78					+4.0	+28.6	9.82	872										
79	142.0	5.8	118	27.5	+4.1	+21.8	8.90	890	+27	10.77	40.8	9.1	366†	5.63	179			

* 382.7 intracellular + 74.3 extracellular.

† 289 intracellular ± 77 extracellular.

22-37 m.eq. of potassium daily. Muscle biopsy at the end of the balance study showed a severe intracellular deficit of potassium and overhydration, with a high value of intracellular sodium. If the muscle mass is about 80% of the total body mass, the total deficit of potassium is about 800 m.eq. As soon as potassium therapy was started, the patient went into positive potassium balance but continued to collect sodium at her previous rate. In view of the large deficit of potassium, a positive potassium balance of less than 10 m.eq. daily for the first week was surprising. Black and Milne (1952) and Fourman and Ainley-Walker (1952) have shown that repletion of potassium deficits is usually more striking; but they were studying healthy people who were depleted of potassium by a gastro-intestinal rather than a renal route. At the start of repletion of potassium case 3 was collecting extracellular fluid at the rate of 212 ml. a day, and both urine and faeces were sodium-free.

At the end of seven days' potassium therapy she showed no signs of potassium intoxication (pulse-rate and electrocardiogram unchanged), therefore her intake of potassium was raised to 103 m.eq. daily. She immediately went into a more strongly positive potassium balance and decreased the rate of sodium collection. The volume of urine increased from 500-600 ml. to 700-800 ml. a day, although both urine and faeces were still sodium-free. The rate of accumulation of extracellular fluid was reduced to 104 ml. a day. The serum-sodium level rose to 112 m.eq. per litre, and the patient began to improve clinically. Although she lost her peripheral oedema, ascites was still accumulating and she had to be drained.

When her intake of potassium was increased to 144 m.eq. a day, her positive potassium balance increased, her positive sodium balance decreased, the volume of her urine increased to 800-900 ml. a day, her serum-sodium level to 140 m.eq. per litre, and her serum-chloride level to 106 m.eq. per litre.

Her potassium intake was raised to 200 m.eq. a day three days before the last balance study. This produced completely normal serum chemistry, her positive sodium balance fell to 4 m.eq. a day, and her positive potassium balance fell to 20 m.eq. a day, indicating that she was becoming saturated with potassium. Since the balance was not studied throughout the repletion period, the cumulative potassium balance is not known, but it can be estimated that the patient retained about 800-900 m.eq. of potassium. At the end of the balance study only 27 ml. of extracellular fluid was accumulating daily, and, most important of all, sodium appeared in the urine for the first time in eighty days, amounting to 8-13 m.eq. a day. The daily volume of urine reached more than 1 litre for the first time in eighty days. Biopsy at this time showed muscle of normal composition, revealing that potassium repletion had increased the intracellular potassium and lowered the intracellular sodium and water. The intracellular total base increased considerably, while the amount of extracellular water in muscle remained the same. This latter observation indicates that the positive sodium balance went into the formation of ascites during potassium repletion.

The accompanying figure shows the daily partition of ingested potassium (represented by the total height of each column) into faecal and urinary excretion and retained portions in three balance studies during therapy. It shows that (1) in the presence of a renal loss of potassium a high intake of potassium for one or two weeks was necessary to establish a significantly positive balance; and (2) in the absence of significant renal failure (which often accompanies congestive heart-failure) the potassium that was not retained was excreted in the urine, protecting the patient to some degree against potassium intoxication.

Discussion

It must be emphasised that cardiac patients with hyponatraemia and resistance to mercurial diuretics are extremely ill and liable to die suddenly. Because of this, oral potassium therapy was started at a relatively low level, and maintained at this level long enough to make quite sure that there was no chance of potassium intoxication. During treatment bradycardia, prolonged Q-T values with raised T waves in the electrocardiograms, and a raised serum-potassium level were looked for. In the absence of any of these signs after several days on a given dosage, it was felt safe to increase the potassium intake. The importance of this careful procedure and the firm establishment of potassium deficiency before starting potassium therapy cannot be overemphasised.

It is well known that patients accumulating oedema excrete little or no sodium in their urine. In the presence of a relatively normal anion excretion, increased excretion of cations other than sodium would result. If some potassium loss is sustained because of this and alkalosis results (Black and Milne 1952), or if mercurial diuretics have produced alkalosis (Squires et al. 1951a), the excretion of urinary titratable acidity and the formation of urinary ammonia would be inhibited (Pitts 1950). This in turn would accelerate the loss of cations other than sodium, ammonia, and hydrogen ion. Therefore the combination of a lack of sodium excretion and alkalosis might well lead automatically to potassium depletion. The fact that extreme potassium depletion has been observed in patients who have had vigorous mercurial therapy suggests that mercury may play some part in accelerating this mechanism, either at a renal tubular level or perhaps even directly at a cellular level. There was some increase in intracellular sodium, and a possible mechanism for this has been discussed by Cooke et al. (1952).

We have also confirmed the observation of Squires et al. (1951b) that there is gross overhydration of cells in this syndrome. It appears difficult to attribute this to increased cellular osmolarity, and an alternative mechanism involving water extrusion from cells has been suggested by Robinson (1950) and Deyrup (1953).

The presence of any degree of renal insufficiency will complicate any attempt at potassium therapy, because of the increased danger of the accumulation of extracellular potassium before potassium is transferred into the cells. This should be taken not necessarily as a contraindication to therapy but as a reason for even more caution than would otherwise be required.

A low intracellular potassium content or, for that matter, any intracellular electrolyte disturbance cannot be considered as an isolated abnormality. Potassium is bound in part to glycogen and protein within the muscle-cell, and an electrolyte abnormality will probably indicate a more widespread biochemical disorder. An intracellular potassium deficit will not ensure a rapid uptake of administered potassium by cells, and the absence of a strongly positive potassium balance immediately after the start of potassium therapy does not indicate the absence of intracellular potassium deficiency (Black and Milne 1952).

A most significant feature was the appearance of sodium in the urine as the saturation point of cellular potassium was approached. This may have been merely because of the rise of serum-sodium level as potassium displaced sodium in the cells, but it must be noted (table II) that the serum-sodium level rose one or two weeks before sodium excretion began. We are inclined to the view that this excretion was due to more than the mechanical result of increased sodium filtration at the glomerulus. The sodium excretion was well correlated with the dramatic fall in the rate of accumulation of extracellular fluid (chloride space). The dietary intake of

sodium does not affect the response, since there was no change in the sodium intake during the development of and the recovery from hyponatraemic failure and potassium deficiency.

At no time did these patients show the usual electrocardiographic signs of potassium depletion. Digitalis effects could have masked these, but it remains to be seen what correlation such changes have with intracellular levels of potassium in cardiac muscle.

A low serum-sodium level does not necessarily mean sodium depletion, and, if oedema is present, the amount of total body-sodium may be abnormally great. The administration of sodium to hyponatraemic patients not excreting sodium will do little more than increase the oedema.

Squires et al. (1951b) found that congestive failure without depressed serum-sodium levels could also involve potassium deficiency. Hyponatraemia appears to be an end-stage of a prolonged loss of potassium either complicated or caused by the administration of mercurials, and it is more than likely that potassium deficiency plays a part in the clinical picture of congestive failure and masks the true extent of debility caused by haemodynamic insufficiency alone. The question may be raised whether attention to potassium balance should play a more important part in the treatment of congestive failure. Case 3 seems to show that considerable clinical improvement may result from correction of potassium imbalance.

Summary

Three patients with congestive heart-failure, resistance to mercurial diuretics, and hyponatraemia were submitted to electrolyte balance studies and electrolyte tissue analysis of muscle-biopsy specimens.

These studies showed a large deficit of potassium and overhydration in the cells. The sodium content of the cells was also probably increased.

One of these patients was treated with a high-potassium intake and the maintenance of digitalisation but no mercurials. Balance studies were continued during therapy, and a second muscle biopsy was done fifty days after the first. Potassium therapy was associated with the following changes: the electrolyte and water composition of muscle was completely corrected, oedema was decreased, cyanosis disappeared, there was considerable clinical improvement, hyponatraemia was corrected, and sodium began to be excreted in the urine.

The rôle of potassium depletion in the clinical picture and in the treatment of congestive failure is discussed, and its possible significance in the development of hyponatraemia is pointed out.

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SYNDROMES OF RHEUMATOID ARTHRITIS

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RHEUMATOID arthritis may begin in many ways. Of particular interest in a recent series of 750 cases were those of hyperacute, monarticular, and episodic onset and those that began and progressed for years with complete absence of pain.

Acute Arthritis

In 38 of the 750 cases the onset of rheumatoid arthritis was so acute as to resemble rheumatic fever. In 10% of the whole series a past history of rheumatic fever was given. The attacks often followed within two weeks of a throat infection, but in only 1 did rheumatic carditis develop, and each progressed later into typical rheumatoid arthritis.

Case 1.—A man, aged 25, developed acute rheumatism and pericarditis after a sore throat, and four months later multiple evanescent nodules appeared, together with mitral and aortic disease. Gradually wasting of the interossei became apparent, and radiography showed generalised osteoporosis. Biopsy of a nodule showed a picture rather intermediate between that usually seen in rheumatic fever and that of rheumatoid arthritis (fig. 1). The patient eventually died of congestive heart-failure eight months after the onset of the illness. No necropsy was done.

A second case developing carditis has since been seen. After a typical onset of rheumatoid arthritis at the age of 29 there was a gradual remission, and then, after an acute episode eight years later, mitral stenosis and aortic disease appeared. The normality of the heart before the acute episode was agreed after full cardiological examination.

An acute onset immediately introduces the differential diagnosis of rheumatic fever, gout, gonococcal arthritis, and septic arthritis. In gout (see below, under "Episodic Rheumatoid Arthritis") the diagnosis is not likely to be long in doubt, but the therapeutic test with colchicine will help, except in the occasional case where both gout and rheumatoid arthritis coexist. In gonococcal arthritis and septic arthritis the therapeutic use of antibiotics will assist in diagnosis. Only in the differential diagnosis from rheumatic fever in adults may serious difficulty arise when salicylates fail and no past history of juvenile rheumatism has been elicited.

Rheumatic fever in younger people is often followed by rheumatic pains and minimal periarticular swelling, and by occasional acute episodes in later life. Such cases seldom progress to true rheumatoid arthritis (Kersley 1939), but there are exceptions—e.g., case 1.

The cardiological picture in rheumatoid arthritis is still confused. Clinically heart lesions in any way resembling those of rheumatic fever are uncommon in rheumatoid arthritis, but at necropsy lesions resembling those of rheumatic fever are found in a high percentage of cases (Bayles 1943, Fingerman and Andrus 1943, Rosenberg et al. 1943). Jonsson (1952) on careful clinical cardiological examination found some heart abnormality in 30% of rheumatoid arthritics compared with 8% of controls.

Though rheumatoid arthritis and rheumatic fever are normally quite distinct, being completely different in clinical course, cardiological complications, prognosis, and therapy, occasional borderline cases should make us wary of regarding them as separate entities.

Monarticular Cases

When only one joint is involved, the differential diagnosis from tuberculosis must be considered. In 11



Fig. 1.—Section of nodule from case 1, clinically and histologically borderline between rheumatoid arthritis and acute rheumatic fever.

cases this question was raised at some stage of the disease. The erythrocyte-sedimentation rate (E.S.R.) was somewhat increased in all these cases. 2, after a lag of a year, developed signs in other joints and became typical rheumatoid arthritis. In 2 the diagnosis was proved to be rheumatoid arthritis by biopsy, and 1 developed into ankylosing spondylitis. In 2 a tuberculous focus in the synovial membrane was discovered. In the remaining 4 cases the diagnosis has not been proved, but they are thought to be oligarticular rheumatoid arthritis.

Case 2.—A woman, aged 28, was diagnosed as having a tuberculous right knee at the age of 14—this was arthrodesed. At the age of 17 the right elbow became painful, was considered to be tuberculous, and was allowed to stiffen. At the age of 27 the left knee became swollen and slightly painful. The E.S.R. was 80 mm. in 1 hr. and haemoglobin 72%. Radiographs were reported as showing arthritis, either rheumatoid or tuberculous.

Operation and Findings.—A synovial biopsy specimen was typical of rheumatoid disease. On synovectomy the synovial membrane was found to be hypertrophied and there were early articular erosions at the synovial fringes. Histologically the synovial reaction was, in general, that of active rheumatoid arthritis. There was villous proliferation, fibrosis, and thickening of the synovia, with Allison-Ghormley foci. There were, however, small foci of early necrosis and epithelioid reaction, in one of which a giant cell was found, these foci suggesting tuberculosis (fig. 2). No acid-fast bacilli were found.

Follow-up.—The result of the synovectomy was satisfactory, and after the usual post-operative manipulation a good range of painless movement has been obtained a year after the operation. The E.S.R. is 16 mm. in 1 hr., and the patient feels fit and maintains her

improvement in spite of going out to work and running her home. For the last three months, however, she has had slight pain, stiffness, and minimal swelling of the proximal interphalangeal joints of the second right and third left digits of the hands. Radiography shows no abnormality.

Case 3.—A man, aged 25, developed slight pain and swelling of the left elbow at the age of 15 and had had only 20° of movement since. A year later his left knee became painful and swollen, and then gradually improved, though it swelled up again on any strenuous exertion. Gold therapy seemed to help the condition. At the age of 24 the E.S.R. was 21 mm. in 1 hr., and radiographs were reported on as "arthritis, pathology doubtful." The condition was considered to be rheumatoid, and surgery decided on.

Operation and Findings.—The head of the ulna was removed and found to be severely eroded, and its synovium hypertrophied and pallid. Synovectomy was done at the same time on the knee, and here there was polypoid proliferation of the synovium, with pannus invading the femoral cartilage. The condition was still considered by the orthopaedic surgeon to be rheumatoid, but microscopy showed that the whole of the cartilage of the radius had been replaced by inflammatory fibrous tissue containing fibrinoid, and there was one large tuberculous focus. The synovial membrane of the knee showed many tuberculous foci with giant cells (fig. 3). Both knee and elbow were submitted to fusion operations. Since then there has been no pain, the patient's general condition has improved, and he has gained 3 stone in weight; and his E.S.R. is now 1 mm. in 1 hr.

Some monarticular cases in children and in adults are undoubtedly rheumatoid arthritic, as proved by surgery and by the subsequent course of the disease, but occasionally biopsy shows a few typical tubercles when rheumatoid arthritis has been diagnosed with considerable confidence. It is very important in this connection to remember that microscopy of a small biopsy specimen may be extremely misleading.

Poncet (1902) described "rhumatisme tuberculeuse," and Copeman (1936) has reviewed the subject in the light of modern thought. Tuberculous rheumatism is usually divided into two types; acute (very similar to rheumatic

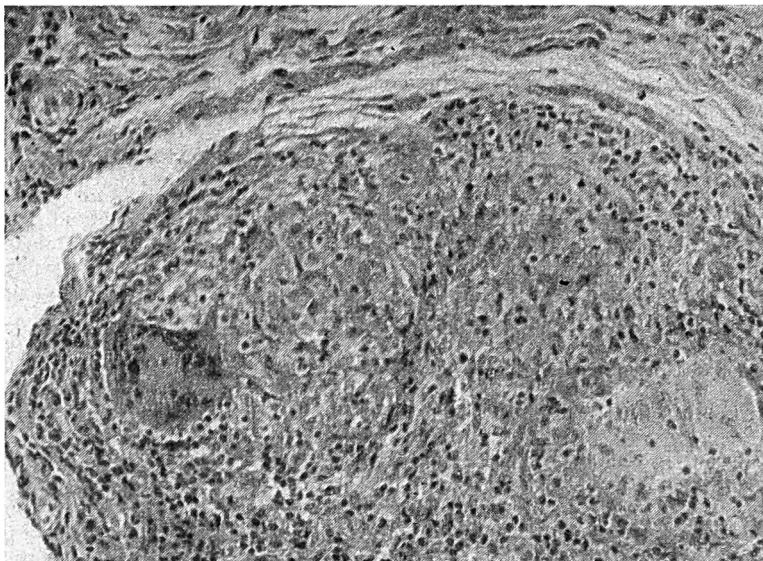


Fig. 3.—Section of synovial membrane from case 3, diagnosed as rheumatoid arthritis, but histology showing definite tubercles.

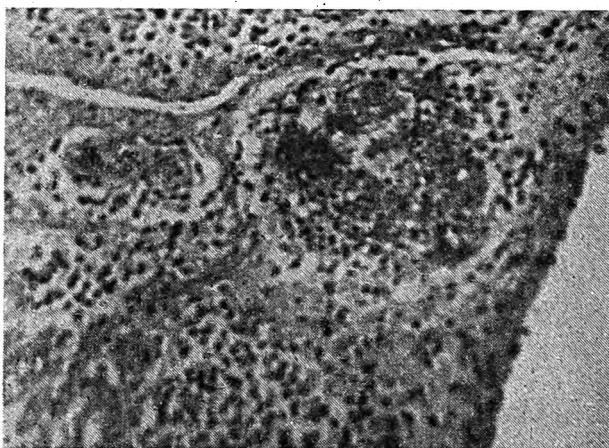


Fig. 2.—Section of synovial membrane from case 2, diagnosed first as tuberculous and then as rheumatoid. Histology mainly of rheumatoid type with one small focus of necrosis and one giant cell suggesting tubercle.

fever) and chronic (resembling rheumatoid arthritis). Suggested criteria for the diagnosis of tuberculous rheumatism are atypical rheumatoid arthritis, with a strong family history of tuberculosis; hypersensitivity to tuberculin; fever; fatigue; and, possibly, definite tuberculosis in a joint. It has been thought by some workers that a chronic leakage of toxic material may produce inflammation in a sensitised joint—possibly in the same way as rheumatoid arthritis is said to arise after gonorrhoea, when the joint shows no signs of specific infection. Fletcher (1951), however, on biopsy and joint culture of 5 cases of rheumatoid arthritis with active tuberculosis, found no evidence of tuberculosis in the joints examined. Moreover Dickson (1936) pointed out that, in true tuberculosis of joints, more than three joints are affected in 5% of cases. Ropes and Bauer (1953), from examinations of synovial fluid from tuberculous joints, found that the lowered sugar content was one of the most striking differences from rheumatoid fluid, but even the sugar level was normal in 4 of 24 fluids. The viscosity was often a little lower, and there were more red cells, in many tuberculous fluids, but neither of these findings was in any way pathognomonic. In their series 21 of 28 gave a positive guinea pig test, and all of 13 cases in which biopsy was done gave histological evidence of tuberculosis. These results were, however, in clear-cut tuberculous conditions rather than in early doubtful cases. There seem to be two distinct problems; the differential diagnosis of monarticular rheumatoid arthritis from tuberculosis, and the possible interrelationship of tuberculosis and rheumatoid arthritis. In this connection we should recall the effect of tuberculosis on experimental allergy, its possible effect as a stress factor, and the suggested interrelationship of silicosis, tuberculosis, and rheumatoid arthritis in Caplan's (1953) syndrome. When, however, tuberculous and rheumatoid foci appear side by side in the same joint, it is difficult to avoid the conclusion that the situation may not be fortuitous, and that the "rheumatoid" reaction may in some cases be due to some non-specific reaction of the joint to a sensitisation to tubercle.

Episodic Rheumatoid Arthritis

The episodic onset of rheumatoid arthritis raises the differential diagnosis from gout, palindromic rheumatism, and intermittent hydrarthrosis. The diagnosis from gout does not stay long in doubt, except where both conditions coincide.

In the present series 13 cases were episodic and could be subdivided into three groups: (1) in 3 males radiography and a raised plasma-uric-acid level suggested

gout, but concomitant rheumatoid arthritis was proved by biopsy; (2) in 5 cases the E.S.R. and the radiographic appearances were persistently normal, and in 1 other the E.S.R. was raised on one occasion out of four examinations; and (3) in the remaining 4 cases there appeared to be definite rheumatoid exacerbations with almost complete remissions lasting on an average about a month.

When gout and rheumatoid arthritis are combined, both diagnosis and treatment are difficult.

Case 4.—A man, aged 51, had for two years had acute attacks of pain and swelling in his feet, ankles, and index finger, followed by complete remissions. He appeared to improve both on colchicine and on gold. Both his E.S.R. and plasma-uric-acid level were raised. Radiography suggested gout, but synovial biopsy showed typical rheumatoid arthritis. Gradually the remissions became less complete and the rheumatoid picture became apparent.

It is, however, the differential diagnosis from palindromic rheumatism and hydrarthrosis that is really difficult.

Case 5.—A girl, aged 18, had developed at the age of 10 pain and swelling of her right knee for about a week; this recurred each year till the age of 16. Radiographs were persistently normal. The E.S.R. in 1946 was 3 and 5 mm. in 1 hr., in 1950 32 mm. in 1 hr., and in 1953 again normal—8 mm. in 1 hr. For two years there had been no symptoms.

Case 6.—A woman, now aged 53, had had rheumatic fever at the age of 17 and then remained well until the age 49. She then, after hysterectomy, began to have attacks of severe pain and swelling in her left knee, lasting about twelve hours every twelve days. This condition persisted for two years. The E.S.R. and radiographs were normal.

Treatment.—Synovectomy cured the local condition. The synovial membrane was typical of rheumatoid arthritis. Shortly after the operation attacks of pain and swelling began in the right knee, occurring again every ten to twelve days and lasting three days. These attacks were completely controlled on two occasions by courses of chrysotherapy, relapse occurring when gold was withheld. During the last course dermatitis ensued, prohibiting further chrysotherapy. Sodium gentisate 10 g. daily and 'Mobilene' (diacetyl-pyrocatechol) 2.5 g. daily both seemed to reduce the severity of the attacks. Procaine injected into the joint had no effect; nor had a course of phenylbutazone 600 mg. daily. Cortisone 100 mg. daily for two weeks did not prevent the attacks, but they were less severe. Corticotrophin 50 mg. aqueous solution and 50 mg. gel at the onset of an attack and thereafter 50 mg. gel daily eased but did not prevent an attack or hasten its resolution. Intra-articular hydrocortisone 50 mg., however, cut short an attack within an hour.

Follow-up.—Now, seven years after the onset of the condition, at the age of 56, radiography shows only slight osteoarthritic changes, and the E.S.R. is only 4 mm. in 1 hr.

Palindromic rheumatism, first described by Hench and Rosenberg (1941), consists in recurrent attacks of articular and para-articular inflammation lasting hours or days, with complete resolution, no constitutional disturbance and, even after hundreds of attacks, no residual radiographic or pathological abnormalities. The joint changes are those of acute inflammation with polymorph reaction. Wolfson and Alter (1948) collected 52 published cases, but some of them did not meet all the above-mentioned criteria. Men and women were affected in equal proportions, and the age-distribution was from 13 to 68. Bywaters (1949) described 3 cases resembling palindromic rheumatism but exhibiting some features of rheumatoid arthritis or of generalised lupus, and he remarked that "pigeon-holing . . . is a necessity for the clinician in his general craft but a hindrance in the pursuit of truth." Boland and Headley (1949) claimed that chrysotherapy was beneficial. Two somewhat similar syndromes are the angioneurous arthrosis of Solis-Cohen (1914) and the allergic arthritis of Kahlmeter (1939).

Intermittent hydrarthrosis, described by Perrin (1845), is distinguished by the regularity of the recurrence of the arthritis and by the fact that usually only one or two joints are affected. Ropes and Bauer (1953) found the

synovial fluid similar to that seen in mild rheumatoid arthritis, containing fewer red cells and polymorphs than are seen in the average rheumatoid fluid. Cohen (1948) states that it may eventually progress to a typical rheumatoid condition.

Episodic rheumatoid arthritis is difficult both to diagnose and to treat, but gold is well worth a trial; synovectomy may be considered, and hydrocortisone may be used to terminate an episode.

Arthritis Without Pain

In 5 of the 750 cases the rheumatoid arthritis was painless. In each case, as might be expected, there was gross destruction of bone and joint but no evidence of any neurological disease. Apart from the lack of pain the lesions appeared typical in every way. In 2 cases where the painless arthritis had been confined to the wrists and hands, pain developed twenty-four and sixteen years later, when the ankles became involved.

Case 7.—A man, aged 57, had had grossly swollen wrists (fig. 4) for sixteen years but had continued to work as a carpenter without any pain. For a year painful swelling of the ankles had been present, the wrists still remaining painless. The E.S.R. was 58 mm. in 1 hr. Radiography showed gross rheumatoid destruction of the wrists, and biopsy a typical rheumatoid synovial membrane.

Case 8.—A man, aged 50, had had an increasing number of rheumatoid nodules on his fingers (fig. 5) since the age of 19. Only for a year had he had any pain, which had then developed in his hands, feet, and knees. His E.S.R. was 35 mm. in 1 hr.

Whether the absence of pain can bear any relationship to rheumatoid lesions of the perineurium, as described



Fig. 4.—Wrists and hands which have been swollen for 16 years with complete absence of pain (case 7).

by Morrison et al. (1952), seems very doubtful. In our cases several painless joints were present at the same time, and yet there was no obvious neurological lesion.

The variation of degree of pain experienced with swollen joints has previously been noticed in gonococcal arthritis (Kersley and King 1942) and seems to be out of proportion to normal variability of pain sensitivity. The occurrence of pain in 2 cases later when further joints were involved certainly rules out any question of the general threshold of pain playing any major part in this phenomenon.

Summary

Of 750 cases of rheumatoid arthritis in adults 38 began so acutely that rheumatic fever was considered in the differential diagnosis. Only 1 developed carditis resembling that of rheumatic fever.

In 11 monoarticular cases the diagnosis of tuberculosis arose, and in 2 of them small tuberculous foci were found rather unexpectedly in the synovial membrane.

13 cases were episodic. Their diagnosis and treatment is discussed.

5 cases progressed for years without any pain, but 2 of them developed pain twenty-four and sixteen years later with a subsequent exacerbation of arthritis.

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VOMITING AND REGURGITATION DURING ANÆSTHESIA

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VOMITING has been defined as the forcible expulsion of stomach-contents into the pharynx. Physiologically, the mechanism of vomiting consists in a series of coördinated movements as a result of which a relaxed stomach is squeezed between the descending diaphragm and contracting abdominal muscles (Best and Taylor 1950). This mechanism is governed by a centre in the medulla, which may be influenced by impulses arising in the stomach or any other viscous, or in practically any region of the body. It may also be excited by substances carried in the blood-stream. The centre may be depressed by general anaesthetics, and the peripheral mechanism paralysed by relaxant drugs.

Regurgitation, on the other hand, may be regarded as a passive process (Morton and Wylie 1951) depending entirely on differences of hydrostatic pressure between the stomach and the pharynx. Thus, if the patient is in a head-down position and the cardia and the circumpharyngeal orifices are open, any fluid in the stomach

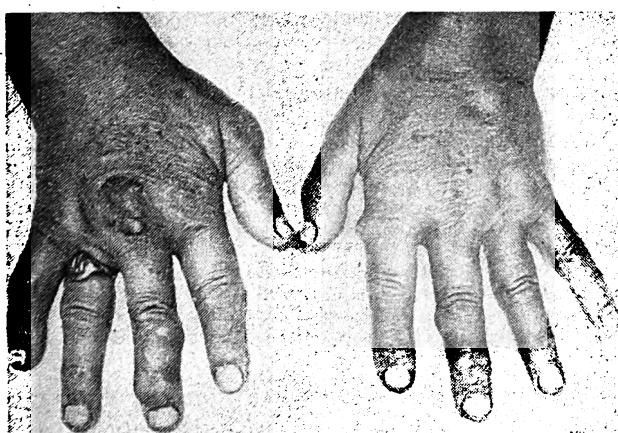


Fig. 5.—Rheumatoid nodules, gradually increasing in number for thirty years, with complete absence of pain until last twelve months.

will flow into the pharynx. Morton and Wylie therefore advocate that the foot-down tilt be adopted before inducing anaesthesia with thiopentone and muscle-relaxants in patients whose stomachs may not be empty. Presumably the assumption is that the hydrostatic pressure within the stomach is insufficient to force the stomach contents, against gravity, up to the level of the vocal cords when the abdominal muscles and the diaphragm are paralysed.

The present investigation was undertaken to test the safety of the above technique and to study the mechanism of vomiting and regurgitation during anaesthesia.

Method

The investigation was made on conscious volunteers and on patients undergoing anaesthesia for various operations. 'Polythene' tubes 1-2 mm. in diameter were passed into the stomach in the conscious volunteers and in the patients after anaesthesia had been induced. A slow steady flow of saline was maintained through these tubes to prevent blocking. Pressure recordings were made directly on a water manometer, or by a tambour on a moving drum. The necessary adjustments were made for differences in hydrostatic levels and for resistance to the flow of saline. *d*-Tubocurarine chloride and succinylcholine chloride were the relaxant drugs; hexamethonium bromide and 'Arfonad' [*d*-3,4(1',3'-dibenzyl-2'-keto-imidazolido)-1,2 trimethylene thiophanium *d*-camphor sulfonate] were used as ganglion-blocking agents. The cardia was infiltrated with 1 : 1000 amethocaine hydrochloride from within the abdomen; this was deposited in the subperitoneal area of cardia and oesophagus. Saline solution was used in all cases to fill the stomach to the extent of 500-1000 ml.

Results

FACTORS AFFECTING INTRAGASTRIC PRESSURES

The accompanying table shows average readings of gastric tone expressed in cm. H₂O in two groups of people: (1) those with distended abdomens—e.g., due to gravid uterus—in the supine position; and (2) those with concave abdomens in the supine position.

The intragastric pressures contrast strongly in the two groups, and are also affected differently by anaesthesia, relaxants, and posture. The table shows the enormous increase in the intragastric pressure obtained in group 1 (people with distended abdomens) by the adoption of the lithotomy position. In group 1, when totally paralysed, patients showed very little drop in pressure on the adoption of 20% foot-down tilt, and in one full-term pregnancy the pressure did not drop below 10 cm. H₂O.

FACTORS AFFECTING CARDIA

Muscle Relaxants.—Nine patients were anaesthetised with small doses of thiopentone (250-500 mg.) and full doses of muscle-relaxant. After the trachea had been intubated with a cuffed endotracheal tube, the stomach was filled with 500-1000 ml. of saline solution. Pressure was applied to the abdomen with sandbags so that a

AVERAGE READINGS OF GASTRIC TONE (CM. H₂O)

Group	Awake	Light anaesthesia	Deep anaesthesia	Total paralysis				
				Supine	Foot-down 20%	20° Trendelenburg	Lithotomy	
1 (ten people)	From +5 to +18	From +2 to +18	From +5 to +15	+9	+6	+12	+15	
2 (twelve people)	From -2 to +5	From -2 to +5	From -2 to +3	-3	-5	+2	-2	

constant intragastric pressure of 15-20 cm. H₂O was maintained throughout the experiment. The tube was withdrawn from the stomach. The patient was tipped head-down, the pharynx and upper oesophagus were sucked dry, and the table was levelled again. The subjects were then ventilated for 3-5 minutes, after which the table was again tipped and the pharynx and upper oesophagus were examined for the presence of saline solution; in no case was any detected. Saline solution was now aspirated from the stomach to confirm that it had not emptied during the experiment.

Three patients underwent oesophagoscopy after these observations, and no fluid was seen in the oesophagus until the cardia was broached (see below). A number of other patients underwent laparotomy for various reasons, yet the surgeons could not empty the gastric contents into the oesophagus by manual compression of the stomach. The intragastric pressure recorded in one of these patients amounted to 19 cm. H₂O—a figure which is well above the highest pressure recorded in paralysed subjects in the supine position (see table).

Ganglion-blocking Drugs.—Ten subjects were treated as just described, and ganglion-blocking drugs were given until the blood-pressure could not be further reduced. This was taken as evidence of autonomic block, though it could not be accepted as being total. Systolic blood-pressure of 40-60 mm. Hg were recorded in most cases. Under these conditions the previously mentioned manipulations failed to empty the stomach, even if full doses of muscle-relaxant were injected as well.

Local Analgesia.—In this group of subjects local analgesia of the cardiac region of the stomach had no effect on the integrity of the cardiac valve.

Attempts to Make Cardia Incompetent

From these experiments it may appear that true regurgitation from the stomach into the oesophagus does not occur in normal people, and that when, for example, the vomiting centre is put out of action by general anaesthetics, the stomach cannot empty its contents into the oesophagus. This, however, is not so.

The cardia was made incompetent in two patients in the following way:

After preliminary endotracheal intubation under thiopentone and suxamethonium each patient was run on fairly deep cyclopropane anaesthesia but with spontaneous respiration. The stomach was next filled with saline solution, as in the earlier experiments, and attempts were made to mimic the somatic contribution of normal vomiting by increasing the intra-abdominal pressure (see above) and at the same time obstructing the airway while the diaphragm was descending during inspiration.

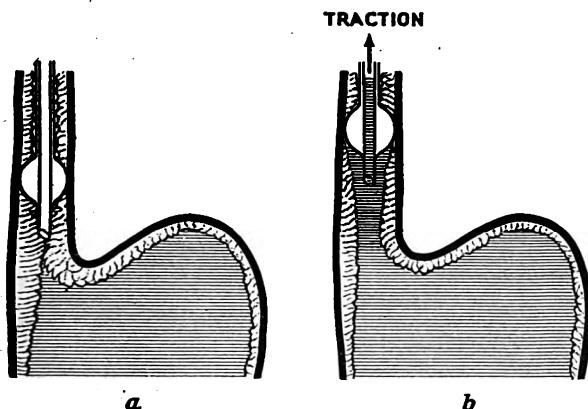
On every occasion saline solution was aspirated or pushed (or both) into the oesophagus at each attempted inspiration. This fluid was recovered from the oesophagus but did not appear in the pharynx under these conditions (see below), and during oesophagoscopy on one of the patients the reflux was very well demonstrated during attempted inspiration.

In a further three patients the cardia was made incompetent by the following manoeuvre:

A double-lumen tube, with a distensible balloon at the lower end and a terminal opening, was placed in the oesophagus, the end of the tube reaching to within an inch or two of the oesophageal opening in the stomach. The balloon was now distended with about 40 ml. of saline solution. Traction on this tube stretched the very friable mucous layer of cardiooesophageal junction (see figure) and allowed saline solution to flow from the stomach, and this fluid was collected from the inner tube. When the traction was discontinued, the fluid ceased to flow. This was repeated several times in each patient.

FACTORS AFFECTING CRICOPHARYNEAL SPHINCTER

In the first set of experiments the patients were anaesthetised to light surgical anaesthesia with cyclopropane and oxygen, intubated, and had their stomachs



Method of rendering cardiac valve incompetent with double-lumen tube and distensible balloon : a, balloon inflated and cardiac valve intact ; b, traction applied to tube puts cardiac valve out of action and allows fluid to pass upwards from stomach into inner tube.

filled with saline solution as described above. The abdomen was then compressed until a reading of more than 10 cm. H₂O was attained, after which the stomach-tube was withdrawn into the oesophagus and 200 ml. of saline solution was introduced. The oesophageal tube was withdrawn, and the fluid was retained in the oesophagus because the pressure in the stomach was already so high.

There was no leak into the pharynx when the quantity of fluid was limited to approximately 200 ml., even in the Trendelenburg position. A slight leak took place, however, when fairly strong manual pressure was applied to the rebreathing-bag, presumably owing to pressure of the lungs on the oesophagus. When the anaesthesia was deepened, or when a small dose of muscle-relaxant was given, there was a considerable leak when the head-down position was adopted or when slight pressure was applied to the rebreathing-bag.

In the second set of experiments the patients were anaesthetised with thiopentone and succinylloholine chloride intubated with a cuffed tube, and maintained on nitrous oxide and oxygen. The pharynx was filled with saline solution, and the endotracheal tube cut so that about an inch protruded from the mouth. The face-mask of the anaesthetic machine was now applied, incorporating the endotracheal tube within the mask. Strong inflation of the lungs under conditions of total paralysis produced by succinylloholine chloride did not force any detectable quantity of fluid into the oesophagus. When the paralysis had completely worn off, spontaneous respiration against strong resistance at the expiratory valve (thereby raising the intrapharyngeal pressure) also failed to make the fluid disappear from the pharynx. When the patient was made to gag, however, some of the fluid disappeared into the oesophagus. Ball-valving of the tongue in the pharynx was excluded as an explanation of these findings, because the same results were obtained when a pharyngeal airway was in position.

It was thought dangerous to raise the pressure in the pharynx without raising the intratracheal pressure at the same time, even though a cuffed endotracheal tube was in place, in case a leak should take place round the cuff. Instead, the endotracheal tube was obstructed during inspiration, thereby giving an appreciable pressure difference between the fluid in the pharynx and the oesophagus, and in these circumstances there was no apparent loss of fluid from the pharynx.

Discussion

From this investigation it appears that the technique of Morton and Wylie (1951) for the induction of anaesthesia in patients whose stomachs are not empty is safe, because the cardia is not made incompetent by

total somatic paralysis. If the cardia were incompetent, the intragastric pressure would not remain high enough to force fluids against gravity up to the level of the vocal cords unless the abdomen were greatly distended.

There are, however, some points concerning this technique which require notice.

Vomiting may occur after sleep has been induced but before the relaxant has had time to take effect. If this happens, the gastric contents may be in the mouth and pharynx when paralysis sets in ; and as they cannot run back into the oesophagus they will tend to run down into the trachea. This complication may be minimised by giving the relaxant before, with, or immediately after thiopentone if this agent is used for induction, so that sleep and relaxation come on simultaneously. If an inhalation technique is used instead of thiopentone, the relaxant must be given as soon as consciousness is lost.

The fact that the cardiac valve may be made incompetent by simple obstruction of inspiration is important, since this can easily happen under anaesthesia. Thus inspiratory stridor, or obstruction of the airway by "ball-valving" of the tongue in the pharynx, may lead to aspiration of stomach contents into the oesophagus with each inspiratory effort, especially when the intra-gastric pressure is high, as in the lithotomy position (see table). This may explain the frequent occurrence of regurgitation during anaesthesia for obstetric manoeuvres.

The oesophagus is normally empty although its pressure is lower than that in the stomach and pharynx, owing to the cardiac valve and the cricopharyngeal sphincter. It may, however, contain material under certain conditions : (1) incompetence of the cardia, which may result from diaphragmatic hernia, neoplasms in the region of the cardia, and various operations such as cardioplasty for achalasia ; (2) obstruction of the cardia or of the oesophagus (e.g., neoplasm, and by achalasia) ; and (3) oesophageal diverticulum. Further, owing to the distensibility of the oesophageal walls a large quantity of fluid can be kept in the oesophagus without much increase in intra-oesophageal pressure. While the patient is conscious or under light anaesthesia, this material is prevented by the intact cricopharyngeal sphincter from entering the pharynx. If the sphincter is paralysed, however, the angle of elevation of the head and shoulders and hence simple gravity determine whether the pharynx is flooded or not.

One further possibility remains : when a patient with oesophageal obstruction has not regurgitated (or been aspirated) since his last meal, the intra-oesophageal pressure may be so high that paralysis of the cricopharyngeal sphincter may cause regurgitation into the pharynx, even with a steep foot-down tilt. This, however, is unlikely to happen if the oesophagus is first decompressed by applying suction to an oesophageal tube in situ.

Vomiting in the infant differs from that in the adult since up to 6 months of age there is little tone in the abdominal muscles and therefore insufficient power to raise the intra-abdominal pressure except by contraction of the diaphragm. The infant vomits by a series of reversed peristaltic waves which begin at the pylorus and run up to the cardia. There is no evidence that this type of vomiting is affected by paralysis of the somatic muscles, though the mechanism is probably depressed by deep anaesthesia.

Conclusions

The so-called sphincter at the lower end of the oesophagus acts not as a sphincter but as a valve, which allows fluids and solids to pass easily from above downwards but obstructs their passage from the stomach into the oesophagus. The competency of this valve is

independent of either somatic or autonomic nerve-supply. It was found to be completely competent during full muscular paralysis, after full doses of ganglion-blocking drugs, and after infiltration of the area with local anaesthetics.

The cricopharyngeal sphincter, on the other hand, acts like a sphincter normally, but as a valve when paralysed although not quite so efficiently as the cardia. It gives easy exit to fluids from oesophagus to pharynx but not in the reverse direction. The muscle of this sphincter is relaxed by muscle-relaxants, but even in its paralysed state tends to obstruct the entrance of either fluid or air from the pharynx into the oesophagus but not in the reverse direction.

The oesophagus can hold an appreciable quantity of fluid, which may only make its appearance in the pharynx when the cricopharyngeal sphincter is relaxed by deep anaesthesia or by muscle-relaxants, and a positive pressure difference exists between the oesophagus and the pharynx.

The cardia may be made incompetent by obstructing inspiration during anaesthesia when the intra-abdominal pressure is high.

I should like to thank my colleagues in the Department of Anaesthetics, and particularly Dr. W. D. Wylie, for their interest and encouragement. I am also grateful to those members of the surgical staff of the hospital who have permitted me to make these investigations on their patients, to the patients who volunteered to help; and to Miss J. F. Davenport for secretarial assistance and the illustration.

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AMINO-ACIDURIA IN PERNICIOUS ANÆMIA AND SUBACUTE COMBINED DEGENERATION OF THE CORD

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PRELIMINARY observations reported here indicate that patients with untreated pernicious anaemia or subacute combined degeneration of the cord excrete abnormal amino-acids in their urine. After the administration of either vitamin B₁₂ or liver extract the pattern of amino-acids in the urine reverted towards normal.

Pernicious Anæmia

Initially ten patients were studied: five with pernicious anaemia and five (as controls) with equivalent degrees of other varieties of anaemia. The diagnosis of pernicious anaemia was based on the presence of macrocytic anaemia, histamine-fast achlorhydria, and megaloblastic bone-marrow, and on an adequate response to therapy.

The method used was paper partition chromatography (Datta et al. 1950). The quantity of urine used in each case was that containing 250 µg. of total nitrogen as determined by micro-Kjeldahl.

The accompanying table summarises the relevant haematological and biochemical findings, and fig. 1 shows the pattern of amino-acid excretion in case 2 before and after treatment. Before treatment there was abnormal excretion of taurine, with some overexcretion of lysine,

FINDINGS IN FIVE CASES OF PERNICIOUS ANÆMIA

	1	2	3	4	5
Sex	M	M	M	F	M
Age (yr.)	47	56	64	57	63
Hb % (Sahli)	26	57	60	49	43
Red cells (million per c.mm.)	1.64	2.29	2.04	1.78	1.53
Mean corpuscular volume (c. μ)	94	102	118	124	120
Serum-bilirubin (mg. per 100 ml.)	0.8	1.1	2.3	1.5	1.1
Alkaline phosphatase (King-Armstrong units)	7	9	14	..	7
Thymol turbidity (units)	2	1	1	..	4
Serum-albumin (g. per 100 ml.)	5.4	4.6	5.2	..	5.2
Serum-globulin (g. per 100 ml.)	2.1	2.3	1.8	..	1.9

cystine, and leucine. These chromatograms are typical of those found in the five cases of pernicious anaemia examined. In all these cases there was much taurine excreted, sometimes accompanied by leucine, cystine, and lysine; but after treatment with vitamin B₁₂ the pattern reverted towards normal.

Subacute Combined Degeneration of the Cord

The findings in the following case of subacute combined degeneration of the cord suggest that the demonstration of excessive taurine excretion may be of clinical value.

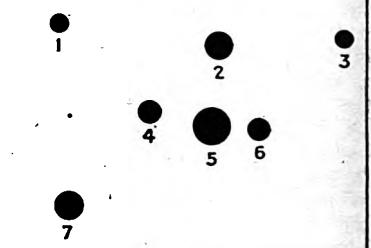
A housewife, aged 66, complained of unsteady gait and weakness of the legs over the previous three months. She had also noticed some tingling in the hands.

On admission to hospital in March, 1954, the patient had a continuous horizontal nystagmus which she stated had been present from childhood. There was severe incoordination of both legs with a staggering gait and rombergism. Without assistance she walked very uncertainly and unhappily. There was proprioceptive uncertainty of toe movements, and vibration sense was absent to the mid-lumbar region. The ankle-jerks were absent and the knee-jerks were much reduced. The plantar response was flexor. There was blunting of light touch and superficial pain over the distal part of the left foot, and both calves were tender.

The cerebro-spinal fluid contained 25 mg. protein per 100 ml. and 1 lymphocyte per c.mm.; Wassermann reaction negative. Blood Wassermann and Kahn test negative; Hb 14.6 g. per 100 ml., white cells 3500 per c.mm., packed-cell volume 42%. Bone-marrow examination: "The sample is moderately cellular. No abnormal cell forms are seen and there is no abnormal number of any of the usual primitive cells. Erythropoiesis is normoblastic." Fractional test-meal showed histamine-fast achlorhydria.

Subacute combined degeneration of the cord was provisionally diagnosed, and the patient was given vitamin B₁₂.

BEFORE TREATMENT



AFTER TREATMENT

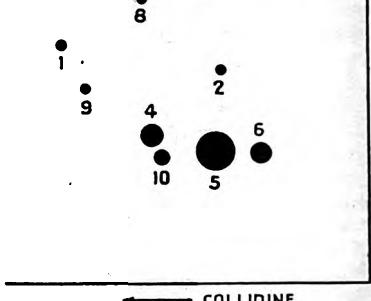


Fig. 1.—Urinary excretion of amino-acids in pernicious anaemia (case 2). 1, Leucine. 2, Taurine. 3, Cysteic acid (from cystine). 4, Alanine. 5, Glycine. 6, Glutamic Acid. 7, Lysine. 8, Tyrosine. 9, Valine. 10, Glutamine. Circles are roughly proportional to colour density of ninhydrin-developed spots on chromatograms.

100 µg. by intramuscular injection daily for fourteen days, followed by 100 µg. twice weekly.

Follow-up five weeks after the start of treatment showed that the patient's general condition was much improved, and she could now walk much better. Vibration sense was now appreciated in the pelvis and there were no paresthesiae.

Fig. 2 shows the amino-acid excretion before and after treatment. It will be seen that the excretion of taurine is in this case greater than that of glycine. In normal chromatograms taurine is rarely detected.

Discussion

The abnormal excretion of amino-acids in the urine in untreated cases of pernicious anaemia is of interest because at necropsy much fatty infiltration of the liver is found (Boyd 1953). The low oxygen-carrying power of anaemic blood has been commonly offered as an explanation for histological damage in the liver. Previous studies of hepatic function in untreated pernicious anaemia have shown no definite evidence of dysfunction. Schilling and Harris (1952) investigated twenty untreated cases of pernicious anaemia by the following tests: cephalin flocculation, thymol turbidity, alkaline phosphatase, prothrombin concentration, and plasma-proteins. The tests revealed no consistent abnormality. The present patients showed no abnormality of plasma-proteins, thymol turbidity, or alkaline phosphatase. That patients with an equivalent degree of anaemia due to iron deficiency do not show an abnormal amino-acid pattern in their urine suggests that anoxic damage of the liver may not be the mechanism involved.

Lack of vitamin B₁₂ may possibly cause liver damage directly. Experiments by Drill and Hall (1950) show that supplements of crude liver extract were more effective than choline in completely protecting rats against hepatic damage produced by high-fat or low-protein diets. The factor present in liver extracts exerting this lipotrophic action was not identified. Amino-aciduria could also be due to a renal defect or to some primary fault in amino-acid metabolism. Though at least two tubular mechanisms are concerned in the reabsorption of amino-acids (Beyer et al. 1947), there is no evidence at present that vitamin B₁₂ influences this tubular function. It is known that vitamin B₁₂ is involved in methyl synthesis and transmethylation of certain amino-acids—e.g., homocysteine (Jukes et al. 1950) and choline (Arnstein and Neuberger 1951). This action of vitamin B₁₂ and its failure in untreated pernicious anaemia may be the basis of the development of the megaloblastic bone-marrow. Vilter et al. (1950) suggest that megaloblastic development is due to the failure to convert thymine to thymidine. Evidence of the importance of amino-acids in the formation of red cells has been obtained by Sebrell and McDaniel (1952), who show that histidine, valine, leucine, and lysine are essential in this respect.

The amino-aciduria of untreated pernicious anaemia requires further study because it may help in determining the basic action of vitamin B₁₂.

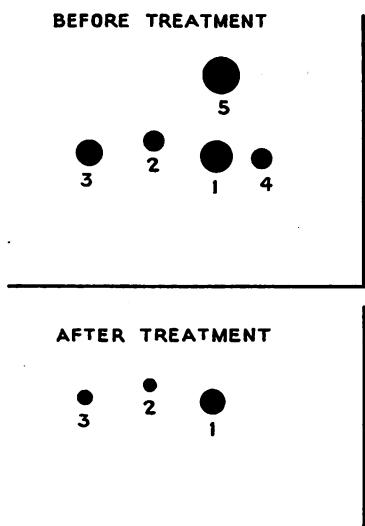


Fig. 2.—Urinary excretion of amino-acids in a case of subacute combined degeneration of the cord. 1, Glycine. 2, Alanine. 3, β-Amino-isopropionic acid. 4, Glutamic acid. 5, Taurine.

It is well known that subacute combined degeneration of the cord can occur without any evidence of pernicious anaemia in the peripheral blood and bone-marrow. Diagnosis of such cases is extremely difficult since the only criterion is the clinical picture associated with achylia gastrica; final proof of the diagnosis depends on the response to liver therapy. The urinary amino-acid excretion in the case described here was entirely in keeping with that found in untreated cases of pernicious anaemia. With treatment the excessive taurine excretion ceased. We therefore suggest that in the presence of a clinical picture resembling subacute combined degeneration of the cord, the associated features of achylia gastrica and increased taurine excretion in the urine may enable the diagnosis to be made at an early stage in the illness.

Our thanks are due to the physicians of the Royal Victoria Hospital for permission to investigate their cases; to Dr. M. G. Nelson, clinical pathologist, Royal Victoria Hospital, for the haematological studies; and to Dr. J. A. Smyth, physician-in-charge, metabolic department, Royal Victoria Hospital, for the use of the facilities of the Biochemical Laboratory.

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ANÆMIA FROM BLEEDING OF THE FETUS INTO THE MOTHER'S CIRCULATION

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In 1948 Wiener wrote a paper "to present cases of severe anemia of the newborn infant due to occult placental hemorrhage." Three cases were presented.

The first was in a baby delivered by caesarean section because of central placenta praevia. Immediately after birth the Hb was 8.7 g. per 100 ml. Wiener suggested that there had been "occult hemorrhage from the fetal surface of the placenta . . . which would not be manifest because the fetal blood would be mixed with the maternal blood lost at the delivery."

The second case was in a first-born child, born by a normal labour, with Hb 6.5 g. per 100 ml. immediately after birth. "In retrospect," Wiener wrote, "it seems evident that despite the apparently normal delivery, this infant was suffering from post-hemorrhagic shock caused by occult placental bleeding. Had this patient been seen after Case 1, the true nature of the condition might have been recognized." In these cases the bleeding was regarded as being "from the fetal surface of the placenta"—i.e., into the amniotic cavity

The third case was in the third baby of a woman whose second baby, born in 1943, had "developed hemolytic anemia and was treated by numerous transfusions of the Rh-negative blood." It is not recorded that she had Rh antibodies at the time. The third pregnancy ended at term on March 31, 1947. No antibodies had been found in the mother's blood up to and including March 15. At birth the baby had severe erythroblastosis with Hb 7.4 g. per 100 ml. and died. The mother was now found to have "anti-Rh agglutinins of 16 units titer." Wiener states: "The simplest way to account for the findings in this case would be to postulate some defect on the fetal side of the placenta, appearing during the two-week interval between the last antenatal Rh antibody titration and

the delivery of the patient. . . . A slow ooze of fetal blood from such a placental defect could also account for the extreme anemia and shock-like condition of the infant at birth." "The anemia was apparently due primarily to hemorrhage rather than hemolysis." On the other hand, "the liver cells [of this baby at necropsy] were filled with hemosiderin pigment," surely indicating haemolysis.

Though I think Wiener's argument is somewhat dubious in this case, nevertheless here is, so far as I know, the first suggestion that a fetus could become anaemic by bleeding into its mother's circulation, and it was because of this hypothesis that the present investigation was made. Wickster (1952) has reported a case (his case 6) which, he thought, illustrated Wiener's hypothesis, and I believe it did. Observations on a baby and its mother have allowed us to prove the hypothesis.

Case-report

The mother, aged 25, belongs to blood-group B, Rh-negative (cde/cde). She was married in 1952, and that year had a pregnancy that lasted about six weeks and ended in spontaneous abortion. She had never had a blood-transfusion. She became pregnant again early in 1953, her expected date of delivery being Nov. 1. Her blood was tested at three months and seven months, and no Rh antibodies were found. On Nov. 14, after a completely uneventful pregnancy, she gave birth to a girl weighing 6 lb. 4 oz. There was no unusual bleeding during the labour. The baby's pallor within an hour of birth led to examination of its blood. It was found to have Hb 7.8 g. per 100 ml. and red cells 2,300,000 per c.mm. (normoblasts 1239 per c.mm., late erythroblasts 426 per c.mm., and early erythroblasts 213 per c.mm.). It belonged to blood-group B, was Rh-positive, Coombs-negative, was given a replacement transfusion of 390 ml. of group-B, Rh-negative (cde/cde) blood, and made a good recovery.

Proof of Wiener's Hypothesis

DIFFERENTIAL AGGLUTINATION

The blood-grouping of the family was as follows :

Father: O, MS, P+, CDe/CWDe, kk, Lu(a-), Le(a-), Fy(a+).
Mother: B, MNS, P+, cde/cde, KK, Lu(a-), Le(a-), Fy(a+).
Baby: B, MNS, P-, CWDe/cde, kk, Lu(a-), Le(a-), Fy(a+).

The baby differed from its mother in having the antigens C^w and D. When the mother's blood was tested with saline anti-C^w and with saline anti-D in the capillary tube, minute agglutinates could be seen. When an indirect Coombs test was done on the mother's cells with blocking anti-D serum, there was gross partial clumping. Since we did not have a saline anti-D serum that would allow of accurate differential agglutination by the Ashby method, we made a rough quantitation by setting up parallel indirect Coombs tests with (1) the mother's cells; (2) the final specimen from the replacement transfusion; and (3) the following dilutions of Rh-positive in Rh-negative blood : 20, 10, 5, 2.5, and 1.25%. All readings of the Coombs test were done on an illuminated glass slide. We judged the number and size of the clumps that formed in the mother's blood to be about equal to those in the post-transfusion specimen, and to be greater than the 5% but less than the 10% Rh-positive in Rh-negative blood suspensions.

ABSORPTION OF SALINE ANTI-D

(Time in minutes to agglutinate D-positive cells after absorption of anti-D with various cells)

Cells used for absorption	No. of absorptions			
	1	2	3	4
Donor's (cde/cde)	3'	4'	4'	4'
Baby's (C ^w De/cde)	>60'
Mother's (cde/cde + C ^w De/cde)	10'	23'	35'	60'
Post-transfusion (cde/cde + C ^w De/cde)	9'	22'	35'	60'

ABSORPTION OF ANTI-D BY MOTHER'S BLOOD

The strength of a saline anti-D serum may be measured by the time taken for D-positive cells to agglutinate in the capillary tube (Chown et al. 1948)—the weaker the serum the longer the time. Four aliquots of a saline anti-D serum that would agglutinate the baby's cells in three minutes were absorbed four times with equal volumes of packed (1) donor's cde/cde cells; (2) the baby's C^wDe/cde cells; (3) mother's cells, considered to be 90-95% cde/cde and 5-10% C^wDe/cde cells; and (4) post-transfusion specimen cells, estimated to consist of 90-95% cde/cde and 5-10% C^wDe/cde. The results are set out in the accompanying table, from which it appears that there was D antigen in the mother's blood in roughly the same proportion as in the post-transfusion specimen.

DISAPPEARANCE OF BABY'S CELLS FROM MOTHER'S CIRCULATION

By the indirect Coombs method with anti-D the following observations were made :

Nov. 24, day of delivery : 5-10% D-positive cells.
Dec. 14, twenty days post partum : reduced by half or more.
Jan. 11, forty-eight days post partum : none demonstrable.

DEVELOPMENT OF ANTIBODIES IN MOTHER'S BLOOD

On the day of delivery there was no anti-D in the mother's blood; on the twentieth day saline anti-D, titre 1, and weak indirect Coombs reaction; on the forty-eighth day saline titre 2, albumin 4, indirect Coombs 16. Anti-C^w was not demonstrable.

FETAL OR REFRACTORY HÆMOGLOBIN IN MOTHER'S BLOOD

Through the kindness of Dr. George Delory, associate professor of biochemistry, the mother's blood was quantitated for fetal or refractory Hb by the method of White et al. (1950), with the following results :

Day of delivery	11%
Twenty days post partum	5%
Forty-eight days post partum	5%

The estimation depends on the rate of conversion of Hb to alkaline globin haematin on the addition of sodium hydroxide. From 60 to 75% of the Hb of the fetus and newborn (from 5 to 10% of the Hb of the adult) is "refractory" to conversion by the method used. The above percentages represent the total refractory Hb and indicate that something more than 6% of the Hb in the mother's circulation at delivery was derived from the baby. This is in good agreement with the estimation based on differential agglutination.

VOLUME OF BABY'S BLOOD IN MOTHER'S CIRCULATION

Mother's weight before pregnancy, 56 kg.
Red-cell volume before pregnancy at 30 ml. per kg., 1680 ml.
Add 200 ml. acquired during pregnancy, 1880 ml.
Estimate of baby's cells in her circulation, 5-10%, 90-180 ml.
Weight of baby at birth, 2840 g.
Normal red-cell volume at 42 ml. per kg., 120 ml.
Add 50-75% for red cells in placenta and cord, 180-210 ml.

We therefore reach the conclusion that from a circulation which at the moment of birth should have contained 180-210 ml. of red cells there had been transferred to the mother, over an indefinite period of time, 90-180 ml. of red cells, or almost 160-320 ml. of whole blood.

Or we may approach this question more indirectly from the state of the baby at birth :

Normal red-cell volume for 2.84 kg. newborn baby, 120 ml.
Normal blood volume for hematocrit 56, 215 ml.
Hematocrit five hours after birth, 27.
Red-cell volume, 27% of 215, 58 ml.
Red-cell volume missing, 120 minus 58, 62 ml.
Add 50% for placental circulation, 93 ml.

So by direct rough estimate we reach the conclusion that the mother's blood contained 90-180 ml. of fetal

red cells, and by calculation that there were 93 ml. of red cells missing from the fetus and placenta. The agreement is good enough; the mother's balance was probably made up of repeated donations, some of which, like many donations, had worn out and been discarded, and yet the final result might be cumulative; the baby's deficit had been reduced by increased production, a sound procedure that Mr. Butler would endorse, though export had reduced the baby's living standard to a bare minimum.

TIME OF ENTRY OF FETAL BLOOD INTO MATERNAL CIRCULATION

When Rh-positive blood is injected into an Rh-negative volunteer, it takes three or four months before Rh antibodies can be demonstrated (Race and Sanger 1950). They were demonstrated in our patient's blood twenty days after her delivery. It therefore appears that some Rh-positive blood, or the Rh antigen in some form, entered her blood two or three months before delivery. This deduction leads to the suggestion that, if the sole stimulus of the mother was fetal blood, the amount of blood lost by the fetus may have been even greater than appears from our calculations given above, for at least some of the blood would have been destroyed after the first entry from sixty to ninety days before birth. On the other hand, the amount first entering may have been trifling, and the bulk of that found mixed with the mother's may have entered shortly before birth.

Discussion

The proof of the presence of the fetal blood mixed with the mother's is direct and beyond question. Our estimate of the amount of fetal blood present agrees sufficiently well with the state of the baby, and of the baby's blood at birth, to make it highly probable that the fetus, by being the donor for a fetomaternal transfusion, had produced in itself a condition of haemorrhagic anaemia and something verging on haemorrhagic shock. The condition only verged on shock, for the baby had had time, before it was born, to make up its plasma deficit, and it was doing its best to rebuild its depleted red-cell supply. Most cases of non-haemolytic anaemia of the newborn are perhaps due to acute external haemorrhage at or close to the time of delivery. In them shock may be severe.

That proof of the fetomaternal transfusion was possible depended, first, on the mother's not having antibodies that would destroy the transfused cells and, secondly, on the easily demonstrable antigenic differences between the two bloods. Such differences between mother and baby in the Rh, MNS, Kell, and Duffy systems are not too uncommon and should allow proof in a fair proportion of such cases. The ABO system seems less likely to be useful, since only the O cells of the fetus of an A or a B mother could be demonstrated through their inagglutinability. However, in the hands of an expert in the method of differential agglutination there are possibilities here too.

There are some other situations in which investigations along this line may prove of value. It seems theoretically possible that a fetus could kill itself in this way. It may then be possible to explain some fetal deaths by examination of the mother's blood for "transfused" cells. The father's blood antigen structure will indicate what antigens, absent from the mother, the fetus *might* have that could be used as tags. If the fetus is born within a few days of death, one can do pretty complete blood-grouping on the cells that can be shaken from the clots in the large vessels of the fetal surface of the placenta, and know exactly what antigens to look for in the mother's blood. Of course, if the mother already has antibodies against the fetal cells, direct proof may not

be possible. Antibody depression, followed by a rise and then a fall, might be suggestive.

If the mother had had antibodies against the cells of her fetus, and if the fetal blood had entered her circulation rapidly, could she have had a transfusion reaction of some sort? There seems to be no good reason why she could not. Some patients have quite sharp reactions to as little as 5 or 10 ml. of transfused blood—chills, severe back pain, shock, and haemoglobinuria. I recall one Rh-negative woman, highly sensitised by multiple Rh-positive transfusions, who had, in two succeeding pregnancies, influenza-like chills just before the death of her fetus. Perhaps they were "transfusion reactions." Could some cases of atypical acute toxæmia or a rare case of jaundice in pregnancy be so explained? In the older published reports there are records of women who became jaundiced in more than one pregnancy and bore babies who developed *icterus gravis*.

The following case, seen with Dr. Ida Armstrong after the above report was prepared, lends support to the suggestion of a transfusion reaction in a woman with antibodies against the cells of her fetus.

Case-report

At noon on Saturday, Feb. 6, 1954, Dr. Armstrong on my recommendation ruptured the membranes of a sensitised (albumin Rh antibody titre 32) Rh-negative woman three weeks before term. Sunday passed without event; the patient went to sleep about 10 P.M. At 6 A.M. on Monday she woke and said she was cold. She passed 4 oz. of urine. The fetal heart sounds were good. By 8 A.M. she was flushed, her temperature was 98.4°F, and the fetal heart sounds were no longer heard. At 9 A.M. she had a rigor, her temperature was 103.4°F, and pulse-rate 132; she was nauseated and vomited. Labour set in, and she was delivered at 11 A.M. of a boy weighing 6 lb. Her temperature had returned to normal.

The baby was in shock; Rh-positive, Coombs-positive; Hb 11.6 g. per 100 ml.; bilirubin 3.1 mg. per 100 ml. Twenty minutes after birth the baby began to bleed from the nose; this bleeding increased in spite of a transfusion of 50 ml., and the baby died two hours later. At necropsy there was blood in the lungs and airways only. On the maternal surface of the placenta was a ragged hole 7 × 3 mm. and 12 mm. deep.

Comment.—The pathological study is not yet complete, but the suggestion is that the baby bled into its placenta at the point where the hole in that organ was found, and that some of the baby's blood entering the mother's circulation caused her to have a transfusion reaction chill. The effect of this on the baby is not clear.

Summary

When the blood of a woman, who that day had given birth to a baby with severe normoblastic anaemia, was examined by differential agglutination, antibody absorption, and biochemical analysis, it was proved that 5–10% of the red cells in her circulation were derived from the baby. She developed antibodies against the baby's cells within three weeks of delivery. It is suggested that fetomaternal transfusion may cause, in addition to non-haemolytic anaemia of the newborn, fetal death, atypical toxæmia, and, rarely, jaundice of pregnancy.

This investigation could not have been made had it not been for the whole-hearted co-operation of Dr. A. M. Goodwin, Dr. Harry Medovy, and Dr. J. Bowman. Dr. Medovy's suggestion that the baby's condition illustrated Wiener's hypothesis led to the investigation.

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**POST-TRAUMATIC VERTIGO
WITH SPECIAL REFERENCE TO POSITIONAL
NYSTAGMUS**

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IN the course of recovery from a head injury many patients develop the cardinal symptoms of headache, giddiness, and mental disturbances. These symptoms may cause protracted ill health, and the disability which results may be difficult to assess, especially when the case is complicated by questions of compensation. Although organic changes can be presumed to have taken place at the time of the accident, clinical evidence of such changes is often difficult to elicit. When this is so, the symptoms are sometimes wrongly attributed to psychogenic causes, a mistake which may seriously complicate the patient's further management.

Post-traumatic giddiness varies in type, degree, and causation, and the first step in its investigation must always be a detailed analysis of its subjective features. It may then be found that when the patient uses the word giddiness he means that he has a feeling of instability and not true vertigo with illusions of movement. If, however, the symptoms at all suggest true vertigo, a full examination of the vestibular system becomes imperative. In this connection the caloric tests, using both cold and hot stimuli, have acquired an outstanding importance and should always be used. In addition, however, the examination should include tests for positional nystagmus, a condition which occurs in certain critical positions of the head.

Positional nystagmus was first described by Bárány (1921), who said that it might be of either central or peripheral origin. In the light of further knowledge it seems that either condition may sometimes result from head injury. Of the two varieties, positional nystagmus of peripheral origin appears to be the commoner. Its clinical features and certain points in its diagnosis, prognosis, and treatment are described below.

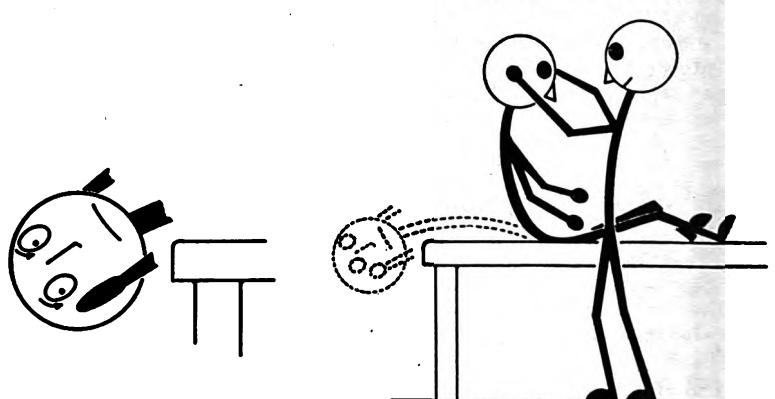
Bárány (1921) emphasised that, in the peripheral variety of positional nystagmus, the position of the head in space and not its movement was the essential factor in evoking the nystagmus, and for this reason he attributed the disorder to a lesion of the otolith apparatus within the labyrinth. This conclusion was in agreement with the results of the contemporary experiments of Magnus and de Kleyn (1920) on animals and has since been supported by a good deal of clinical evidence, which has been very fully reviewed by Lindsay (1945, 1947), Gerlings (1948), and Nylén (1950). Direct evidence of the existence and morbid anatomy of the labyrinthine lesion has been put forward by Dix and Hallpike (1952), who lay particular emphasis upon the benign course and upon the paroxysmal character of the nystagmus, both of which features distinguish it clearly from Bárány's central type of positional nystagmus. For these reasons Dix and Hallpike propose that it should be known as the benign paroxysmal type of positional nystagmus. Their argument that the lesion is limited to the labyrinth was supported by the absence of associated evidence of any involvement of the central nervous system, and by the finding of aural disease in a considerable proportion of their patients. In some of these the disease was unilateral, and then it was noted that the nystagmus was characteristically directed towards the affected ear when this was placed undermost in the test procedure.

Dix and Hallpike lay stress on the fact that in many of their cases no evidence of any severe loss of labyrinthine function could be obtained from the caloric tests. For this reason they regard the lesion as irritative and occurring in a partially disorganised end-organ. Support for this conclusion was provided by the morbid-anatomical changes disclosed by histological examination of the temporal bones in a characteristic case. The patient had had positional vertigo of the benign paroxysmal type for many years, the attacks occurring with the head back and to the right. Well-marked tissue changes were found in the otolith macula within the right labyrinth, the utricular macula being particularly affected. The otolith membranes were absent and the sensory cells disorganized, with considerable thickening and fibrosis of the subepithelial connective tissue, within which were irregular cellular infiltrations. These findings were considered to be in agreement with the hypothesis of a chronic lesion caused either by low-grade infection or trauma.

Clinical Features of Benign Paroxysmal Positional Nystagmus

The nystagmus most often occurs spontaneously without any discoverable cause, but when it arises after trauma it seems to present exactly the same clinical picture. The patient often gives a characteristic history of brief attacks of giddiness coming on when he takes up certain postures. He may have found out for himself that the attacks are brought on by lying down or when looking upwards—e.g., to hang clothes on a line. The vertigo is brief and is therefore infrequently associated with nausea or with vomiting, and there is usually no deafness. Particularly in post-traumatic cases the patient may complain of headache and inability to concentrate, in addition to giddiness. Routine clinical examination may show no abnormal physical signs, and the diagnosis depends on the demonstration of vertigo and nystagmus when the head is placed in a certain critical position. The correct procedure for eliciting the reaction and the character of the nystagmus is shown diagrammatically in the accompanying figure.

The patient should be sat on a couch and his head turned to one side and brought back over the end of the couch while he gazes at the examiner's finger. If this does not cause an attack of giddiness, the manoeuvre should be tried with the head turned to the opposite side. When the test is positive, the nystagmus and associated vertigo may come on almost at once or after a few seconds. The patient will show obvious signs of discomfort, and, unless he can be reassured, will shut his eyes and try to sit up. However, if he can be persuaded to stay supine, the nystagmus, which is usually rotary and directed towards the lower ear, will increase in rapidity and die away, the whole cycle lasting less than half a minute. At the same time the vertigo will cease and the patient will be content to remain in that particular



Manoeuvre to induce benign paroxysmal positional nystagmus.

position for as long as required; but, when he sits up again, a briefer and less severe attack of nystagmus and vertigo may result. If the test is repeated at once, the response will often be much less marked or absent. This "fatigability" of the response may be connected with the fact that often the nystagmus cannot be demonstrated on every occasion; and, if the history is suggestive, the diagnosis should not be abandoned on the basis of a single examination.

Illustrative Case-reports

In the past year five patients attending the outpatient department of the National Hospital, Queen Square, gave a history of a head injury followed by giddiness and were found on examination to have positional nystagmus.

Case 1.—A man, aged 47, hit his head on a steel door-frame. According to witnesses he lost consciousness for several minutes, but he was allowed home after attending a local hospital. For the next six weeks he complained of headaches and of "never feeling clear in the head." He could not concentrate, and his memory for recent events appeared to be affected. About two weeks after the injury he was leaning out of bed to pick something off the floor, when suddenly the room started to revolve for a brief period and he vomited. Since then he had had similar attacks of giddiness and had noticed that they only tended to occur in certain postures.

On examination six weeks after the accident the only positive finding was an attack of paroxysmal nystagmus and vertigo on putting his head backwards and to the left.

Case 2.—A woman, aged 37, was involved in a road accident. A car ran into the back of a motor-cycle on which she was sitting. She was unconscious for about four hours and was detained in hospital for several days. Since the accident she had had headaches, which she described as a pain at the back of her nose and a feeling of pressure in the centre of her forehead. She also had an almost continuous pain up the left side of her neck. Finally she had complained of giddiness on change of posture, particularly on leaning her head backwards. This giddiness seemed to last for a minute or two, and objects appeared to rotate in a vertical direction. It was associated with palpitations and a "limp" feeling, but she was not sick.

On examination two months later no abnormal physical signs were elicited apart from positional nystagmus of the paroxysmal type on putting the patient's head back and to the left. Radiography of the skull and cervical spine showed no abnormalities.

Case 3.—A woman, aged 38, had injured her head two years before attending the National Hospital outpatient department. She was a conductress on a bus which had had to pull up suddenly, throwing her against a steel bar and knocking her unconscious for several minutes. Since the accident she had been liable to headaches and attacks of giddiness, when the room would appear to revolve about three times and she would feel sick. She had noticed that these attacks were particularly liable to come on after moving her head upwards or downwards.

There was well-marked positional nystagmus of the paroxysmal type on putting the patient's head backwards and to the right, but examination was negative apart from this. Radiography of the skull showed no abnormalities.

Case 4.—A man, aged 48, had fallen and struck the right side of his head and must have been unconscious for several hours. Ever since this accident he had complained of headaches associated with nausea and increased irritability, and of a swirling sensation in his head whenever he tilted it backwards or made a sudden quick movement. He had never had any impairment of hearing.

When he was examined more than two years later his symptoms had improved somewhat, but there were still paroxysmal nystagmus and vertigo on putting the head backwards and to the right. This was the only abnormal finding, and radiography of the skull showed no fracture.

Case 5.—A woman, aged 40, had been liable to brief attacks of giddiness at intervals since a severe head injury fourteen years previously. She was liable to attacks of vertigo on sudden changes of posture—e.g., on getting out of bed quickly, and on reaching up to hang clothes on the

line. If she kept still, the sensation of movement would stop in a minute or two.

When the patient's head was put backwards and to the left, an attack of vertigo was precipitated, associated with nystagmus. It lasted for about ten seconds. A similar attack occurred on sitting up again. No other abnormal physical signs were elicited, but radiography of the skull showed an old fracture line running obliquely in the right frontal bone to the superolateral margin of the orbit.

Discussion

It will therefore be seen that among the various causes of post-traumatic vertigo there is a small but well-defined group in which posture plays an all-important rôle. The nystagmus will not be elicited unless it is examined for with the patient's head in various positions, and if this is not done an erroneous assessment of his disabilities may be made. This in turn may cause the patient to respond unsatisfactorily to treatment. When the patient has this type of positional nystagmus, much can be accomplished by simple reassurance and a mild sedative. He should be told that the giddiness is due to a slight injury of the balance mechanism in one ear, and it should be demonstrated that the vertigo only comes on when his head is placed in certain definite positions. He can then take steps to avoid these, with resulting increase in confidence. The diagnosis will also be of obvious importance when a medical opinion is requested in a law-suit arising from an accident.

The duration of post-traumatic positional nystagmus is very variable, but in most patients the condition seems to behave in the same way as the spontaneous variety, and runs a course limited to a few months. In fact the clinical pictures of the two conditions are so identical that it seems necessary to believe that both arise from lesions of the otolith apparatus, these being due to mechanical injury in the post-traumatic cases.

However, it must be emphasised that, although this condition presents such a well-defined clinical entity, it is by no means common and is only one among the various causes of post-traumatic vertigo. The symptom of giddiness arising after trauma is often of psychogenic origin, or may result from lesions of the vestibular apparatus and its central connections at other levels. The history and the finding of signs of damage to other systems often suggest its site of origin.

The vestibular connections apparently reach the cortex mainly in the temporal and parietal lobes, and vertigo may arise from an irritative lesion in these areas. After concussion, or when there has been no definite evidence of cerebral contusion or laceration, epileptic fits are particularly liable to arise in the temporal lobe. The aura of such attacks may be varied in the extreme, but occasionally they will consist in a brief period of vertigo before consciousness becomes impaired. That vertigo can occur in focal epilepsy is supported by the experimental studies of Penfield and Kristiansen (1951), who found that the aura of rotation most frequently arose from the superior temporal or temporoparietal areas.

In severe head injuries, particularly if there has been a long period of unconsciousness, the brain-stem will usually be the site of considerable damage. This may involve the vestibular connections at this level and cause vertigo, but other associated symptoms and signs will often help in localisation. Certain types of positional nystagmus may develop after central lesions of this kind, but several workers have pointed out the clinical differences between positional nystagmus of central and peripheral origin (Bárány 1921, Lindsay 1947, Nylen 1950). Central positional nystagmus may not be associated with vertigo. The nystagmus tends to start immediately the critical position is taken up, without any latent period, and to last for as long as this position is maintained. Another characteristic of central positional nystagmus is that it may alter in direction when the

position of the head in space is changed, but this is by no means always so. This latter fact is not in favour of the classification suggested by Nylén (1950), who associated the central type with direction-changing positional nystagmus and the peripheral type with direction-fixed positional nystagmus.

The eighth nerve or labyrinth is sometimes directly involved by an injury, especially when the base of the skull is fractured. The vertigo that often results tends to occur in prolonged attacks, and the caloric tests will show abnormal responses. In addition some degree of deafness will almost always be present.

Summary

Among the various causes of post-traumatic giddiness the small group due to positional nystagmus of the benign paroxysmal type is considered in detail.

This condition may be missed unless examined for by placing the patient's head in the critical position.

Lesions of the vestibular apparatus and its central connections that may also cause vertigo after a head injury are briefly considered.

I wish to thank the medical committee of the National Hospital for Nervous Diseases for allowing me to use the case-records, and especially Dr. C. S. Hallpike for his helpful criticism and advice and permission to use the illustration.

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DEATH FROM CORTICOTROPHIN

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UNTOWARD reactions to corticotrophin are being published with its more general use. Most of these reactions are so-called "side-reactions": hyperadrenalinism, endocrine depression of the thyroid gland and the gonads, potassium deficiency, psychoses, peptic ulcer, occult oedema, Cushing-like syndrome, secondary infection and increased susceptibility to infection, and purpuric and thrombo-embolic phenomena. About 2% of patients show hypersensitivity reactions ranging from urticaria, angioneurotic oedema, and bronchospasm to anaphylaxis through either specific or non-specific sensitivity to this protein (Brown 1952).

Specific Hypersensitivity

Feinberg et al. (1951) reported the case of a woman, aged 60, who, after cortisone therapy for rheumatoid arthritis, was given 25 mg. of corticotrophin, and within 5 minutes had generalised urticaria, angioneurotic oedema of the larynx, asthma, and profound shock. Recovery followed emergency therapy. Skin tests with corticotrophin from pigs, oxen, and sheep produced positive reactions to dilutions up to 1 : 10,000,000. Muscle extracts of beef and pork gave negative skin tests, whereas pituitary preparations, such as 'Antuitrin,' gave positive reactions. Passive transfer reactions were positive to porcine corticotrophin but not to cortico-

trophin from oxen and sheep or to other pituitary compounds which gave positive direct skin reactions. This patient subsequently gave a history of having had a course of corticotrophin a year before when urticaria developed after the first injection. The urticaria became worse after each successive injection, and finally corticotrophin was discontinued when the twelfth dose was followed by angioneurotic oedema and shock.

Reports of hypersensitivity to corticotrophin are discussed by Brown and Hollander (1952), who observed 208 patients treated with corticotrophin. Only 7 (3%) of these patients showed hypersensitivity, but in 1 it was alarming. They reported as follows:

"That a hypersensitivity state was established as a result of Pork ACTH (Armour) and perhaps, in one instance, consequent upon the use of Beef ACTH. In each instance apparent species sensitivity existed, but in none were we able to demonstrate organ sensitization."

"The relatively small incidence of allergy produced by the administration of ACTH in our experience, leads us to place far less significance on its existence than we had previously anticipated."

All their 7 hypersensitive patients gave positive skin tests to pigs' corticotrophin and responded to anti-histamines and/or adrenaline therapy.

Stevenson (1952), in the discussion of these cases, stated that his group had found 6 of 113 patients hypersensitive to corticotrophin; 1 patient, who received 25 mg. of corticotrophin 133 days after discontinuation of a 32-day course of corticotrophin, developed within 30 minutes a severe reaction characterised by shock, syncope, vasodilatation with severe congestion of the conjunctiva, and muscular irritability to the point of involuntary spasm. He revived completely after 6 hours. This reaction was considered to be due to hypersensitivity to corticotrophin; skin tests, though positive to corticotrophin, were not positive to porcine muscle extract. Stevenson advised a test dose of 5 mg. of corticotrophin injected intramuscularly before larger amounts are injected, if more than 10 days have elapsed since the previous injection of corticotrophin.

Route of Administration.—Intravenous, intramuscular, and subcutaneous routes are all incriminated in published reports:

Wilson (1951) reported protein shock, from intravenously administered corticotrophin 20 mg. in saline solution 500 ml., in 2 patients. Within 15 minutes of the onset of the therapy both patients developed nausea, headache, low back pain, and shaking chills; the injection was stopped at once, and an hour later both patients had circulatory collapse and became acutely ill. Both patients recovered. Skin tests done with the same batch of corticotrophin were negative.

Intermittent Therapy.—Increased susceptibility to hypersensitivity appears to be more likely after corticotrophin has been given for some weeks or when corticotrophin is given again after an interval of weeks or months.

Dosage.—Total dosage, or the amount of corticotrophin necessary to provoke a reaction of hypersensitivity has not been fully investigated.

Allergy.—A history of allergic reactions or allergic disease seems to favour somewhat untoward reactions to corticotrophin.

Species or Organ of Origin of Corticotrophin.—Anaphylactic and hypersensitivity reactions may attend the use of both bovine and porcine corticotrophin, even though the pituitary extract is thoroughly hydrolysed in the manufacture. Preparations available in this country are of bovine origin (Crookes) and porcine (Organon) and contain a small amount of posterior lobe of pituitary gland with pressor and oxytocic substances, which, however, are less in more recent methods of extraction.

Types of Reaction.—Sensitivity reactions to corticotrophin, or to some factor produced in its preparation,

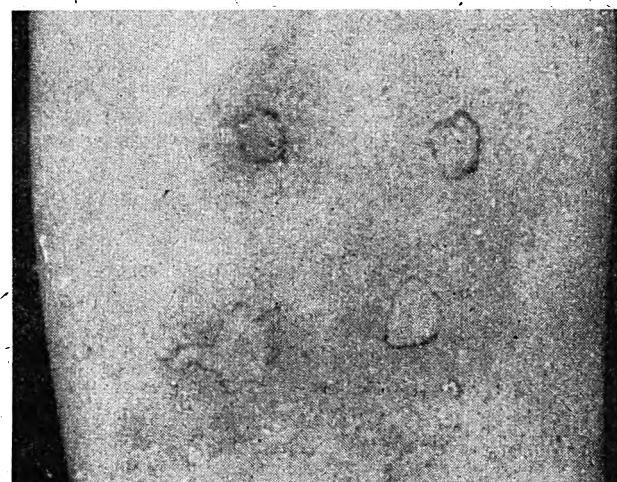
may be of two types (Thorn et al. 1953) : (1) immediate (i.e., within minutes of intramuscular or intravenous administration), producing bronchospasm, angioneurotic oedema, itching, urticaria, and very rarely anaphylactic shock ; and (2) delayed (i.e., several hours after the start of corticotrophin therapy). Further, Thorn states that a responsive adrenal cortex will protect the patient to a considerable degree against sensitivity, and therefore there is more likelihood of adverse reactions if the patient has undergone bilateral adrenalectomy or has either Addison's disease or panhypopituitarism.

Case-record

A merchandise storeman, aged 27, was referred to one of us (B. H. R. H.) for dermatological consultation in October, 1952. In June of that year he had developed on his face and neck an irritable and exudative dermatitis, which had spread to his groins, thighs, and upper arms. He had been admitted to the Memorial Hospital, Hastings, in August, 1952, and given a course of intramuscular corticotrophin (Organon) of porcine origin 10 units 6-hourly for 27 days, followed by 25 units 6-hourly for 6 days, with partial improvement in his skin condition. On Sept. 28, 1952, he was permitted to leave hospital for the afternoon, and on his return was given his evening dose of corticotrophin. Within 15 minutes he became prostrate and weak and developed a rigor, weak pulse, and transient loss of consciousness. He recovered rapidly after vomiting and was quite normal within 30 minutes. This reaction was thought to be either a petit-mal attack or due to hypokalaemia. Corticotrophin therapy was discontinued, and the patient was given phenytoin sodium ('Dilantin'). He was discharged from hospital on Oct. 2, 1952. He gave no history of either skin disease or allergic disorder. There was a history of asthma in his maternal grandfather. He had had no previous illness except mild concussion from a football injury 2 years previously, and of minor attacks of loss of consciousness without tonic muscular movements, provoked by emotional upset ; a physician had diagnosed them as hysterical fits. No occupational cause was found for the dermatitis, and patch-tests to likely occupational and domestic substances were negative. The patient was under treatment until June, 1953, during which time the dermatitis on his face, neck, and thighs recurred several times and showed no great improvement with a rest from work. The only significant feature elicited was sensitivity to streptomycin ointment. He was admitted to Napier Hospital on June 22, 1953, with acute dermatitis which had been present with varying severity on the face, neck, and groins for 2 years.

On examination nothing abnormal was found apart from dermatitis. The urine, chest radiographs, and a differential blood-count were normal.

Second Course of Corticotrophin.—On June 23, 1953, at 9 p.m., 25 units of corticotrophin (Crookes) of bovine origin was given intramuscularly. 10 minutes later the patient complained of feeling queer and sick. He had a severe rigor and became unconscious. Signs of peripheral circulatory failure then developed ; he sweated and became deeply cyanosed, with cold and mottled extremities. His heart sounds became inaudible and his blood-pressure unobtainable ; his respiration became shallow and irregular. The administration of nasal oxygen was started. Intravenous nikethamide 2 ml. and subcutaneous adrenaline 10 minims were given. A 'Plasmosan' drip containing 10 minims of adrenaline was next infused rapidly, and the patient's condition slowly improved. His blood-pressure became recordable at 80/40 mm. Hg, and pulse-rate 140 ; his colour improved, his respirations became deep and rapid, and he became restless. Severe shock lasted 25 minutes. For the next 10 hours the patient was extremely restless. His blood-pressure was maintained, at about 90/60 mm. Hg with 'Neo-Synephrine Hydrochloride' in a glucose-saline infusion. 12 hours later he was semiconscious. He reacted to painful stimuli and could swallow fluids. His colour was good, and his blood-pressure normal and sustained. An infusion of 450 ml. of 50% glucose produced little change in his condition. For the next 8 days his consciousness remained somewhat impaired. He was given milk, glucose, and 'Casilan' by mouth, an adequate fluid and caloric intake being maintained. Lumbar puncture on June 25 produced cerebrospinal fluid under a pressure of 250 mm. H₂O and containing protein 75 mg. per 100 ml. ; and on June 29 under a pressure of 130 mm. H₂O and containing protein 90 mg. per 100 ml., but otherwise



• Passive-transfer intradermal reactions in upper arm to patient's serum and (from left to right in upper row) to physiological saline solution, to 'Antuitrin S.' 1/100 (both negative), and (from left to right in lower row) to porcine corticotrophin (Organon) 1/100 (positive) and to bovine corticotrophin (Crookes) 1/100 (negative). Sites sensitised 48 hr. before test with 0·1 ml. of patient's serum. Test solutions diluted with physiological saline solution, and 0·1 ml. of 1/100 injected into sites intradermally. Readings as above after 20 minutes.

normal. The level of total non-protein nitrogen in the blood was 46 mg. per 100 ml. on June 27 and rose to 138 mg. per 100 ml. on July 1. Blood-counts were normal. Tarsorraphy for corneal ulceration was done on June 29.

Tests for Allergy.—Prausnitz-Küstner passive-transfer intradermal tests gave the results shown in the accompanying figure.

Patients treated with the same batch of bovine corticotrophin as the patient had no untoward reactions.

Outcome.—On July 1, after several cyanotic attacks, the patient died.

Necropsy Findings.—The cerebral convolutions were moderately flat, and the brain and its venous channels were much congested. The lungs showed subpleural ecchymoses, basal congestion, and terminal bronchopneumonia. The heart was normal. The alimentary canal, abdominal organs, and suprarenal and pituitary glands were normal. The histological appearance of the brain and pituitary and suprarenal glands was normal.

Summary

An immediate anaphylactoid reaction to bovine corticotrophin which was fatal is reported.

The reaction must be considered to be non-specific, judged by passive-transfer skin tests.

A reaction after a long course of porcine corticotrophin 9 months earlier was undoubtedly due to anaphylaxis.

Neither previous history nor direct scratch skin tests in the patient elicited any hypersensitivity to pork or beef.

Death was the result of prolonged cerebral anoxia, produced by the anaphylactoid state, and associated circulatory collapse of 25 minutes' duration.

There were no clinical signs of urticaria, angioneurotic oedema, or bronchospasm before or during the anaphylactoid reaction.

Necropsy indicated that death was directly due to anaphylactoid shock.

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MALLET FINGER

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MALLET finger, a deformity due to a lesion of the extensor tendon of a terminal phalanx, is met with in both general and hospital practice.

Lloyd (1949), Kirkham (1949), Le Vay (1949), and Gissane (1949) have discussed the poor results of the usual treatment. Lloyd also noted the financial loss to the patient and the community that this treatment often entailed.

That the disability may not be very great is well recognised, and consequently often no special splintage is advised.

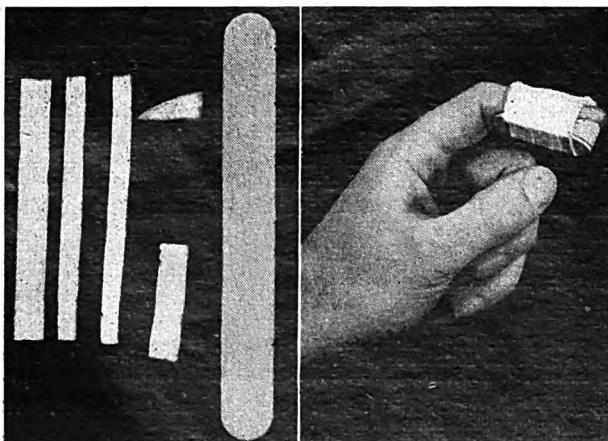
To give the extensor tendon of the affected finger its best possible chance of repair, it is generally considered that the terminal interphalangeal joint should be kept in hyperextension and the proximal interphalangeal joint held in flexion for six weeks. This is usually achieved by putting the finger in a full plaster-of-paris cast with the proximal interphalangeal joint flexed to 90° and the terminal interphalangeal joint hyperextended. This cast is very difficult to apply correctly, and it invariably softens at the pulp of the finger and allows the terminal interphalangeal joint to flex. Moreover, by virtue of its bulk, the patient experiences great difficulty in using the affected hand. He is handicapped in his normal work because right-handed patients usually sustain the deformity in the right hand, and left-handed patients in the left hand. Unfortunately, even after six weeks' immobilisation, which often necessitates being off work for six weeks, the deformity may remain unchanged.

The simple "Enid" splint described below, although not improving the final results, does allow much greater use of the finger and hand.

METHOD

Fifty-two patients with mallet finger were treated and followed up. Twenty-six patients were treated by the plaster technique, and twenty-six with the "Enid" splint. Each patient of the two groups was treated within two days of the injury, all others being excluded from the survey. There was no selection of cases for either group.

Only twenty-six patients (thirteen in each group) regained full extension of the terminal interphalangeal joint of the finger after six weeks' immobilisation. The patients of either group whose radiographs showed a



The "Enid" splint : a, adhesive strapping, cork, felt strip, and wooden spatula ; b, the splint applied.

flake fracture of the base of the terminal phalanx usually regained full extension of the joint.

Almost all the patients treated with the "Enid" splint could do their normal work during treatment. Most of the patients treated in a plaster-of-paris cast could not, or did so with difficulty. If mallet finger is to be treated at all, therefore, the "Enid" splint has a definite advantage over the generally used plaster method in allowing freer use of the finger and hand without impairing the final result.

THE "ENID" SPLINT

The splint consists of a wooden spatula (tongue depressor) cut to a length which allows flexion of the proximal interphalangeal joint of the affected finger.

Between the splint and the end of the finger is inserted a wedge-shaped piece of cork, with its thick end distally, which is fixed to the rounded end of the spatula either with glue or by covering both the cork and the spatula with adhesive strapping.

The splint is applied to the finger so as to hyperextend the terminal interphalangeal joint, and bound to it with strips of adhesive tape, after the dorsum of the finger has been protected with a strip of felt. The proximal interphalangeal joint is left free (see figure). The strapping, which can be waterproof, is reinforced by the doctor or the patient as required. The splinted finger can be protected with a rubber finger-cot.

No originality is claimed for this splint.

I wish to thank Mr. R. Mason for the photographs.

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PROGRESS IN RHEUMATIC CHOREA
A SIMPLE TEST

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THE course of rheumatic chorea is very capricious and its pattern so variable that assessment of progress may be difficult. When the grosser movements have subsided much superfluous muscle activity often persists, and associated movements may also linger. These are often difficult to assess objectively and to record in such a way that daily or weekly progress may be determined. For the most part there is only an impression that movements are made more or less clumsily, or that the associated movements are increased or diminished.

In attempting to assess the response to treatment with corticotrophin Dixon and Bywaters (1952) used three methods :

(1) *Clinical Grading*.—This is the simplest method, but the grading is relatively crude and the distinction between grade 1 (just discernible chorea) and the more severe grades may be difficult.

(2) *Dexterity Test*.—The time taken by the patient to put 100 small plastic pegs in a standard peg-board is used as an index of severity. Dixon and Bywaters suggest an arbitrary normal upper limit of four minutes, but observation has shown that a patient with obviously active chorea can often complete the test in less time than this. Further, there is no doubt that skill in doing the test improves with practice, irrespective of activity of the chorea, and that older children perform much better than the younger.

(3) *Kinetic Bed*.—Movements of the child lying on an inflated cushion are recorded through a tambour on to a smoked drum. This is quite an elegant method but is too elaborate for routine use.

PRESENT METHOD

One of the most constant signs in chorea is unsteadiness of the grip, giving a type of "milking" movement when one or two of the examiner's fingers are gripped by the patient's hand. With a sphygmomanometer cuff it is possible to measure the degree of fluctuation of the grip and thus to assess the degree of steadiness. The cuff is rolled up into a cylinder and, after it has been attached to the sphygmomanometer, it is inflated so that fairly gentle pressure will push the mercury up to 100–120 mm. After making sure that there are no leaks in the system the operator asks the patient to grip the rolled-up cuff so as to keep the mercury steadily at say, the 100 mm. mark. The normal child can keep it quite steady, with fluctuations of not more than 1 or 2 mm. above and below, for at least two minutes. Even with quite mild chorea, however, considerable fluctua-

tions occur, which increase as the child tries to correct them. As the chorea settles down, the fluctuations become less and eventually fall to the normal range. The range of fluctuation can be recorded at intervals, and a graphic record can easily be made by attaching the cuff to a water manometer or a tambour recording on a smoked drum.

Other involuntary movements, such as tremor, would also give abnormal fluctuations, but these would be regular, unlike the complete irregular pattern which is typical of chorea. Similarly, in myasthenia there would be a steady fall in the mercury column with no well-marked fluctuations.

The test, which is extremely simple, seems to give a fairly reliable objective assessment of progress.

REFERENCE

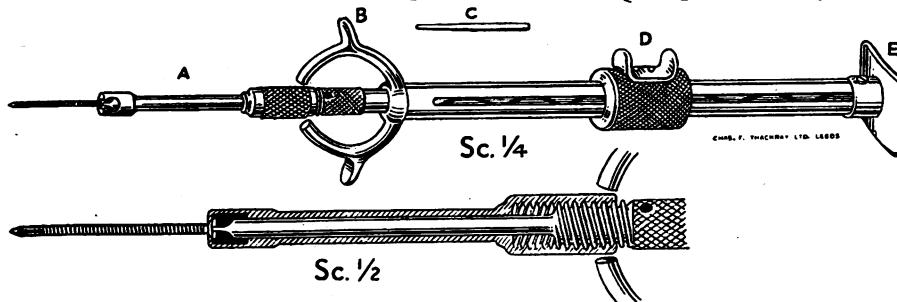
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New Inventions

MECHANICAL SCREWDRIVER FOR THE NAIL-PLATE OPERATION

PROBABLY the most time-consuming, and certainly the most laborious, stage of the operation for the application of a nail-plate in such conditions as pertrochanteric fractures of the femur is the insertion of the long screws which hold the plate to the femur.

The screwdriver illustrated provides a means whereby this stage can be reduced in time and effort. It was made by modifying a disused Kirschner wire drill of the Sven Johansson type. The modification consisted in removing the clamping screw which held the Kirschner wire and replacing it by a metal boss with screw thread, from which projected a short screwdriver blade. Over the blade was fitted a screw-holding sleeve (A) of the



Muller and Bishop type, which is similar in principle to that described by Thomas.¹ The distal portion of the original finger-grip was also removed.

In use the instrument is held horizontally, being supported by two fingers of the left hand on the finger-grip (B), at the same time slight pressure being exerted by the body against the plate (E). The knurled collar (D) is moved to and fro, providing a continuous clockwise rotation of the screwdriver blade.

The screw-holding device allows the instrument to be handed ready loaded with a screw to the operator after each drill hole has been made. As is the case with all screw-holding screwdrivers, it is necessary to leave about $\frac{1}{8}$ inch of the screw projecting so as to be able to slacken the sleeve and to remove the screwdriver with ease. If perchance the screw is driven too far home, a small tapered Tommy bar (C) fitting into a hole in the shaft allows an anti-clockwise turn or two. The final tightening-up of the screws is done with an ordinary screwdriver.

I wish to thank Mr. Geoffrey Hyman, on whose patients this instrument has been used, for his encouragement and enthusiasm at all times; and Messrs. Chas. F. Hackray Ltd., of Leeds, who are now manufacturing this instrument, for their skilful execution of the modifications described and for supplying the illustrations.

STANLEY HULMAN

M.B. Leeds

Orthopaedic Registrar to the Halifax Group of Hospitals, Yorks

1. Thomas, F. B. *Lancet*, 1946, i, 310.

Reviews of Books

The Power of Poison

JOHN GLAISTER, professor of forensic medicine, University of Glasgow. London: Christopher Johnson. 1954. Pp. 262. 18s.

IN this comparative study of well-known poison cases of recent times Professor Glaister examines the defences of society against the poisoner and the subterfuges that have been used to penetrate them.

He discusses the technique of notorious poisoners, their personalities, their defences in court, and the mistakes that led to the detection of their crimes, illustrating his argument from evidence given, speeches of counsel, and addresses to juries from presiding judges. He discusses the establishment of proof, the diagnosis of poisoning from disease, the evidence

of poison, the way in which it can be administered, how the Poison Acts can be defeated, and the safeguard of death certification. The book ends with an extended description of four trials involving a charge of murder by the administration of a different poison, the last being the Merryfield case.

Professor Glaister believes that with present-day methods of pathology and toxicology the poisoner has "but a poor chance of escape." But there are frightening loopholes in the law. Phosphorus rat poison can be bought at a chemist's shop without signature. Arsenic can be obtained in a variety of ways. For instance one witness explained that he got the arsenic at the place where he worked, that arsenic was used in glass-making, and that it was kept in a big barrel about two feet in height. He said that he was able to remove some without anybody noticing. So far as he knew, it was never missed. He appropriated two or three pounds of it, placed it in a paper bag, and handed it to a friend to destroy rats. This book, besides providing interest and information, may well serve a useful purpose in promoting stricter regulation of the distribution of poisonous substances.

Surgical Infections

Prophylaxis, Treatment, Antibiotic Therapy. EDWIN J. PULASKI, M.D., D.M.Sc. (surgery), deputy director, division of surgery, Walter Reed Army Medical Center. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954. Pp. 332. 55s. 6d.

IT is the ramifications, as well as the multiplicity, of drugs at his disposal which bewilders the surgeon when he wishes to apply antibiotic treatment. Will he disturb the bacterial flora to the exclusion of organisms in competition with the one he wishes to discourage? Will a new and resistant species thus develop? Is the selected dose too small or too great, and has the appropriate drug been chosen? These are some of the questions which

tend to be shelved rather than solved in the hurly-burly of the daily surgical round. Dr. Pulaski has gone some way to answer them in the first part of his monograph, which is concerned not only with the chemistry, biochemistry, and bacteriology of each antibiotic but also with its disadvantages and dangers. Indeed the dominant note of the first of these two chapters is a timely warning of the serious consequences of indiscriminate or imperfect use of these drugs. He also includes valuable tables giving the concentration of penicillin, streptomycin, aureomycin, and chloramphenicol to be expected in the various body-fluids for any given dose.

Dr. Pulaski originally intended to limit his monograph to the use of the antibiotics in surgery, but his surgical instinct persuaded him that this might prove misleading. "Antibiotic therapy is adjunct therapy and can be properly discussed only in the light of the surgical therapy which it supplements" is how Dr. de Bakey expresses it in his foreword. And so Dr. Pulaski added six chapters describing the clinical features associated with infections in every site of the body, and the treatment appropriate for each. But he has been less successful in implementing his afterthought, and many readers will wish that he had given the space to broaden the scope and add to the detail of his valuable first intention.

Cold Injury

Transactions of the Second Conference, November, 1952, New York. Editor: M. IRENÉ FERRER, assistant professor of clinical medicine, Columbia University College of Physicians and Surgeons, New York. New York: Josiah Macy, Jr., Foundation. 1954. Pp. 225. \$4.00.

Two papers in the present collection have a general interest beyond their immediate context.

The first of these describes the application of epidemiological methods to an inquiry into the incidence of a non-communicable disease: Commander Schumann of the United States Public Health Service thereby succeeded in demonstrating, in Korea, a higher incidence of frostbite in Negro as opposed to white troops. A number of possible alternatives were reviewed in a lively but inconclusive debate on the interpretation of this finding. In the second paper, Dr. Dugal deals with ascorbic acid as a protective against the general effects of cold in rats. Further study of this action pointed to a possible synergism between ascorbic acid and corticotrophin.

The remaining full-length paper, by Dr. Adams-Ray, is more concerned with the locally injurious effect of cold. Histological examination of small superficial areas of tissue from amputated limbs, which had been frozen with ethyl chloride before operation and then warmed up at different rates, revealed less damage after rapid than after slow thawing. The subsequent discussion centred on vasomotor factors in relation to environmental temperatures and included a brief account of the "photogrammetric" method of measuring volume-changes in various parts of the living body. This ingenious procedure relies on serial stereoscopic photography.

Experimental Studies in Psychiatric Art

E. CUNNINGHAM DAX, M.B., B.Sc., D.P.M., late medical superintendent, Netherne Hospital, Coulsdon, Surrey. London: Faber & Faber. 1953. Pp. 100. 18s.

Dr. Dax disclaims any attempt to describe ways in which art activities could be used therapeutically for mental disorder: he is content to give a detailed account of the facilities available to patients in the large mental hospital of which he was medical superintendent, and to discuss the patients' use of them.

He gives special attention to the examination of some features in patients' paintings—particularly representations of the eye—which throw light on their state of mind. He describes interesting, but apparently crude, experiments on the response of patients to different compositions, as shown by what they painted after hearing the pieces played on a gramophone. It was found that the type of music had no significant effect on the colourfulness, artistic merit, or emotional turmoil discernible in the ensuing paintings, but that it did influence the amount of movement and the gaiety or depression attributed to them by the observers. The

experiment is unfortunately described in very general terms, and no precise information is given which would permit the evidence to be examined. The findings after cerebral injury—mainly leucotomy—are likewise presented in broad outline. The concluding chapters deal with the relation between art and mental illness, and the need for fuller investigation. The work is illustrated with 51 plates, and has a rather patchy bibliography, containing nearly 80 titles.

Acute Renal Failure

ARTHUR GROLLMAN, M.D., PH.D., F.A.C.P., professor and chairman, department of experimental medicine, Southwestern Medical School of University of Texas. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954. Pp. 92. 30s.

INTEREST in this condition was stimulated during the second world war when it often occurred in battle casualties and in crush injuries during air-attack. Professor Grollman in this excellent monograph has clearly summarised the results of the vast investigations of the last fourteen years.

The chapters on aetiology and pathology deal with the proximal tubular necrosis of metallic intoxications and the more diffuse and patchy tubular lesions of acute tubular necrosis. The importance of renal ischaemia in the aetiology of the latter is correctly emphasised, but symmetrical renal cortical necrosis and the anuric type of acute glomerulonephritis are less adequately described. The clinical management outlined is in accordance with modern physiological principles and will offer an excellent guide to the physician in charge of these patients, though many clinicians in this country consider that cation-exchange resins for removal of excess potassium are of greater value than Professor Grollman allows. He does not mention parenteral administration of 40% glucose into the superior or inferior vena cava in patients unable to tolerate fluid by mouth, and some would hold that the more dilute glucose solutions he recommends are of inadequate calorific value and of less efficiency in inhibiting endogenous protein breakdown. He gives an excellent practical account of treatment by peritoneal dialysis and briefly discusses other dialysis methods which are less effective or which need apparatus available only in a few specialised centres.

Collected Works of C. G. Jung

Editors: Sir HERBERT READ; MICHAEL FORDHAM, M.D., M.R.C.P.; GERHARD ADLER, PH.D. Vol. 7. *Two Essays on Analytical Psychology.* Vol. 12. *Psychology and Alchemy.* London: Routledge & Kegan Paul. 1953. Pp. 319 and 553. 25s. and 35s. respectively.

AMONG the least inviting books on library shelves are those opera omnia which attest a once powerful system, a widely debated philosophy—the lifework of some La Mettrie or Duns Scotus who was great and fertilising in his time but now offers only dusty food for historians and thesis writers. It is impossible to judge which of the sages of our day must soon share this fate, and which will remain for generations to come potent intellectual forces, less perhaps than Kant or Aquinas but at least as strong as Locke or Malebranche. Many people would confidently promise C. G. Jung a continuing credit and respect: for them the appearance of the first two volumes of his collected works, in an English translation, is an earnest of his enduring influence.

The first of the volumes to be published is from an expanded version of the lectures on individuation, redemption, and alchemy which were translated in *The Integration of the Personality*; the other volume is derived from a likewise much expanded version of the *Two Essays on Analytical Psychology*. The books, though chronologically out of turn, are rightly given precedence, for the studies of alchemy set out the main theme of Jung's later work, and the *Two Essays* are fundamental to his psychology. As the *Two Essays* in their original German have been much modified in successive editions, the editors have appended translations of the original drafts, thus permitting comparisons which illuminate the change in Jung's views over twenty-five years. In this as in other respects they have done their work well: the bibliographical date, format, type and illustrations are excellent and the translation, by Mr. R. F. C. Hull, is idiomatic and faithful.

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* (Journal of Pharmacology and Experimental Therapeutics, Dec. 1952, p. 376).

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LONDON : SATURDAY, JUNE 12, 1954

Leucotomy: a Responsibility

WHEN frontal leucotomy was introduced, over fifteen years ago, in the treatment of severe and long-continued mental illness, the earlier results were very impressive. Patients who had been withdrawn and inaccessible for years seemed able, after operation, to regain contact with the world around them; while those whose aggressive outbursts had required their continual confinement in the refractory ward or the padded cell could be allowed to move freely among their fellow patients and take part in the limited social activities of the hospital. In some, the social amelioration was such that they could go home again and even return to employment. When months and sometimes years confirmed these improvements, the new treatment was regarded as revolutionary by those familiar with the previous outlook for chronic psychosis and especially for schizophrenia. And within limits this revolutionary promise has been fulfilled. Young schizophrenics no longer fill the hospitals, waiting for the inevitable march of deterioration, nor are the refractory wards occupied by large numbers of unpredictably aggressive or catatonic patients; and this change is certainly due in part to leucotomy. True, these results are gained at a price—some flattening of the personality, a certain apathy and loss of discriminative behaviour in the emotional and perhaps also the intellectual sphere; but in the case of the established psychotic whose personality is already disorganized most people would not think this price too high for what seems to be gained both by the patient himself and the community. This certainly appears to be the view of the mental-health authorities of those State governments in the United States, and more recently in Australia, which are sponsoring widespread leucotomy programmes.

The operation, however, is no longer confined to patients with psychotic illness. Its power to reduce tension and mental distress suggested its use in the symptomatic treatment of severe obsessional and anxiety neuroses and in cases of intractable pain caused by incurable disease such as neoplastic secondaries; and it has now been used in both these fields. Here the problem of personality changes is of preponderant importance. In these patients the finer shades of behaviour—tact, self-restraint, the ability to appreciate "the substance of things hoped for, the evidence of things not seen"; those features that give the individual flavour to personality and make someone the well-loved friend or relative—are still preserved, even though at times they may be clouded by disease. Hence in contemplating any operation that may work a lasting change it is essential that the

patient so far as possible, and above all the relatives, should be fully informed both of what is at risk and of how large or small the risk is. When it is a matter of intolerable suffering in the incurable, and when death cannot be far off, the decision may be relatively easy. Though leucotomy will not have any direct effect on the perception of pain (which may indeed be manifested with less restraint) it will usually induce a placid indifference to the expectation of a further attack; and where (as so often) the apprehension of what is to come is a large element in the patient's distress, the operation may in practice be preferable to the liberal administration of sedatives and morphine, which also damage personality. The case of neurotic illness, however, is in a different category. Here the patients may have most of life before them, and may be expected to live it in the world and not in a mental hospital. The symptoms of their illness may be making existence unendurable for them, and almost unendurable for their relatives, and the demand for relief may thus be so imperative that any suggested treatment will be welcomed and its risks ignored; but, if so, the doctor must take all the more pains to ensure that those concerned fully understand the dangers of the procedure as well as its likely benefits. If a standard leucotomy is being considered, these dangers undoubtedly include a small possibility of producing an apathy so profound that life is lived on a vegetable level, or a lack of restraint and inhibition so great as to disrupt all the usual amenities of social life. Such catastrophes are very rare, especially now that the more posterior cuts are avoided; but this is no consolation to an unprepared family when they do occur. In America (as we report on p. 1233) some urge that the chief risks should be stated in detail on the form of consent to operation, as a safeguard not only for the patient but also for the neurosurgeon.

In the treatment of neuroses a standard leucotomy is now seldom if ever used. Other and more limited procedures have been specifically devised for the purpose, and a measure of success has been reported with partial leucotomies, orbital undercutting, excision of parts of the frontal cortex (including cingulectomy), and even direct coagulation of parts of the anterior thalamic nuclei. With all these operations the personality changes are less; but there are always changes. In ordinary social intercourse they may not be obtrusive, or even detectable; but, when the texture of life includes the subtler harmonies of emotional and intellectual response, the difference in the patient may be crucial to those who are near to him. Often these potential disadvantages will be quite outweighed, for patient and relatives, by the increase in his happiness and efficiency; but (to put it no higher) an operation with such effects can never be recommended as one might prescribe a seaside holiday or a course of the latest antibiotic. It is the doctor's clear duty to ensure that all the consequences of the treatment are appreciated as fully as possible, so that neither relatives nor patients can afterwards feel that the decision would have been different if they had been more fully informed. This will at times require discussion of ethical, religious, or even æsthetic problems: but if the doctor presumes to advise on matters of such ultimate importance he should be prepared to fit himself for the responsibility.

Is Hypertension a Disease?

VARIOUS upper limits to the normal arterial pressure have been suggested, without any good evidence in support of the chosen figure. Such evidence might be obtained from two types of inquiry : first, whether there is a level at which the height of the pressure begins adversely to influence survival ; and, secondly, whether study of the distribution of pressures in the whole population will reveal the constituent distributions of normal and pathological pressures. There is a good deal of information on the first issue from life-assurance records.¹ These show that high pressures do lessen life-expectancy, while at the opposite end of the scale the advantage of a low pressure persists however low the level. Since people with low pressures do not usually suffer any inconvenience, one may suspect that the "normal" pressure is unnecessarily and wastefully high. The answer suggested by the first sort of evidence is then that the whole human race, or at least the Western part of it, is hypertensive. The second question has now been carefully studied by PICKERING and his colleagues.² They find that the distribution of pressures at all ages is of the quasi-normal type usual in biological measurements. The mean and variance of the pressures both increase steadily with age, but there is no suggestion of the segregation of a group of "pathological" high pressures. The inheritance of the pressure level was also studied³ ; and it was found that, allowing for the effect of age, first-degree relatives do resemble each other in the height of their pressures, the correlation coefficient being about 0.2. For example, relatives of a group of hypertensives whose average pressure at a certain age is 50 mm. Hg above that of the general population, will themselves have at that age an average pressure some 10 mm. above the general average ; but the distribution of pressures within the group will be similar in form to that in the whole population. This type of inheritance is similar to that for most body measurements, and suggests multigenetic determination. The correlation is lower than that found with many other measurements, but is not far from that shown, for instance, by ear measurements and does not necessarily imply that genetic factors are less important than environmental.⁴ There is obviously no support here for the notion that a single gene is responsible for pathological hypertension.

The implications of these facts are far-reaching. There appear to be no grounds for regarding essential hypertension as a disease, or as anything other than an arbitrary upper section of the normal range of pressures. Certainly life-expectancy decreases as the pressure rises ; but the same is true for weight, and we do not feel it necessary to postulate a disease of essential obesity. The association between high pressure and cardiovascular complications is after all not very close—one patient will succumb in middle life to cardiac failure while another will maintain a pressure of the same order into his seventies without even ventricular hypertrophy. Moreover, in extreme

age, we can meet the same complications in patients whose pressures are not above the average for their age. Morbid anatomists often ignore this feature by invoking the doctrine (not shared by clinicians) that the blood-pressure commonly drops greatly with the onset of cardiac failure ; but there need be no difficulty in regarding ventricular failure, for example, as determined by the interaction of various factors : quality of the muscle, work load, and length of exposure—that is, age.

To accept such a view of essential hypertension is not, of course, to deny that pathological rises of pressure occur, as in renal disorder, or that there are circumstances (notably when arteriolar necroses are occurring) when the lowering of the pressure is a proper, and indeed urgent, object of therapy. But this view does emphasise the importance of the state of the vascular system rather than the height of the blood-pressure.

After Hospital

WHAT, in fact, are the results of hospital care ? Do the people who leave hospital cured or improved maintain their health ? In an attempt to answer this question Prof. THOMAS FERGUSON and Dr. A. N. MACPHAIL¹ have studied an unselected group of 705 men treated in acute medical units in the West of Scotland—two in teaching units in city hospitals, two in key provincial hospitals. Their chief finding is summarised, in their preface, as follows :

"It seems clear that further breakdown is sometimes precipitated by the transition—often sudden and dramatic—from the protective care of the modern medical ward to spartan conditions outside. Hospital treatment is usually only an episode in the general care of the patient ; and the health services cannot stand in isolation from other social services. There is a limit to what Medicine can do to preserve fitness in the face of bad conditions of living and working."

Their study was made between 1950 and 1953. Of the 705 patients originally seen in hospital, 548 were seen three months later in their own homes and 474 were seen two years after leaving hospital. By that time, 171 of the original group had died, and the remaining 60 were untraceable. Of the 474 seen after two years, 265 were working at their old jobs, though 30 were judged to need lighter work and 18 were unfit for work under ordinary conditions. Of 91 who had found new jobs, 3 were thought to be unfit for work, and 33 could have done their former jobs. Some 50 had done very little work, and 106 had done no work at all, since leaving hospital. Nearly a fifth of those in work at the end of two years were in jobs which were unsuitable, having regard to the demands of the job and the conditions of the men ; and the proportion doing such unsuitable jobs was highest among those between the ages of 45 and 65, and among unskilled rather than skilled labourers. After two years, only 111 of these 474 men could be regarded as cured, though a further 193 had maintained the improvement achieved in hospital ; 106 had not improved, and their health was unsatisfactory ; 64 were worse than when they left hospital and some were going downhill. Moreover, 129 had been readmitted to hospital on more than one occasion during the two years. These

1. Dublin, L. I., Lotha, A. J., Spiegelman, M. Length of Life. New York, 1949.
 2. Hamilton, M., Pickering, G. W., Fraser Roberts, J. A., Sowry, G. S. C. *Clin. Sci.* 1954, 13, 11, 38.
 3. Hamilton, M., Pickering, G. W., Fraser Roberts, J. A., Sowry, G. S. C. *Ibid.* p. 273.
 4. Tanner, J. M. *In Clinical Genetics*. London, 1953.

1. Hospital and Community. London : published for the National Provincial Hospitals Trust by the Oxford University Press. 1954. Pp. 157. 9s. 6d.

figures gain life from the case-histories which FERGUSON and MACPHAIL quote. They write of gross overcrowding; of walls "soaking and falling down" or "running with water"; of parents and children sleeping in box-beds sunk in these soaking walls; of men with failing hearts housed at the top of tenements; of unskilled labourers with heart and lung conditions returning to their jobs as navvies; of stokers with angina shovelling coal; of men finding work within their compass, but being ordered to take on heavy extras by officious charge-hands: in short they describe unending waste—waste of life and health, waste of hospital resources. These authors are admittedly writing of an overcrowded industrial area where housing is notoriously shocking, and the paper by Professor LANE and his colleagues which we publish on p. 1229 shows that in Salford at least the picture of reablement and resettlement is far more cheerful. Nevertheless FERGUSON and MACPHAIL are able to quote surveys from other regions where the findings have been similar.

Where these conditions exist, what is the remedy? One, they suggest, is to provide more "convalescent rehabilitation" hospitals, like the Astley Ainslie Institution in Edinburgh, to which patients could be transferred from the acute hospitals as soon as they were fit, and before they were sent home. Patients who have no-one at home to look after them might

also benefit from a "half-way house" type of hostel; and better follow-up services would certainly help. But in many cases rehousing offers the only hope of improvement. Finally, far too many of the men left hospital to return to work which could scarcely fail to precipitate another breakdown. Many of those studied were "substantially handicapped" by illness from finding suitable work; yet few of those who had registered as disabled persons had received training in new work, and this lack of suitable training courses kept them from returning to industry, or forced them back into unsuitable work. As FERGUSON and MACPHAIL point out, "the cost of training suitable disabled persons in new work, geared to a reasonable prospect of employment at the end of the training period, has to be set against the cost of expensive, recurrent, and often prolonged hospital treatment, together with other associated charges on public funds." The cost of decent housing, too, must be set against the costs of hospital treatment. The living conditions described by these authors were destroying the health not only of the patients who were studied, but of their wives and children. This impressive study shows once more how our very intentness on cure can take our minds off prevention. We provide the best repair service we can and then too often allow the car to be driven straight out into a brick wall.

Annotations

MAJOR ACCIDENTS

THE Ministry of Health, having examined the organisation for dealing with big accidents, has issued recommendations to hospital authorities¹ and local health authorities.²

The Ministry is satisfied with existing arrangements for summoning police, fire, and ambulance services by emergency telephone calls. Hospital boards should ensure that, after an accident, the ambulance authorities can at once get detailed information about the number of beds available at hospitals in the neighbourhood; and in particular, when a hospital that normally receives casualties can no longer do so, the ambulance staff should know. The Ministry remarks that experience has revealed a need for coöordination of activity at the site of an accident involving many casualties; "and it is considered that this can best be provided by the dispatch of a mobile team from the appropriate hospital." Boards should therefore arrange for suitable hospitals to be ready to provide such teams, which, it is suggested, should comprise an experienced doctor and four trained nurses. On the scene this team would open and man a casualty-post, and the doctor would assume responsibility for controlling and coöordinating all medical and first-aid resources. Each hospital board should ensure that any doctor who may be sent to an accident in charge of a mobile team knows in advance the hospitals which will ordinarily receive casualties and the hospitals to which they should turn for support, so that he can advise the ambulance authorities where to take patients. "Front-line" hospitals should also know from which hospitals they can draw additional staff. At each of the hospitals that would receive casualties this responsibility would rest with an appointed senior medical officer, who would also decide whether, in the light of reports from the ambulance service, to dispatch a mobile team. (But

"the senior member of the medical staff immediately available on duty might by chance be a senior registrar or less, and he might have to act at once pending the arrival of a more senior officer.") Likewise he would inform the ambulance staff and those at the scene of the accident of the space remaining at his hospital "so that casualties could be directed to the right destination." This information could probably best be sent via the hospital office to the ambulance control station, which would in many cases be in touch with the scene of the accident by wireless. The ambulance officer on the scene would need to work closely with the doctor in charge of the casualty-post in directing the ambulances. "Should it be necessary to call upon more distant 'support' hospitals, the hospital medical officer in charge of a mobile team will know which of them should receive casualties and will keep the ambulance service informed."

Accidents are not like formal exercises: they are liable to happen at times and places that defeat precise planning. But this does not mean that there should be no precise plan; and the Ministry's advice (though issued only for general guidance) seems sadly lacking in precision. In this country we gain at least one advantage from living so thick on the ground, in that help can be brought to the scene of most accidents within the hour, and of some within minutes. Within an hour or two, whatever the advance plan, or lack of it, the work goes smoothly forward. In the critical period before this, much depends on a few key posts being manned by people who know what they are about. The Ministry's recommendations do not make this clear. Thus the Ministry seems to accept that in this period the responsible doctor at a main hospital accepting casualties (which will usually have 300 or more beds) may be "by chance a senior registrar or less." In such a hospital it should be possible to recruit two or more senior members of the staff (perhaps whole-timers) who would be willing to acquaint themselves with this work so that if one were absent another could do duty. Similarly, according to the Ministry, a great deal is to depend on the doctor in charge of the mobile team. If a mobile team is really needed, this doctor's hands will be full directing it; indeed,

1. H.M.(54)41.
2. Circular 13/54.

they may be over-full if he also coördinates the additional voluntary medical aid that mercifully is brought to bear at nearly every large accident. It does not seem sensible that this doctor should be further charged with the duty of advising the ambulance service on the hospitals to which casualties are to be sent. This is an expert's job ; and it is best left to experts. Such work might be undertaken by one of the regional board's officials or, in parts remote from a regional centre, by one of the management-committee staff. The Ministry's memorandum has one notable omission : there is no mention of the help, if any, that the civilian services may ask of the Armed Forces. The Harrow disaster,³ where the Forces, including notably Americans, came voluntarily to the scene, showed how valuable such help can be. In each area the authorities should know whether, if need arises, they may call, for instance, for an R.A.F. mobile medical team.

TREATMENT OF KELOIDS WITH HYALURONIDASE

KELOIDS vary from minor cosmetic blemishes to crippling deformities. They may be caused by severe trauma such as a bad burn, or by trifles such as acne or chickenpox. The cause may be so slight as to be forgotten ; indeed some keloids have been thought to be spontaneous. Of greater importance than the provocation is the soil, for some people are more prone than others to keloids when exposed to the same kinds of injury ; this proclivity is relied on by some races for the production of cicatricial tribal markings and adornment.

Keloids are a therapeutic problem, for they rarely disappear spontaneously. They respond ungratefully to surgery, commonly recurring in the scar and points of suture. Small keloids can be treated by radiotherapy, particularly at an early stage. Old and extensive lesions are often excised and the region then exposed to X rays, but even this combination may fail to prevent recurrence. Any useful addition to our therapeutic methods would therefore be popular.

Braun-Falco and Weber⁴ treated early keloids by local injections of hyaluronidase on empirical grounds, and reported favourably on a small series. Asboe-Hansen⁵ found accumulations of metachromatic ground-substance in keloids, which encouraged a further trial of hyaluronidase in their treatment. Braun-Falco and Weber⁶ published a further report in which they claimed that even extensive lesions were improved by this treatment. They injected hyaluronidase for six to eight weeks, at first daily and later at longer intervals according to response. The injections were painful and at first were made with great difficulty because of the density of the lesions ; but after the first few treatments the fluid spread more easily. Good results by this method have also been reported from France⁷ ; and Cornbleet⁸ in the U.S.A. has described its use in 26 cases. He found that small, early lesions responded to the enzyme treatment alone ; while large and long-standing keloids diminished in bulk, facilitating their treatment by radiotherapy or a combination of this and surgical excision. Cornbleet also noticed that the injections were painful, even when mixed with a local anaesthetic. Because of this, the force required to drive the solution into the lesion, and the need for repeated treatments, the method is unsuitable for children. Popkin⁹ has described the treatment of scleroderma by the iontophoresis of hyaluronidase ; but it seems doubtful whether such a large molecule can be driven into the skin even

with a current of painful intensity, and the few trials of the method in this country have failed completely.

It seems to be putting the cart beside the horse to treat keloids by removing the connective-tissue ground-substance, which is presumably a concomitant rather than the cause of exuberant connective-tissue formation ; but Cornbleet suggests that removal of ground-substance stimulates the activity of the fibroblasts to the point of exhaustion—like the action of a hormone weedkiller. Braun-Falco and Weber may be nearer the truth in suggesting that the effect of hyaluronidase in keloids may be due not so much to its specific action on excess ground-substance as to its inflammatory stimulus.

ALDOSTERONE IN ADDISON'S DISEASE

Two years ago Simpson et al.¹ described the isolation of a potent salt-retaining fraction from the adrenal cortex, which has since been crystallised² ; because of the presence of an aldehyde group at the 18 position on the steroid ring the name "aldosterone" has been proposed (in place of "electrocortin"). Mach et al.³ now report its effects in 2 patients with Addison's disease in whom other treatment had been temporarily stopped. They gave 150–300 µg. daily in three injections. The response to these minute doses was dramatic : symptoms of adrenal insufficiency were relieved in a few hours, before there could have been any notable changes in the total amounts of sodium and potassium in the body. Over several days' treatment there was a gain of sodium and a loss of potassium from the body comparable to that found by Mach et al. with 4 mg. of deoxycortone, but without as much retention of water or rise in the blood-pressure. There was a suggestion that, unexpectedly, the new hormone may improve the hypoglycaemia of Addison's disease. Perhaps even more surprising was the finding that after only a few days' treatment the patients were less pigmented. Cortisone produces a loss of pigmentation, but only after several months. Other effects of "11-oxysteroids" were not observed with aldosterone ; in particular, the number of circulating eosinophils did not fall, and the abnormal diuretic response to water was not affected.

The work of Mach et al. marks another milestone in the study of Addison's disease, and it gives hope of an important addition to the treatment.

DESIGN OF CRASH-HELMETS

Now that many motor-cyclists have realised the importance of wearing a crash-helmet, the design of these protective hats requires careful consideration. The British Standards Institution recently issued a standard specification (B.S. 2001 : 1953), but opinion differs as to the relative importance of some of its specifications.

The specifications which will not be disputed include a strong attachment under the chin which will also cover the ears, a smooth external surface, light weight, resistance to moisture, and avoidance of brittleness. Some doubts have, however, been expressed about the specifications concerned with the rigid strength of the hat shell. Thus the standard stipulates that a 4-lb. weight falling four feet shall not displace the shell towards the top of the head-harness by as much as 1 inch, and that an end-to-end or side-to-side thrust of 30 lb. shall deform the helmet less than $1\frac{1}{4}$ inches. Critics point out that such a helmet is useful if the wearer is hit over the head with a hammer, but that the usual mechanism of head injury in the motor-cyclist is quite different. His protective hat should have a surface that will skid, and padding that will provide a cushion to reduce the effect of sudden deceleration. Cushioning is much more important than rigidity ; and emphasis on

3. *Lancet*, 1952, ii, 1117.

4. Braun-Falco, O., Weber, G. *Derm. Wschr.* 1951, 124, 798.

5. Asboe-Hansen, G. *Acta derm.-venereol.* Stockh. 1951, 30, 221.

6. Braun-Falco, O., Weber, G. *Derm. Wschr.* 1952, 125, 465.

7. Leclercq, R. *Ann. Derm. Syph.* 1952, 79, 264.

8. Cornbleet, R. T. *J. Amer. med. Ass.* 1954, 154, 1161.

9. Popkin, R. J. *J. Invest. Derm.* 1951, 16, 97.

1. Simpson, S. A., Tait, J. F., Bush, E. *Lancet*, 1952, ii, 226.

2. *Ibid.* 1953, ii, 551.

3. Mach, R. S., Fabre, J., Duckert, A., Borth, R., Ducommun, P. *Schweiz. med. Wschr.* 1954, 84, 407.

rigidity, with a space between helmet and head-sling, involves taking up weight and space which may be better used for cushioning material. Furthermore, a rigid helmet with a sling support is commonly uncomfortable. Certainly if one banged one's head against a wall, the blow would be softened better by a cushion than by a plastic pudding-bowl. Obviously, too, a protective hat should not be rigid and uncomfortable unless this is proved essential. Tests now being undertaken by the Road Research Laboratory may settle this question. Meanwhile any helmet is better than none.

APPOINTMENTS SYSTEMS

An interesting lethargy, partly financial in origin (but also, possibly, partly psychological), still prevents some hospitals from accepting the reasonable, practical, and kindly duty of arranging appointments systems for outpatients. In returning to the charge of stirring them to action, the Minister of Health¹ reminds regional hospital boards, hospital management committees, and boards of governors of four main criticisms: that patients called for an appointment at a particular time often have to wait an hour (and often much longer) before they are seen by a doctor; that consultants are responsible for some of these delays when they arrive late; that some appointments systems are badly organised; and that little attempt is made to explain the reason of delays to patients, or to win their confidence, or consider their comfort or needs. The first of these, the Minister notes, is a statement of fact; as for the second, lateness on the part of the consultant staff may be inevitable at times, but could become much rarer if the medical staff would coöperate better. For the last two, he says, there is no justification.

Good hospital management, is, of course, the key to better things; and this comprehensive term includes better coöperation between medical, nursing, and other staff working in outpatient departments, and a greater concern for the convenience of patients. These things cannot be conferred like a knighthood or a medal; but they can be inculcated, and they can in time grow into part of the spirit of a hospital. Boards and committees can help their growth by encouraging those who are trying to develop them, by providing the right kind of propaganda (aimed at staff as well as patients), and by checking up on efficiency from time to time. Of course many boards and committees are doing this already, so far as their funds, premises, and man-power allow; but he asks all of them, whether they are doing these things or not, to review the existing outpatient arrangements in their hospitals and see what can be done to remove all reasonable causes of complaint.

In particular he urges that the old practice of "multiple" or "block" appointments (by which everyone is called for, say, 2 o'clock, though the session is likely to last 3 hours) should be discontinued; and that proper appointments systems should become not only universal, but designed to ensure that each patient is called, as far as possible, for the time when he is expected to see the doctor. Periodical reviews will show whether the system is working, and if not, why not. Such information should be the basis of fresh action, not merely an interesting objective finding. The Minister draws attention to the need for special plans for patients who have to attend several departments on the same day, for parents who have left small children at home, and for patients coming from a distance and badly served by buses or trains.

Punctuality has two aspects: patients should be discouraged from coming too early in the hope of being seen before time; and consultants should recognise that the success of the whole system depends on their own punctuality. If they are going to be delayed they should let the hospital know in good time; and if experience shows that they are often unavoidably late, then "the number of clinics or the times should be reduced or

altered to fit in better with the calls on the consultant's time."

The running of appointments systems should be in the hands of a senior administrative officer; and he should discuss and agree with the medical staff on any necessary alterations or improvements. Reports on the arrangements, and on any difficulties encountered should be made regularly to the board of governors or management committee. The Minister again draws attention to the special responsibility which lies on those who receive patients. They should be specially chosen for the work, and should be encouraged to remember that "patients are often anxious, bewildered, or even frightened, and that it is essential to attend to their needs and comfort all the time they are in the outpatient department." He reminds boards and committees that lay receptionists often have the right qualities for this task, and that voluntary organisations are often ready to lend helpers on a part-time basis. A receptionist should anticipate any complaints that may be made, and try to remove any sense of grievance the patient may feel at being kept waiting: and a reasonable explanation is usually enough to achieve this. Patients should either be conducted whither they have to go, or helped to find the way by adequate signposts. A friendly reception in hospital is an important factor in good public relations. These are further fostered and maintained by considerate manners in everyone the patient encounters in hospital, and by talks to local bodies and messages in the press, designed to interest people in the work of their hospitals, the difficulties encountered in ensuring comfortable care of patients, and the measures taken to overcome these difficulties. The Minister proposes, in due course, to call for reports from boards and committees on the running of their hospital outpatient departments and clinics, and on the extent to which waiting-time has been eliminated. This human and enlightened circular deserves a human and enlightened response.

CHEMOTHERAPY IN ORTHOPÆDIC TUBERCULOSIS

"STREPTOMYCIN is a useful adjunct in the treatment of tuberculosis. This may well be an overstatement in tuberculosis of bone and joint, in which group we have little knowledge and less hope."¹ This rather gloomy opinion was expressed in 1947; but further experience has been more heartening, as Harwood Stevenson² makes clear in a report from the Royal National Orthopaedic Hospital. While MacKenzie,³ emphasising that antibiotics are no panacea, suggests that they should be reserved for the critical phases in the disease—progressive or multiple lesions, sinuses, operations, and synovial infections—Stevenson reports series in which chemotherapy has been used routinely as an adjuvant. In the conservative treatment of the tuberculous hip he found that the addition of chemotherapy roughly halved the average time both for the appearance of the first radiographic signs of healing and of the patient's stay in hospital. This series was treated with streptomycin and *p*-aminosalicylic acid (P.A.S.), but he has no doubt that the addition of isoniazid would increase their combined effectiveness. He advises a dosage of P.A.S. 15 g., streptomycin 1 g., and isoniazid 4 mg. per kg. body-weight, daily for three months. Streptomycin and isoniazid together have double the bactericidal rate of either alone, and P.A.S. delays the emergence of drug-resistant strains; a three-month course of this combination does not apparently carry much danger of drug resistance.

Stevenson notes similar improvement in results in tuberculosis of the knee, and he reports a few cases of synovial tuberculosis of the knee treated with a combina-

1. Report to the Council on Pharmacy and Chemistry. *J. Amer. med. Ass.* November, 1947.

2. Stevenson, F. H. *J. Bone Jt Surg.* 1954, 36B, 5.

3. MacKenzie, I. G. *Lancet*, March 27, 1954, p. 652.

tion of intramuscular and intra-articular streptomycin without any splinting apart from rest in bed. He found an effective streptomycin level in the joint a week after an intra-articular injection. About 60% of sinuses treated with streptomycin and P.A.S. healed and stayed healed for not less than two years; and in most of the failures some cause, such as the presence of a sequestrum, was found.

Fifty years ago bold surgical attacks were made on tuberculous joints, but the results were so often disastrous that conservatism became the rule, at least in this country. Streptomycin restores the power of healing to tuberculous tissues so that the ordinary principles of surgery can again be applied. Once the dangers inherent in surgical intervention (dissemination, local spread, and failure to heal) have been overcome, there are obvious advantages to be gained; pus can be released, necrotic debris cleared out, and even grafts inserted directly into tuberculous tissues. A fresh blood-supply can be brought to the centre of the lesion, into which, as MacKenzie points out, antibiotics otherwise penetrate so little that their only effect may be to produce resistant strains of the organism. Wilkinson⁴ has for some years been recommending earlier and more radical surgery, and there now seems to be no doubt that a new era is opening in which, as Stevenson says, "the type of case in which prolonged abscess formation and successive involvement of vertebral body after vertebral body by subligamentous spread—possibly with sinus formation and secondary infection—may become a thing of the past." But there is a danger that we must keep in mind. Tuberculosis of bone and joint is a metastatic manifestation of a general disease, with foci of infection in the lymph-glands and elsewhere deep in the body. We can now make the patient's fight much easier in the local skirmishes, but final control of the disease still depends on his own resistance: first-class general conservative treatment remains essential; and if the period of this is greatly reduced recurrence is liable to ensue.

GLUCONEOGENESIS FROM FAT

THE possibility of gluconeogenesis from fat remained in doubt so long as there was no firm evidence of carbohydrate utilisation in the diabetic organism. Now that we have this evidence, it is clear that the breakdown of protein cannot supply sufficient sugar for both utilisation and excretion, so the sugar must be derived from fatty acids as well as from protein. Burns and Marks⁵ perfused the glycogen-poor livers of fat-fed dogs and of a pancreatectomised cat, and showed, from dextrose:nitrogen ratios, that more sugar was produced than could have been formed from protein alone even if all the carbon in the protein had been converted to glucose. Isotope studies^{6,7} have proved beyond doubt the conversion of fat to carbohydrate via the tricarboxylic-acid cycle.

Kinsell and his group in California have long been studying the possibility that adrenal steroids accelerate gluconeogenesis from fat, and they seem at last to have established this. They first noticed that corticotrophin and adrenal cortical hormones decreased or even eliminated the ketosis normally associated with fasting or high-fat intake in healthy people^{8,9} and with insulin withdrawal in some diabetics.¹⁰ The results of animal studies differ somewhat from those on man. Corticotrophin administered to phloridzinised rats, for instance, caused ketonuria as well as increased glycosuria, but no

increase in urinary nitrogen.¹¹ This was taken to indicate gluconeogenesis from fat via the stage of ketone bodies. Kinsell and his co-workers had to explain the suppression of ketosis by corticotrophin or cortisone in patients subjected to the ketogenic influence of a 3½-day fast.¹² Several possible mechanisms might have been in action. The adrenal steroids might have stimulated ketolysis, or so changed the metabolic path of fatty acids that little if any ketones were formed as intermediary metabolites. The possibility of a decrease in total energy requirement was not supported by studies of oxygen consumption; and, lastly, the possibility that the total oxidative breakdown of amino-acids was stimulated sufficiently to exert a major fat-sparing action was ruled out by the relatively slight increase in nitrogen excretion. In order to test the hypothesis that adrenal steroids stimulate ketolysis, sodium aceto-acetate was given intravenously to healthy and diabetic persons, with and without corticotrophin and cortisone,¹³ but there was no significant difference in the blood and urine ketone levels. In similar experiments the effects of corticotrophin and cortisone were observed during and after standard intravenous infusions of a fatty acid—sodium octanoate.¹³ The blood and urine levels of ketones and octanoate indicated that in some people there was pronounced stimulation of fatty-acid utilisation without any increase in the rate of ketone production. This supports the hypothesis of a changed metabolic path of fatty acid under the influence of adrenal steroids. Later work from Kinsell's laboratory¹⁰ has yielded evidence that these steroids also stimulate gluconeogenesis from carbohydrate. It was then found that more glucose was excreted in the urine than could have been derived from protein, even if all the katabolised protein had been broken down to carbohydrate, and allowing, too, for the sugar formed from the glycerol moiety of katabolised fatty acids. The only other possible carbohydrate source of this extra urinary sugar was hepatic glycogen, but the discrepancy was so great that such a source was improbable. This work must cause us to re-examine the usual assumption that only 10% (representing the glycerol) of dietary fat can be glycogenic; the commonly accepted dictum that only 58% of dietary protein is glycogenic is more patently false. This figure is based on the classical dextrose:nitrogen ratio of 3.65 found in the phloridzinised fasting dog; it is a mean of selected determinations,¹⁴ and takes no account of the undoubtedly glucose utilisation by the animals during the experiments.¹⁵

An interesting sideline of Kinsell's work on administering adrenal steroids to diabetics fed only on protein and fat is the way he overcame the great insulin resistance which threatened to wreck his early experiments.¹⁰ This insulin resistance could be completely eliminated by preventing depletion of potassium and sodium. As long ago as 1936 McQuarrie and others¹⁶ found that the severity of diabetes was eased in children given sodium chloride 1–2 g. per kg. body-weight daily, so long as the dietary potassium was kept low. On the other hand, a high potassium-chloride intake relative to sodium chloride increased the glycosuria. Kinsell's patients may have had enough adrenal steroids to cause a pronounced urinary excretion of potassium, and this may have allowed the diabetes-improving effect of the extra sodium to be dominant. Further work on this interesting relation of potassium to "steroid diabetes" and insulin resistance is to be published soon.

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Special Articles

FOLLOW-UP OF MEDICAL INPATIENTS IN A GENERAL HOSPITAL WITH SPECIAL REFERENCE TO WORKING CAPACITY

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THIS paper gives the results of a follow-up of medical inpatients approximately three years after their admission to Salford Royal Hospital. It is primarily concerned with the ability of these former patients to carry on their normal work after discharge. This aspect of hospital work has the advantage of being capable of direct measurement.¹

We realise that this is the experience of one branch of one hospital only and does not necessarily represent experience in other hospitals or districts. A comparison with similar results elsewhere would be of much value.

MATERIAL

Salford County Borough has some 178,000 inhabitants and is contiguous with Manchester; together these two boroughs form the centre of the "conurbation" of South-East Lancashire of almost 2½ million persons. Salford's main industries are engineering, textiles, and docks, but there is, in addition, a wide variety of other industries. Salford Royal Hospital is typical of many of the older voluntary hospitals. It has served this industrial area for more than 120 years and has been very much a community hospital to which the people of Salford have looked in times of need. It has 256 beds, 71 of which are for medical patients.

METHOD

The names of all persons, excluding children, admitted to the medical wards of Salford Royal Hospital in 1950 were extracted from the inpatient register and the relevant case-book obtained from the records department. A form was then sent to each person with a covering letter from the senior physician explaining the reasons for the inquiry. When answers were received, information was transferred to a card. If after about a fortnight no reply had been received, a reminder was sent. If still no answer was obtained, a visit was made by a member of the almoner's department in all cases where this was practicable. Information about persons who had died in hospital was transferred straight from the case-book to the record card.

In this way records of 973 patients were examined² and information was obtained about the present position of 887 of them. This is a very high response to a predominantly postal inquiry of this type, and may reflect the high regard with which Salford Royal Hospital is held by the people it serves. Even for the 86 (9%) "non-contacted" persons some information was obtained: some had emigrated or moved to other parts of the country; a few were in sanatoria; and 2 were in prison.

- Some of the figures given here formed the basis of part of a presidential address to the Manchester Medical Society (medical section) in May, 1953.
- Among these 973 patients are some who were admitted to medical beds and subsequently transferred to a surgical ward. In the reverse case of transference from a surgical ward the patient's name may not necessarily be included if it does not appear as a medical admission in the register.

THE RESULTS

Numbers Available

Of the 887 persons for whom information was obtained 306 had died, leaving 56% of the male and 64% of the female patients available for further follow-up (table I).

Mode of Admission

379 (39%) of all the patients were admitted from outpatient clinics; 311 (32%) were urgencies or casualties. Of the remainder, 22% were admitted either on the request of their general practitioner or as a result of a domiciliary visit; in 7% of the cases it was impossible to decide the mode of admission in retrospect.

Employment

On admission 413 (80%) of the men were employed, 54 (10%) were retired, 29 (6%) were unemployed, and for 19 (4%) information about employment was not available.

For the women this information was not so easy to obtain, because there was often ambiguity as to whether

TABLE I—PATIENTS ADMITTED TO MEDICAL BEDS

	Men	Women
No. admitted in 1950	515	458
Died in hospital	85 (17%)	63 (14%)
Died since discharge	95 (18%)	63 (14%)
Total deaths	180 (35%)	126 (28%)
Not contacted	47 (9%)	39 (8%)
No. now alive and contacted	227 288 (66%)	165 293 (64%)

in describing herself as having "no job" a woman meant she was unemployed or a housewife. Hence these two categories have been added together into a group "not gainfully occupied outside the home" (referred to below as "not gainfully occupied"). On admission 265 (58%) of the women were not gainfully occupied, 141 (31%) were employed outside their home, 8 (2%) called themselves retired, and for 44 (10%) information about employment was not available.

At the time of the follow-up about three years later the state as regards employment was:

Men	Women
Employed .. 225 (44%)	Employed .. 95 (21%)
Unemployed .. 42 (8%)	Not gainfully occu- pied .. 198 (43%)
Retired .. 21 (4%)	Uncontacted .. 39 (8%)
Uncontacted .. 47 (9%)	Dead .. 126 (28%)
Dead .. 180 (35%)	

Causes of Admission

The admissions were grouped under thirteen main headings,³ and the total number of days in hospital were separated for each of these groups. (If a patient was admitted more than once during the year for the same complaint he is counted only once here.) The chief causes of admission in three age-groups are given in table II.

It will be seen that, measured either by the number of patients admitted or by the length of stay in hospital, circulatory diseases head the list of admissions for

- The thirteen headings, with their International List numbers in parentheses were:
 - Pulmonary tuberculosis (001–008).
 - Blood diseases (290–299, 204).
 - Cancer (140–239, excluding 201, 204).
 - Diabetes mellitus (260).
 - Vascular lesions affecting central nervous system (330–334).
 - Other diseases of the central nervous system (340–357, 024, 026) and of the nerves (360–367), including displaced intervertebral disc (735).
 - Diseases of the circulatory system, excluding rheumatic fever (410–456).
 - Respiratory diseases, including asthma (470–527, 241).
 - Diseases of stomach and duodenum (540–545).
 - Diseases of intestines and peritoneum (570–578).
 - Diseases of the genito-urinary system (580–605).
 - Psychoneurotic disorders (310–318).
 - All other causes, including rheumatic fever (400–402), arthritis and rheumatism (720–727), diseases of liver, gall-bladder and pancreas (580–587), and diseases of thyroid (250–254).

women, whereas respiratory diseases, circulatory diseases, and gastric ulcers between them account for almost half the male admissions.

MacKay,⁴ who examined a sample of patients discharged from National Health Service hospitals in England and Wales during the first six months of 1949, found that peptic ulcers were the chief medical cause for men in both age-groups 15-44 and 45-64. In our series respiratory diseases occupy this position.

Owing to the small numbers in most disease groups, little weight can be attached to the death-rates within these groups.

Length of Stay in Hospital

The average length of stay in hospital for men was twenty-one days and for women twenty-two days; it varied little between the three age-groups. 15 (3%) of the men and 24 (5%) of the women were in hospital for two months or more during the year. The weekly cost of an inpatient was estimated to be about £15; hence each inpatient cost an average of £45 in 1950.

Subsequent Medical Attention

Of the patients now alive and traced 142 (49%) of the men and 177 (61%) of the women are still attending their doctor or the hospital or both. (Diabetes is partly responsible for the larger proportion of women.) All the patients were asked whether they felt better, the same, or worse than before admission. The replies of the men and of the women were almost identical. It is difficult to know how much value can be placed on these replies, since it is generally recognised that patients tend to give a favourable reply to such inquiries when made by a hospital in which they have been cared for. The figures were as follows :

	Men	Women
Compared with time of admission, feel		
Better ..	193 (67%)	205 (70%)
Same ..	52 (18%)	49 (17%)
Worse ..	40 (14%)	37 (12%)
Unknown ..	3 (1%)	2 (1%)
Total alive and contacted ..	288	293

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TABLE III—MEN EMPLOYED ON ADMISSION AND CONTACTED

Present position	Age-group (yr.)			Total
	Less than 45	45-64	65 or more	
Dead ..	20 (15%)	89 (40%)	13	122 (33%)
In same or similar work ..	83 (61%)	93 (42%)	1	177 (47%)
In other work because of health ..	22 (16%)	20 (9%)	..	42 (11%)
Unemployed because of health ..	12 (9%)	14 (6%)	2	28 (8%)
Retired	4 (2%)	..	4 (1%)
Total ..	137	220	16	373

Ability to Return to Work

The capacity of a patient to resume a fully active working life is regarded as the best available measure, when applied to a group, of a return to health or of successful treatment. Our inquiry aimed at discovering what happened to the working capacity of patients three years after discharge. We fully realise that the successful resettlement of patients depends on numerous factors, the most important of which is the state of the labour market. In individual cases resettlement will also depend on the nature of the patient's illness and his psychological make-up as well as the nature of his work and the attitude of his employer.

The general employment situation in Salford in 1950 was good, though it deteriorated somewhat in 1952, largely through a temporary recession in the textile industry. (The number of unemployed persons in Salford in June of each year was 972 in 1950; 518 in 1951; 3038 in 1952; and 1420 in 1953.) Only those men who were employed on admission and have been contacted since are considered in table III.

The apparently more favourable position of the younger men is almost entirely due to the smaller number of deaths in this group. If only those now alive are considered, the proportion still in the same or similar work was 71% for both groups. 70 men have left their normal work for health reasons in the period under review.

TABLE II—CHIEF CAUSES OF ADMISSION

MEN

—	Aged 15-44 yr.	Aged 45-64 yr.	Aged 65 yr. or more	Total		
No. of patients	All causes ..	178	All causes ..	265		
Respiratory ..	33 (19%)	Respiratory ..	46 (17%)	Respiratory ..	88 (17%)	
Gastric ulcer ..	30 (17%)	Circulatory ..	41 (15%)	Circulatory ..	87 (17%)	
C.N.S. other ..	22 (12%)	Cancer ..	40 (15%)	Cancer ..	71 (14%)	
	<hr/> 48 %	Gastric ulcer ..	36 (14%)		56 (11%)	
			<hr/> 61 %		<hr/> 59 %	
Stay in hospital (days)	All causes ..	3621	All causes ..	1377	All causes ..	10,743
Gastric ulcer ..	606 (17%)	Circulatory ..	985 (17%)	Circulatory ..	1863 (17%)	
Respiratory ..	600 (17%)	Cancer ..	931 (16%)	Respiratory ..	1719 (16%)	
Circulatory ..	507 (14%)	Respiratory ..	875 (15%)	Gastric ulcer ..	1449 (13%)	
	<hr/> 48 %	Gastric ulcer ..	726 (13%)	Cancer ..	1280 (12%)	
			<hr/> 61 %		<hr/> 58 %	

WOMEN

No. of patients	All causes ..	207	All causes ..	79	All causes ..	458		
Respiratory ..	23 (13%)	Circulatory ..	48 (23%)	Circulatory ..	24 (30%)	Circulatory ..	91 (20%)	
Circulatory ..	19 (11%)	Diabetes ..	27 (13%)	Diabetes ..	10 (13%)	Respiratory ..	46 (10%)	
C.N.S. others ..	17 (10%)	Respiratory ..	18 (9%)		<hr/> 43 %	Diabetes ..	44 (10%)	
	<hr/> 34 %		<hr/> 45 %				<hr/> 40 %	
Stay in hospital (days)	All causes ..	3574	All causes ..	4704	All causes ..	1878	All causes ..	10,156
Circulatory ..	447 (13%)	Circulatory ..	1401 (30%)	Circulatory ..	779 (41%)	Circulatory ..	2627 (26%)	
C.N.S. other ..	402 (11%)	Diabetes ..	572 (12%)	Diabetes ..	171 (9%)	Diabetes ..	899 (9%)	
Respiratory ..	383 (11%)	Respiratory ..	430 (9%)		<hr/> 59 %	Respiratory ..	891 (9%)	
	<hr/> 35 %	Cancer ..	395 (8%)				<hr/> 44 %	

There were 21 men who were unemployed on admission to hospital and who were now contacted ; 5 only of these were in work three years later.

For the women the same criterion for judging the return to health was not available, owing to the large number of housewives in the group. An attempt was made, however, to substitute their ability to manage their household duties. It is realised that this is a less objective measure than that used for the men but it is the best available. The results are given in table IV.

DISCUSSION

It is an important function of a hospital to provide care during serious or fatal illness. It is therefore no surprise to find that about a third of the patients admitted to medical beds in 1950 were dead three years later.

It is important, however, to know what has happened to the other two-thirds, and how far they have been able to resume a normal life. If they have failed to do so, the question arises how far the hospital or other branches

TABLE IV—WOMEN EMPLOYED ON ADMISSION AND CONTACTED

Present position	Age-group (yr.)			Total
	Less than 45	45-64	65 or more	
Dead	22 (14%)	61 (31%)	43 (59%)	126 (30%)
Manage their housework				
Better	45 (30%)	25 (13%)	8 (11%)	78 (19%)
As well	57 (37%)	64 (33%)	16 (22%)	137 (33%)
Worse	15 (10%)	38 (20%)	6 (8%)	59 (14%)
Unknown	13 (8%)	6 (3%)	..	19 (5%)
Total	152	194	73	419

of the National Health Service might influence events to obtain a better result.

The ability of a man to return to his old work and to continue in it for three years has been accepted as evidence that he has settled well and has dealt successfully with his illness. We admit that in a few instances a man who returned to his old work might for some reasons be better suited to another job, but in most instances a man is wise to return to his previous job and place of work. In this way he is more likely to resettle and more likely to receive sympathetic consideration. That 71% of the surviving men who were working before admission are back at their old or similar jobs is important.

More detailed attention must, however, be directed to the remaining 29% consisting of 70 men who are not still at their old jobs. Of these, 42 said that they had changed their work for health reasons. These have been considered in detail, and in most cases their statement appeared to be well founded. In about half of them this change did not involve downgrading economically or socially. In 22 instances it is considered that the change brought with it a fall in wages or in status, including 4 men who retired prematurely ; but in none of these instances did it appear that further help or advice from the hospital or a doctor could have improved the result. It was the practice to include in the discharge letter sent by the hospital general advice about the patient's work, but usually the details of the return to work were settled between the patient and his own doctor. In the case of patients whose illness was such that a change of work was essential the almoner made the necessary inquiries and arrangements for rehabilitation or re-training. This was usually done, before the patient left hospital, directly with the employer or with the co-operation of the Disablement Resettlement Officer.

A further 28 men were still prevented from working by their illness or their attitude to it. Investigation of these patients shows that in 9 cases further follow-up might have produced better results. For instance, 3 of

these patients had peptic ulcer, 1 diabetes, and 1 a small coronary occlusion. The remaining 19 men were definitely incapacitated and were regarded as unfit for employment, even under sheltered conditions. Thus, of the 251 men employed on admission and contacted since only 9 (4%) might have benefited from more assistance in resettlement. These were the patients who were kept from work largely by their attitude to their illness and who might have settled down after discharge from hospital if extra support had been forthcoming at the outset. Some patients of this kind need encouragement, some firm direction. Whichever it is should be forthcoming from the doctor, if his treatment is to be completed.

Of the 21 men who were unemployed on admission and have now been contacted 14 are still unemployed, and examination of their past record suggests that they belong to that small hard core of unemployables, and that little would be achieved by further efforts at their resettlement.

The assessment of the success of resettlement of the women inpatients is not so easy, since we rely mainly on the answers given by patients about their ability to do housework. As pointed out above, this is not a reliable measure, but for what it is worth it suggests a similar result to that obtained among the men. 73% of the surviving women managed their household duties at least as well as they did before admission. Of those who were unable to manage as well as previously there were a few with crippling diseases—e.g., poliomyelitis and disseminated sclerosis. Too few facilities exist for teaching these young women how they can best run their homes despite their disability. Of the women who were working outside their homes on admission, 60% were still doing so ; 25% said they left for health reasons.

The results shown by this investigation were unexpectedly good. They suggest that, in time of full employment and in a community with mixed industries, the present services are adequate if fully used. There is no evidence that in these circumstances further expenditure of man-power or of money will achieve results commensurate with the outlay. Much, however, depends on the doctor getting the patient back to his own job (or appropriate work) as soon as this is justifiable. The general practitioner has an important part to play in this, but the consultant's is equally great. Many hospital patients look to him for specific instructions about their return to work. Any unnecessary delay in this return to work may cause harm to the patient and hardship to his family. Other patients try to return to work too early. Here, too, it is important that the consultant and the general practitioner should speak with one voice. The 9 cases where resettlement might have been improved if the medical help had been more positive suggest that follow-up clinics should concern themselves with this aspect of treatment. They should inquire particularly about work and should take the necessary steps to ensure early resettlement when the patients have not gone back to their work.

SUMMARY

Patients admitted to the medical beds of Salford Royal Hospital in 1950 were followed up about three years later. Information was obtained concerning 91% of these admissions. 35% of the men and 28% of the women had died.

Of the 251 men employed on admission now alive and contacted, 177 (71%) were in the same or in similar work as when admitted to hospital ; 42 (17%) had had to change their job for reasons said to be connected with their health ; and 28 (11%) had become unemployed for similar reasons. Further investigation of these 70 patients suggests that in only 9 cases further help might have produced better results.

73% of the surviving women were able to manage their household duties at least as well as before admission.

These results suggest that the present facilities for rehabilitation and resettlement are adequate if fully used. The consultant's part in this work is emphasised.

We are grateful to the physicians of Salford Royal Hospital for their permission to follow up their patients. The incidental expenses of this investigation were defrayed by a grant from the Salford Royal Hospital Endowment Fund, and we wish to record our thanks to the members of the Salford Hospital Management Committee for their interest in this work.

INSTITUTE OF UROLOGY

THE Institute of Urology, London, which was formally opened on June 1, is an associated unit of the British Post-graduate Medical Federation. It came into being in 1946 and has already made useful contributions in both teaching and research, even though it has been housed in uncompleted premises. It does not have ready access to any large general hospital; but it has from the beginning been intimately associated with St. Peter's and St. Paul's Hospitals, and more recently it has acquired ward accommodation at St. Philip's Hospital; it now has available a total of 138 beds. In addition to the resources in its own new building it will shortly be able to use new laboratories at St. Paul's Hospital. Also it has links with the Royal Cancer Hospital and (for work on tuberculosis) with Harefield Hospital.

The institute is housed at 10, Henrietta Street (directly

opposite St. Peter's Hospital), which has been extensively modified and now includes a lecture-room, students' common-room, museum, laboratories, records room, library, photographic unit, and artist's studio. The house is old, and for the most part its character has been preserved. Two of the rooms are tastefully decorated in the Regency style, and there is an Adam mantelpiece (although a rather undistinguished example). The exterior of the ground-floor displays an interesting architectural solution of the problem of how to graft an entirely modern design on part of an old building, with a nice balance between boldness and discretion.

At the opening ceremony, held in a marquee pitched in the churchyard of St. Paul's, Covent Garden, the inaugural declaration was made by Viscount Waverley, chairman of the governing body of the British Post-graduate Medical Federation, who remarked that St. Peter's Hospital had engaged in postgraduate training as long ago as 1860, while St. Paul's had taken a share in the work since 1928. The new building, he said, should enable the institute to undertake fundamental researches on which it must rely to justify itself as time went on. There were speeches also by Mr. A. R. G. Hudson, chairman of the committee of management, Mr. Clifford Morson, chairman of the academic board, and Mr. J. D. Fergusson, director of the institute. Afterwards, demonstrations were on view, including notably one of the cytological diagnosis of carcinoma of the prostate.

Personal Papers

LEUCOTOMY

THE face of the clock, white as my own, as I lay there waiting to be pushed into the operating-theatre, indicated the time: 9.10 A.M. I was quite philosophic about it. After all, I myself had asked to have this operation. Lying there thinking back over the past twelve years of suffering, sometimes incredibly agonising, I felt prepared to gamble even my life on the chance of being cured. What use was it to live at all if one was only half-alive?

I suppose it all started way back in my childhood somewhere. An only child said to be "delicate," a home comfortable enough but perhaps rather too strict, parents not very well matched, and a somewhat neurotic mother—my early life was the typical breeding-ground of subsequent neurosis.

To suffer from what is popularly miscalled "nerves" (and is really fear in various disguises) is at once humiliating and frustrating: humiliating, because one gets scant sympathy in an illness which is usually neither mentally nor physically visible; frustrating, because the sufferer often knows quite well why he is ill, but insight into causes is, by itself, rarely enough. I have few pleasant memories of adolescence, for by then my inner difficulties had multiplied apace. Usually I sought escape in the comparatively "safe" world of my studies. At the university in 1939, two days before my honours examinations were due to begin, I experienced my first real breakdown. I had a midday meal as usual; by nightfall I could not keep even a cup of tea down. In the end I chose not to inform my family of my wretched state and, remaining in digs, somehow managed to drag myself through the next three weeks. By then I was so emaciated that, if held up against a strong light, my hand could literally be seen through. At last, when the exams were over, I went home to begin the long, long road to recovery.

In a slightly less severe form this nervous dyspepsia overshadowed my life for the next three years. In

1943 I experienced nine months of continuous depression so intense that I more than once prayed, in all sincerity, never to wake up again. No-one—not even the doctors—seemed to realise just how ill I was feeling. I learned, for the first time, how cruel is the trite phrase: "Oh, it's only nerves." But I never lost a single day's work through "nerves."

Not long after the end of the war I met my future wife; and a few months later we were married. I doubt if either of us was sufficiently mature to marry when we did—intellectual people are often "late-starters" in emotional growth. It soon became fairly obvious that there was very little hope of our ever living together happily; and a separation was followed by divorce. Having, to outward appearances, shouldered the responsibility for all that had gone wrong between us, I felt pretty awful, and at last decided to enter hospital to get straightened out.

Once in hospital—which I did not enter even as a "voluntary" patient, but on exactly the same terms as a patient going into any general hospital—I picked up. Modified insulin treatment built me up physically; discussing my problems with impersonal medical advisers created a new outlook; occupational therapy and the life of the ward somewhat restored my self-confidence. Nevertheless I remained "stuck" in certain vital respects, especially in relation to my problems in the world outside. The day came, therefore, when I had to choose between leaving hospital as I was, in order to have "another go at life," and the only worth-while alternative, which was to have leucotomy.

I was interviewed by a panel of about a dozen doctors, who afterwards discussed my case in private before deciding that I was a reasonably suitable patient for this operation. Even then I was not completely satisfied. I secretly read one or two reliable medical books on the subject—I wanted to know all the pros and cons, and the very worst that could happen to me. Having given me their opinion, the doctors left the final decision entirely to me. How I vacillated during those weeks! Eventually I chose to take the plunge into the unknown.

Preparations started soon after that, for it would have been sheer cruelty to keep me in that fearful state of suspense for long; and one fine morning in 1951 I at last found myself in the anteroom of the operating-theatre. I surprised myself immensely by being quite calm and resigned about the outcome of my "psychological adventure." As for the possibility of dying—I had reflected during the night that for over twelve years I had been half-dead anyway, and that, whereas I had a fair chance of pulling through, many of those who "go over the top" in war-time have less than a fifty per cent. chance of surviving. If I sincerely wanted to get well, I must risk even my life...

At ten-past-nine the surgeon was standing there at the foot of my stretcher. The anæsthetist stuck the needle into my left arm and asked me to count aloud, slowly. As I did so, the clock on the opposite wall began to revolve, slowly at first, then more and more rapidly, until it seemed to be just a spinning top. Soon it began to recede from me, faster and faster, to become a mere pin-head, incredibly far away, in the whirling vortex of infinity... an ultimate point in consciousness. Then—utter blankness.

Some six hours later I returned from that dreamless void to find myself back in my own bed in the ward. I knew immediately where I was. I knew also what my knowing where I was meant: that it was all over, as far as the physical side of the matter was concerned. So far, so good! Then followed the usual aftermath of an operation. For the first fortnight I experienced blinding headaches. Meanwhile I was timidly exploring my new and somewhat altered "self." Closing my eyes, I discovered a wonderfully coloured inner world of mysterious blues and greens—a sort of "submarine" effect. This was only a passing phase in my convalescence, however.

What was the psychological effect of the operation? One or two well-meaning people have objected that leucotomy is unwarranted interference with the "soul." It is not. One is obviously the same person after as before the operation. There is no black-magical change, no dramatic discovery of an entirely new personality. One's memories remain the same; one's intelligence is unimpaired, if not improved; one's basic feelings about life remain unaltered. The only thing which really changes—and this is a very gradual process—is the ability to alter the badly set pattern of one's life; there is more "drive," more resilience, more objectivity in regard to oneself and one's environment. The leucotomy operation itself is only the very beginning of one's cure. The actual improvement in a human life still remains for the individual himself to accomplish.

What have I myself experienced since the operation? In a remarkably short time I regained a sense of physical well-being, which I had almost completely forgotten. Psychologically, the prison doors are opening at long last; it is up to me to walk through them, so that in time I may complete my own cure. Already it is a truly wonderful release from bondage. For the first time in ten years I can really enjoy a cinema show; I am free to go about without excessive anxiety (even to places my wife and I knew together); my mind is clearer and my intellect, if anything, improved thereby; and when necessary I can again stand up to people.

Am I entirely free from symptoms? No, not yet, because I still have some big problems to solve. These are, of course, the problems common to us all, our human heritage. They include, first and foremost, earning a living again. After being wasted on the academic shelf for some years, this is not easy. Generally speaking,

people "couldn't care less" about one's need for employment during rehabilitation; they have their own problems. Also, there is the old fallacy "once a neurotic, always a neurotic" to be overcome. And there are other problems, including the rebuilding of my self-confidence, and reinstatement into social life with the help of loyal friends who have never doubted me.

Medicine and the Law

Physical Methods in Mental Illness

MODERN physical methods of treatment for mental illness are not without hazards for all concerned. Indeed, it is a nice medicolegal question whether the neurosurgeon, the psychiatrist, or the patient is most in need of protection.

In a letter in our last issue Dr. G. D. Morgan and Dr. Elizabeth Tylden drew attention to a legal case¹ in which a patient, making a claim for damages, lost financially because he had refused to enter a mental hospital for electro-convulsive therapy. It is possible that he would have benefited by the treatment; on the other hand, not all psychiatrists agree that electro-convulsive therapy is the most suitable treatment for the condition from which he is reported to have been suffering. Lord Justice Singleton, in dismissing the appeal, said that if a man was recommended by his own medical advisers and others to undergo a course of treatment, he ought to undergo it, if he was advised that there was a reasonable chance of recovery and that the treatment was reasonable. This is a fair statement of a principle which should hold good in an ideal state, where doctors do not disagree. As things are, the patient, when offered some form of physical treatment for mental or emotional symptoms, can only use his own judgment; and even if he had at his disposal all the information available to the medical profession he might still hesitate—might still decide to exercise his right to refuse the proposed measure. Lord Justice Singleton's ruling may coerce future patients to accept, for fear of financial loss, treatment which is not without some risk, however small, both to their personality and to the actual structure of their brain. There is also the danger that if a psychiatrist, for what seem to him to be good and sufficient medical reasons, withholds such treatment from a patient, he will run a risk of being summoned for negligence.

Similar, but more complex, problems are presented by prefrontal leucotomy; for here, of course, personality and intellectual changes can occasionally be very unfavourable indeed, and pareses and convulsions are among possible sequelæ. The protection of the neurosurgeon was discussed last year by the American Psychiatric Association; and though the legal position in the United States is somewhat different from our own, the problems to be solved are much the same. Dr. Maximilian Silbermann and Dr. Joseph Ranschoff² estimated, in their opening paper, that some 20,000–25,000 people in the U.S.A. have undergone some form of this operation, and that almost every imaginable category of mental illness has been treated in this way. They therefore set out to consider what form of consent should be sought before such operations are done, and who should sign it.

If the patient is legally capable of consenting he must, of course, sign the form himself; but patients treated by leucotomy are often not legally competent. Even if the patient is able to consent Silbermann and Ranschoff advise getting the consent of any close

1. *Times*, May 21. *Marcroft v. Scrutons*.
2. *Amer. J. Psychiat.* 1954, 110, 801.

relatives as well, lest any of them later brings a suit claiming that the person who consented to the operation was himself legally incompetent at the time of signing the form. If the patient is incompetent, the consent of a guardian or a committee appointed to take care of him should be enough; but in America, it seems, such committees can greatly complicate the picture. In most States an insane person is a ward of the State, which acts through the appointed guardian or committee. In some States there are two committees, one charged with the care and treatment of the insane person, and the other with looking after his property and financial affairs. Silbermann and Ransohoff advise getting the consent of *both* committees (for the second committee has to authorise payment of the surgeon), and *also* of any close relatives. Since it is "highly improbable" that either committee will give consent without a court order, the first step is to petition the court to give consent and allocate funds from the patient's estate. The next of kin has to be notified, and a long and expensive proceeding may ensue. Special difficulty arises when (as is usually the case) the patient is indigent and cannot afford legal help in establishing his incompetency. These obstacles seem considerable; but Silbermann and Ransohoff insist that for complete protection against liability they must be surmounted.

There is, moreover, another difficulty: a patient may be legally incompetent at the time of the operation, and may later, by another court, be declared to have been, in retrospect, competent all the time.

In a case quoted by these authors, a woman who was legally incompetent was operated on by a neurosurgeon with the consent of her appointed guardian. Shortly afterwards a court determined, in another proceeding, that the woman was sane and could not be retained in the hospital; and a few months later a jury found that she was sane at the time of the operation. She was therefore allowed to recover damages, from the neurosurgeon, for assault and false imprisonment.

At the opposite pole of injustice seems to be the opinion of the Deputy Attorney-General of Pennsylvania that the friends, relatives, guardian, or other persons have no right to determine what methods of treatment can be given to a patient detained in a mental hospital; and that treatment by shock therapy can be given by the superintendent of the mental institution without the consent of the patient or his guardian. Silbermann and Ransohoff suggest that this theory might possibly be extended, "as a legal proposition," to include pre-frontal leucotomy and kindred operations. "However," they very properly add, "ethically speaking, this might seriously endanger a person's right to decide for himself whether or not he agrees to an operation, the effects of which are irreversible."

This leads them to consider the form of consent; and since, as they say, "loosely worded and general consents, do not afford as much protection as specific consents," they propose that the form of consent should mention possible results in detail, and even state the kind of operation to be performed. The consent form they propose carries the following formidable paragraph, which might well deter most patients from consenting at all—though guardians might accept the conditions in a more robust spirit.

"The nature of the operation and the special risks involved have been explained to the undersigned. In particular a full explanation has been given of the possible occurrence of convulsions, personality or intellectual changes, loss of bowel or bladder control, paralysis or other weakness of the nervous system resulting from this operation and the consent hereby given is with full knowledge of these possible consequences."

Recognising that such an unconditional surrender waives the patient's immunity from operation, the authors suggest that he too should be protected—for instance, against a guardian who grants consent without due deliberation. Perhaps the approval of a panel might be sought before operation; and this safeguard has also been suggested for patients without relatives who are in mental institutions.

Finally, there is the public to be considered: do they perhaps need protection? These operations can produce considerable changes in the patient's affective behaviour, judgment, and concept of abstract ideas. A patient who had criminal tendencies before operation is hardly likely to find a higher standard of ethic among the benefits of operation. After transorbital leucotomy, which is commonly performed in America, a patient may be returned to his ordinary life within a few days. Is there some risk in discharging him so early from close supervision? Quite apart from patients who are not reliable citizens before operation, there are others in whom criminal tendencies develop after it. Silbermann and Ransohoff mention a case in which a patient without previous criminal tendencies committed murder after leucotomy. Dr. Walter Freeman, in discussing the paper, remarked that major crimes by leucotomised patients were "surprisingly infrequent"; but added that he knew of one homicide and had seen newspapers accounts of two others.

This raises a flock of questions about the patient's responsibility. Should the leucotomised patient be held fully responsible for negligent actions? Is he capable of the same care and diligence as a person not so treated? Should the operation affect his ability to contract marriage, obtain divorce, or adopt children? Should the fact that he has been leucotomised be ground for divorce? Should failure to reveal that he had undergone the operation before marriage be ground for an action for annulment? Does the operation change a patient's capacity to make, modify, or revoke a will? Can a contract for a person's services be broken by one contractor on the ground that the operation made the other contractor unreliable? Is there, here, an analogy with the case of the patient "defectively cured" of general paralysis by malarial treatment?

Clearly there are many legal questions to be settled about the results of this operation; and in this respect it cannot be classed with other surgical procedures. If Lord Justice Singleton's ruling in the matter of electro-convulsive therapy should be extended, at some future time, to cover treatment by leucotomy, it would bear very hardly on those patients who prefer the ills—and the character and personality—they know to those they know not of.

Domestic or Professional?

In a case before Lord Wheatley in the Court of Session in Edinburgh, a woman is claiming £5000 damages from the board of management for West Fife Hospitals for burns of both buttocks, legs, and back sustained as a result of her having been admitted unconscious to the Northern Hospital, Dunfermline, on April 11, 1953, and put to bed in contact with a live electric blanket.¹ She claims that the nurses, in preparing her bed and putting her in it, were performing domestic work under the control of the board: in any event they were acting in the course of their employment with the board and it was their duty to do their work carefully. In their defence the board denies that the preparation of a bed for the patient, and settling her in it, were duties performed by the nurses under its direction and control. These were matters falling within their professional skill as nurses.

1. *Dunfermline Press*, May 22.

Reconstruction

HEALTH CENTRE IN MANCHESTER

EXPERIMENTS in methods of running a general practice are beginning to show a healthy diversity. Here and there are a few health centres in which general practitioners work side by side with doctors holding local-authority clinics ; at least one diagnostic centre has been brought into use ; and group practice in various guises is increasing.

At the Darbshire House centre in Manchester, which was being officially opened by the Minister of Health last Wednesday, distinctive features include a plan for



Fig. 1—Exterior of building.

the practitioners, later on, to teach undergraduates and themselves to operate local-authority clinics. District nurses will be attached to the centre and will also run a treatment room for injections, minor injuries, and physiotherapy. It is hoped that health visitors will later work from the centre.

The money for this venture comes from several sources. The building itself has been bought and adapted by the Nuffield Provincial Hospitals Trust, which has promised a substantial grant ; a similar grant is to come from the Rockefeller Foundation ; the university is to meet the research and teaching expenses ; and the city corporation is to provide money for maintenance costs (this will come wholly from local revenue, since the centre does not fall within the definition of a "health centre" in the National Health Service Act).

The aims are : (1) to provide first-class medical care for the inhabitants of the densely populated city area that it serves ; (2) to demonstrate integration of preventive and curative services ; (3) to provide for the teaching of undergraduates ; and (4) to show how medical care can take into account social factors, and to promote sociomedical research.

The four doctors staffing the centre have been working there for nearly three months. Each was already established in practice ; and this transfer to a strange milieu is a

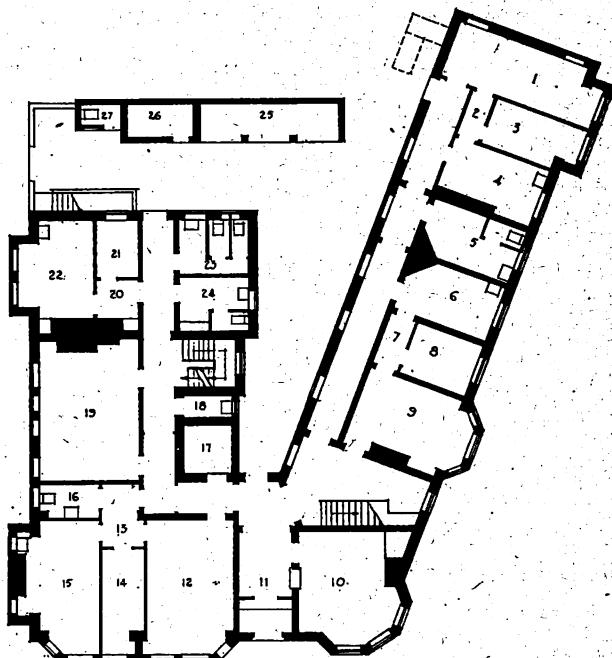


Fig. 2—Plan of ground-floor.

1-4, General-practitioner's suite (1, waiting-room ; 2, lobby ; 3, examination room ; 4, consulting-room). 5, Doctors' toilet. 6-9, General-practitioner's Suite. 10, Office. 11, Entrance hall. 12-15, General-practitioner's suite. 16, Doctors' toilet. 17, Lift. 18, Cleaners' room. 19-22, General-practitioner's suite. 23, Women's toilet. 24, Men's toilet. 25, Pram shed. 26, Caretaker's fuel store. 27, W.C.

courageous act. Eventually these doctors will each run two sessions a week of the local-authority clinics of the school medical service and maternity and child-welfare service ; they will do two sessions a week as clinical assistants at a local regional-board hospital ; and they will be approved as teachers in the medical school. It is proposed that undergraduates, as part of their training, shall take some of their clinical instruction with the doctors in the centre and the district. Furthermore, it is hoped that careful study and recording of the influence of social and economic factors on illness and disablement in the urban population served by the



Fig. 3—A consulting-room.

centre will provide a good basis for research projects, which will be under the guidance of the university department of social and preventive medicine.

The centre, which is within the precincts of the university area, is a former hostel for clerks and domestic-science students, which was bought for £17,500, adapted for £15,000, and equipped for £10,000. The building (fig. 1) is of an awkward V shape, which involved problems for the architects, who have done their best with existing bricks and mortar. On the ground-floor (fig. 2) the four general practitioners have separate suites, each consisting of a consulting-room (fig. 3), waiting-room, and examination-room (fig. 4). These suites are decorated in light pastel colours, with bright

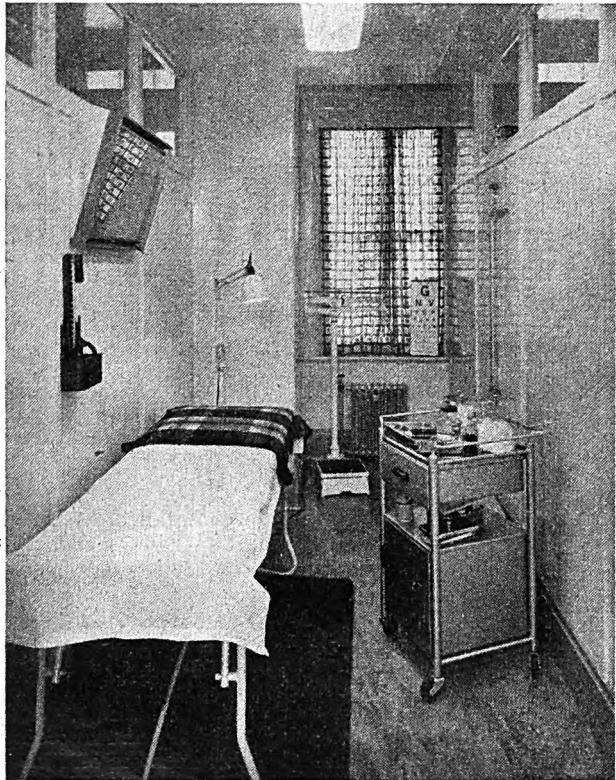


Fig. 4—An examination-room.

curtains and light oak furniture, and, on the walls, lithographs by contemporary artists.

The floors are connected by a passenger-operated lift. The first floor has a small treatment room for the three district nurses, who, in an adjoining room, can give infra-red-ray treatment and simple physiotherapy. There is also a room for clinical pathology, staffed half-time by a hospital technician; specimens for the more complicated biochemical tests and swabs for culture are sent to the clinical-pathology department of the nearby teaching hospital. On this floor, too, is the X-ray room, staffed half-time by a radiographer. Finally, this floor will accommodate the maternity and child-welfare clinics.

The second floor will be used for school clinics; and it has a caretaker's flat and a room for the liaison officer (who is also reader in social and preventive medicine), who will organise undergraduate teaching.

The lay staff includes the secretary, shorthand typists, and a telephonist.

In the brief period that the centre has been open, patients' comments have been generally favourable; they seem to appreciate especially the advantage of an immediate radiographic examination or laboratory test.

Those who would start any sort of health centre set their feet on a stony road. The initiators of the Manchester scheme, who by painful inches have gained their first objective, deserve a resounding success.

Parliament

Control of Television Advertisements

In the House of Commons on May 31, on the committee stage of the Television Bill, Dr. EDITH SUMMERSKILL moved amendments to the Second Schedule (Rules as to Advertisements) to protect viewers—and especially the chronic sick or disabled who were tied to the house—from the glib patter of the salesmen of some drug firms. Mr. ARTHUR BLENKINSOP said that one of the great anxieties in the health service was that doctors were urged by their patients to prescribe for them medicines and drugs which the doctor might feel were undesirable. While the Minister of Health was trying to secure the co-operation of the medical profession in avoiding the prescription of unduly costly drugs, it would apparently be proper for advertisers to promote their sale through the commercial television service.

Dr. BARNETT STROSS agreed that the Minister already had power to prevent unethical advertising. But did he realise what an embarrassment the persuasive advertisement of proprietary preparations might be to the general practitioner who had to waste his most precious asset—his time—explaining to his patients that such and such a thing is not as good as they think it is?

Mr. L. D. GAMMANS, Assistant Postmaster-General, said that everyone would agree with the spirit behind the amendments, which was to prevent the natural hopes and fears of sick people being improperly exploited. The Independent Television Authority already had powers under the Bill, and advertisers, who were as keen as the Government to maintain the general standards of advertising, had volunteered to set up a committee to advise the I.T.A. The Postmaster-General had already consulted the British Medical Association, who had agreed to nominate representatives to sit on the suggested advisory committee. The committee would advise not only on the products to be advertised, but also on the misrepresentations which might take place by someone on the television screen pretending to be a doctor, or a nurse, or saying that he was a herbalist. That would give the medical profession what everyone wanted them to have, the opportunity to express their views. Mr. Gammans added that he would examine the point and if he thought it necessary he would include the committee in the Bill. The amendment was by leave withdrawn.

Dr. STROSS moved an amendment providing that no advertisement should be permitted of any tobacco, smoking mixture, cigars, or cigarettes. He asked for an assurance that the advisory committee would include two members of the Medical Research Council. It might be that the result of the magnificent gift of £250,000 from the tobacco companies would give a solution of the cancer problem within a few years. But today we knew that 83% of all cancers of the lung had an association with excessive smoking, in the main of cigarettes. He held that there should be some safeguard to prevent this type of advertising during the next few years. Sir DAVID MAXWELL FYFE, the Home Secretary, said that he stood by the announcement which had been made by the Minister of Health, but there was a general feeling that it would be unfair to make this prohibition. He undertook to discuss the matter with the Minister of Health and bring to his notice what had been said in the debate. The amendment was by leave withdrawn.

Coroners Act

The Royal Assent was given by Commission to this Bill on June 4.

QUESTION TIME

Group Practice

Replying to a question, Mr. IAIN MACLEOD, Minister of Health, said that applications for assistance in establishing group practice had so far been received from some fifty

groups of practitioners. It was known that some executive councils had other applications under consideration.

Pneumoconiosis Claims

Replying to a question, Mr. OSBERT PEAKE, the Minister of Pensions and National Insurance, said that 5439 people claiming benefit for pneumoconiosis under the National Insurance (Industrial Injuries) Acts were first examined by the pneumoconiosis medical panels in 1952, and 7123 in 1953. Of these 3472 and 4648 respectively were found to be suffering from the disease, representing, for each year, about two-thirds of the number examined.

Army Medical Records

Replying to a question, Mr. ANTONY HEAD, Secretary of State for War, said that the contents of Army medical records might be given, on request, and with the consent of the men concerned, to civil doctors to assist in treatment. It was not the practice to disclose them to the men themselves.

Danger of Teething-powders

Replying to a question, Mr. MACLEOD, Minister of Health, said that no public warning had been issued by the Ministry of Health concerning the use of teething-powders, but in a recent series of notes issued by the Ministry to the editors of women's magazines and to women's page journalists, attention had been drawn to the possible harm in giving repeated doses of teething-powders to infants without medical advice.

Physically Handicapped Children

In answer to a question, Miss FLORENCE HORSBRUGH, Minister of Education, said that in December, 1953, local-education authorities in England and Wales were providing special educational treatment for 6449 physically handicapped pupils accommodated in special schools (other than hospital schools), independent schools, and boarding-homes. Authorities were at the same date seeking special school places for 1613 physically handicapped children. The facilities were being continuously increased, and at present 700 places were being provided, or were shortly to be put in hand.

Hospital Pay-beds

Replying to a question, Miss PATRICIA HORNSBY-SMITH said that during the period July-December, 1953, 32.3% of hospital pay-beds were unoccupied. The number of free hospital beds had been increasing steadily; further increases were planned, and hospital authorities were constantly endeavouring to secure the more efficient use of existing beds.

Psychiatric Treatment of Borstal Prisoners

Miss MARGARET HERBISON asked the Home Secretary whether he had considered the disadvantages of the return to prison conditions in Holloway of borstal girls needing psychiatric observation and treatment; and whether, bearing in mind the fact that Holloway was found not to be the proper place for normal borstal girls, he would consider as a matter of urgency establishing a psychiatric unit under conditions more suited to the needs of emotionally disturbed adolescents where treatment would have a greater chance of success.—Sir DAVID MAXWELL FYFE replied: Admittedly there are disadvantages in sending borstal girls needing psychiatric observation and treatment to Holloway, but there are medical, psychiatric, and nursing services there that are not available in any other penal establishment for women. The number of girls requiring these facilities is so small that it is not feasible to set up a special centre to cater for them. Their conditions at Holloway are governed by the borstal rules.

Miss HERBISON: Does not the Home Secretary agree that it is wrong that borstal girls, particularly emotionally disturbed ones, should be sent to any prison and especially to Holloway? Does he not realise that it would be worth the expenditure to have a small psychiatric unit in one of the borstals? Will he not consider even the sending of visiting psychiatric specialists to one of the borstals?—Sir DAVID MAXWELL FYFE: I should very much like to consider those points. I can assure the hon. Lady that the number does not exceed a dozen a year, and that they remain in Holloway only so long as is necessary for the purpose of the treatment. But I shall consider what she has said.

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN I left Tom and Mabel McGuinness at the door of their caravan last Tuesday afternoon, I was undecided whether they ought to be certified or canonised.

I first met Tom after a talk I had given in the Workmen's Institute on Great English Painters. He asked me if he could see me professionally and I was astonished at his story: A week ago, he said, he had left his home to sweep the streets and when he came back at 6 p.m. found he had drawn a dividend on the pools and was £450 better off.

His wife and he had always had a burning ambition to own a caravan and to live on a small ribbon of land by the wide waters of the Lune not far from the old village of Halton. This was only a mile or so from work and was a place of great beauty and quiet. The dividend was their opportunity. However, news of his luck had reached his relatives—more than he believed existed—who began to put in their claims for his charitable consideration. So many and so urgent were the requests for help that Tom began to grow anxious and sick, wondering how he could dispense his new riches with equity and without offence. It was at this stage he sought my advice. The conflict was solved, before my bromide had a chance to take effect, by his wife who was a woman of steady mind and a singleness of purpose. She told him and his relatives that she had bought a caravan for £450, and had ordered its immediate removal to the elected site by the river. And there, two years ago, they settled in great contentment.

When his work is finished Tom fishes for rainbow trout or works on the small square of green turf between his home and the river, which he has converted into a model garden. His wife spends her day polishing her small home until the brass and the wood shines as brightly as the sun on the waters outside.

Last Tuesday I was asked to visit Tom, who had sprained his ankle. After I had attended to him, my interest was arrested by a picture on the wall. It was, I thought, a fine copy of a Turner landscape showing a part of the Lune Valley near Kirby Lonsdale. It seemed wonderfully true and faithful to his style. I asked if I might take it down and was soon handling it with all the devotion due to the original painting of a great master.

"How did you come by this picture, Tom?"

"It was left me by a great aunt who died in Scotland, last year."

"Do you know who painted it?"

"Yes, an English artist called Turner."

"... You know, of course, that it is worth a lot of money?"

"Mabel," said Tom, turning to his wife who was baking bread in a small gas oven, "How much did that chap from Christie's offer?"

"Six thousand, dear."

"You see," said Tom, limping to the door in order to speak to me more confidentially. "When this valuer chap came down and offered us £6000, I was all for taking it, but Mabel was against it. Mabel is a remarkable woman, doctor. She says to me, she says:

"What do you want in life, Tom?"

"A nice home by the river and peace—and no relations at any cost."

"At any cost? If we get rich where do you think your relations would be?"

"On the doorstep, Mabel."

"And your home by the river?"

"Invaded,"

"And peace?"

"Gone!"

There was a pause while Tom, who had recalled this conversation with relish, savoured it in his memory again. And then he said "In any case it looked nice over the bunk, so we left it on the wall."

that is—we planted ourselves firmly among the silly ones. Setting out for Folkestone from a southern suburb at 11 A.M., we were soon bowling through Maidstone, and after only brief impaction at Ashford won through to the coast by 12.45. This, we said, is too easy. But wait! Setting course for home at 5 P.M. ("my dear, the children must be in bed by half-past seven") we joined a half-mile queue at Ashford, and got through in a quarter of an hour. At Maidstone the queue, double-banked, started over three miles from the town, and was moving at rather less than 1 mile an hour. After three-quarters of an hour of this we acted boldly, cut off on to a by-road, and rejoined the crowd proximal to the obstruction. At Swanley the line was only a mile long; and we reached home—62 miles from the coast—in 4½ hours. By this time our three little wonders were in jubilant form. Not so my missus and I. "Never again," we sighed. But we shall.

* * *

Derby Day always brings its little store of excitement, but our proximity to the racecourse is a doubtful asset. True, all clinics are cancelled, but not with the idea of letting us go to watch the fun. At all other times competition for outpatient appointments is fierce, but on this one day of the year the local inhabitants have no wish to see a specialist. On the other hand the casualty officer is usually provided with reinforcements, and empty beds are kept ready for Pott's fractures, perforated peptic ulcers, and cerebral haemorrhages, which are the chief sporting risks of the turf. Attacks of paranoid hysteria ("I've been robbed!") are not infrequent, and there is said to be a significant increase in the incidence of pediculosis. Complications among inpatients are few, but the house-surgeon always goes round the chronic blocks after the commentary, reducing herniae.

Our first admission was a school-teacher from the Midlands who, in the heat of the final furlong, had a rigor. "And what might a Birmingham schoolmaster be doing on Epsom downs on a Wednesday afternoon?" we asked. "Brushing up his arithmetic, of course," came the reply; then, as a glum afterthought: "Subtraction sums."

But on the whole this was a satisfactory year. Few patients, merry or moribund, could resist backing Never Say Die, and even a confused old granny, who has entertained suicidal notions for years, insisted on 2s. each way.

* * *

By a fortunate coincidence I was again in London this year at the time of the Chelsea flower show. Superlatives do not do justice to the magnificent blooms modern horticulture produces, but I was best pleased by the scientific section where I learnt that while Londoners must expect to water their gardens in >9 years out of 10, Mancunians only need do it in <5. Poor Londoners I thought, how they must long for that elusive <1 year in 10 when they are spared the drudgery of watering-can and hose-pipe. Next morning I returned home to Manchester; persistent rain washed out an afternoon's tennis. I couldn't even get into the garden to tackle the weeds made luxuriant by all this confounded rain.

* * *

Long after everyone else had gone home, a tired and hungry surgeon still sat in the library, uninterestedly turning the pages of *The Lancet*. From time to time he cast impatient glances at the clock on the wall, shook his head, and sighed. At last he rose—"I think it's all right for me to go home; my children should be in bed by now."

* * *

News from School.—The fountain pen broke. I think it could be mended with cellophane. There is a big crack in the plastic above the nib. Everyone was trying to throw balls over and on top of the tower. A lot were lost. We have been planning how to rebel against the Masters. We overpower Mr. Smith-Jones in the shooting range at gun point, (He is the shooting master.) then we raid Catterick Camp on visitors day, capture a plane from Leeming Bar aerodrome from which we scatter pamphlets on Northallerton and nearby appealing to boys to join us. Soon we have an army of 500. In the end we will conquer the earth and rule it.

Love from David.

Letters to the Editor

THE POSITION OF NEUROLOGY

SIR,—It is impossible not to concur, in part at least, with the reasons you proffer for the difficult situation of clinical neurology in this country since 1948. Yet I venture to submit that we must probe a little deeper if we are to gain an effective insight into the situation.

You say that "there is a tendency to believe that in the provinces neurology should be undertaken by general physicians; and that both the practice and the teaching of general medicine would be impoverished by the appointment of neurologists." I do my colleagues the general physicians the justice to say that I do not believe they regard themselves as competent to act as consultant neurologists, and that they would not make any such claim for themselves. Moreover it is not where there are medical schools in the provinces that neurologists are lacking, though they are too few, but in large industrial and in some rural areas where no such schools exist. How, then, can teaching be impoverished where no teaching is, or alternatively how could the teaching of medicine be enriched when neurology is "undertaken"—sinister word—by general physicians.

Let us be frank about this matter, if we are to discuss it at all. The very numerous young men trained for, and eagerly desiring, consulting appointments as general physicians find the number of vacancies woefully inadequate, and the lists of candidates when any vacancy arises as woefully long. What more natural than that they should view with dismay the lessening of consultant openings for them every time, under the present unmeaning system of limitation of consultants, that a neurologist is made a consultant? With no illusions as to their inadequacy to cope with the thorny problems of neurology they are ready to accept the simple notion that the general physician might take over the neurological estate and administer it as a side line, and are prepared to dub neurology a luxury if this will help.

In truth, neurology is nobody's side line. It happens to be a difficult and precise discipline in which we in this country—and let there be no false modesty about it—have long excelled, so that its study has brought more postgraduates to this country from overseas over the past few generations than any other single branch of medicine. It happens also to be an indispensable discipline, and if it is to be allowed to go by the board to meet the complications created by the National Health Service and the present redundancy of potential consultants in general medicine, we shall not be able to restore it, or the damage to the prestige of British medicine which its loss will entail.

The grounds upon which the neurology committee of the Royal College of Physicians submit that there is a deficiency of adequately trained neurologists cannot be gainsaid by anyone who knows the facts, nor their submission that the neurosurgeon is by temperament and training unfitted to "undertake" the whole field of neurology within which the main incidence of illness is medical and not surgical. Yet when, as now, matters of politics and finance, and not the informed and dispassionate view of the needs of the community and of medicine, determine the pattern of development of medicine, situations incompatible with its proper growth and differentiation must arise and will continue to arise.

Unhappily, as I most strongly hold, every professional body that represents medicine with the Ministry of Health has become so deeply entangled in financial controversy over questions of the emoluments and material gratifications of doctors that none is left to speak with single mind and complete disinterestedness upon what is essentially an academic problem—namely, the rational growth and differentiation of medicine as an activity upon which so

much of the welfare of the community hangs. This, perhaps, is where an Academy of Medicine, standing aloof from the chafferings of the market-place, might have filled a rôle of the first importance.

London, W.1.

F. M. R. WALSH.

ARTHROPLASTY v. ARTHRODESIS

SIR.—Your leading article of May 29 discusses the relative claims of arthrodesis and arthroplasty of the osteo-arthritis hip-joint with such fair judgment that I hesitate to criticise. At the same time I must do my best to dismiss the myth you have raised once again that "the variety of methods of arthrodesis reflects the difficulty of producing certain fusion of the hip-joint." If enough people go on saying this long enough, someone will begin to believe it.

Let it be understood quite clearly that there is no difficulty whatever in securing sound arthrodesis of the hip-joint provided only that the first principles of surgical technique and after-treatment are observed. If a surgeon wants to arthrodesse a hip-joint he can always do so. The articular cartilage must of course be removed completely, and there must be internal fixation with grafts or nails, and with protection in plaster for about four months (which never did any harm to a knee-joint provided only that the surgeon knows how to deal with stiff joints by active and not by passive measures).

Your editorial implies that there is uncertainty about arthrodesis of the hip-joint; but the fact is that the certainty of the result of arthrodesis is the very special merit of this operation. The joint will of course be as stiff as it was before; there may be some slight difficulty in reaching the shoe-lace or sitting bolt-upright in a chair; but there can be no doubt at all that the patient will walk ten or twenty miles, jump hedges, vault fences, climb mountains, and engage in every recreation without ever thinking about himself or his hip-joint.

There are of course still older patients, aged 60-90 years, and also those with bilateral osteo-arthritis, in whom arthroplasty is a far better treatment—but here again we must beware recent criticisms; the results can be good if the operation is done well, and most recent failures have arisen not because the operation was bad but because the operation was done badly.

There seems to be no doubt that arthrodesis is best for young and vigorous patients up to the age of about 60 years, but that beyond that age, and for patients with bilateral osteo-arthritis, arthroplasty is better—though I should add that of all the happy patients who see me month by month, I do not know of any more happy than those whose arthritic hip-joints have been arthrodesed. The important point, which should really be obvious, is that neither arthrodesis nor arthroplasty of the hip-joint can succeed unless the operation and the after-treatment are done properly.

London, W.1.

REGINALD WATSON-JONES.

SIR.—In your leading article you mentioned two methods of hip arthroplasty—Smith-Petersen's cup and Judet's acrylic head. In my opinion neither of these methods is satisfactory. Cup arthroplasty, or any such procedure which introduces a "loose body" into the hip, has got obvious mechanical defects. An acrylic head, or other prosthesis which necessitates excision of the head of the femur, is a mistake because if anything untoward should happen further treatment is very difficult.

For upwards of seven years I have been using a steel prosthesis, by means of which the femoral head can be retained. It consists of a hollow cannulated cap which fits over the trimmed head of the femur, and a trifin nail which fixes it to head and neck of the bone.¹ In a fairly large series of cases the following points have emerged:

1. Fitzgerald, F. P. *J. Bone Jt Surg.* 1952, 30B, 120.

1. The diameter of the prosthesis should be 4 mm. less than the femoral head as measured by callipers at the time of operation.

2. The femoral head should be trimmed with a special cutter and not an osteotome, so that an accurate fit can be obtained.

3. A preliminary guide-wire introduced into the head and neck of the bone is essential if the length and position of the prosthesis is to be gauged accurately in advance.

4. The shank should be centrally placed in the neck with the prosthesis in mid position, neither in valgus nor in varus.

5. The point of the prosthesis should not penetrate the femoral cortex.

6. The nail and cap should be riveted together at the time of operation, so that the over-all length is correct. In the original model, which was demonstrated by the makers (Down Brothers) at the British Orthopaedic Association's meeting in Nottingham in 1949, the cap and nail were shown in one piece and the prosthesis is still sometimes supplied in this form. This is a mistake if accuracy is to be achieved, unless a very large stock of prostheses is carried. The two elements can be riveted together by the surgeon at the time of the operation; it takes less than half a minute. This technique has been used for many years; it is simple and perfectly reliable.

7. Finally, meticulous technique, unhurried gentleness, and perfect haemostasis are essential for a good result.

It is too soon to be dogmatic about the ultimate success of this method. This prosthesis is not a panacea, but the results—when the above points have been observed—are promising and it is worthy of further careful trial.

London, W.1.

F. P. FITZGERALD.

REMUNERATION OF HOSPITAL MEDICAL STAFF

SIR.—I received recently bulletin no. 3 of the Central Consultants and Specialists Committee, which purports to explain to the profession the rationale of the recent award to hospital medical staff.

Paragraph 1 states that "Consultants entered the service on the appointed day in 1948 upon 'interim' terms (for example, the maximum salary of a part-time consultant was £1600 per annum)." However, it should be appreciated that this maximum was available for as little as eight sessions. It might reasonably be assumed from this that the rate for a whole-time consultant would commence at £2200 per annum, as a basis for negotiation. In fact, although the statement informs us that a whole-time consultant was entitled to opt, if he so wished, to keep his old pre-service terms (stating that few could have so opted since the prospective new terms were so superior) no new terms were offered and whole-time consultants were obliged to continue at a salary which in many cases was 25-33% below the recommended minimum of the Spens scale in terms of 1939 money values. This deplorable state of affairs continued, not until July 22, 1949 (para. 3), but until January, 1950, when the 1948 scale came into existence. Many by that time were heavily in debt and overdrawn at the bank. Part-time consultants meanwhile could no doubt offset the increase in the cost of living to some extent by higher fees, and in any case had a sessional fee of £200 per annum for their hospital services, plus travelling allowances and allowances for subscriptions, &c., denied to their whole-time colleagues. An adverse differential was therefore applied to the whole-time consultant at the outset of the scheme.

Paragraph 3 informs us that on July 22, 1949, the Joint Committee advised hospital staffs to enter into permanent contracts, but omits to state that this was done only after a promise had been secured from the Ministry that remuneration was a subject suitable for arbitration. This factor, together with other important items, is given in para. 9 of the bulletin but is there given out of its correct context, which is misleading. Furthermore, some coercion was exercised by the Ministry in an attempt to "stampede" the Joint Committee into advising consultants to accept contracts when Sir Lionel Whitby received a letter: "... when any deadlock arises in future discussions, both sides can consider which is the best thing to do, and if arbitration seems best the Minister will certainly agree to it and to be bound by the result, subject only to Parliament . . . but you will appreciate the impossi-

bility of a situation in which consultants and specialists are continuing to be advised to postpone entering into contracts while being assured by us that any solution will be retrospective for them. This is an aspect that we shall be bound sooner or later to review, and we want you to help us to make any such review unnecessary by joining us in speeding the solution."

In the face of this threat to refuse back-pay when settlement was reached, unless this was brought about rapidly, and having secured agreement that remuneration was a matter suitable for negotiation, and with the knowledge that the betterment factor for G.P.S. was 20% (a figure imposed as long ago as 1946 by the Government) and that this was not likely to be exceeded before discussion by Whitley machinery, the Joint Committee advised consultants to sign permanent contracts. These contracts offered a scale of remuneration, subject to "the terms and conditions of service determined from time to time."

A consultant at this stage would reasonably have borne in mind the leading article of the *British Medical Journal* of March 19, 1949, which stated: "The salaries of permanent secretaries and deputy secretaries in Government Departments have been increased by 50% above the salaries of these officers in 1939. It is not unfair to assume from this that the Government regards 50% as a reasonable betterment factor... as the cost of living for the middle and professional classes has risen by 85% since 1939 (B.M.A. economic expert's calculation) consultants and specialists are as unlikely as general practitioners to be content with a betterment factor which is 22% or lower at different points in the range of incomes recommended. Consultants and general practitioners have made joint representation on the betterment factor, and the B.M.A. has put to the Ministry of Health a request for a factor of 70% to be applied to the gross remuneration of general practitioners. Pending the results of the negotiations on this the medical profession will not fail to keep in mind the increase of the salaries of senior Civil Servants by 50% over what they received in 1939."

Another leading article in the same journal, dated July 23, 1949, entitled "Consultants Advised to Sign," remarks: "The Joint Committee may be congratulated on having secured from the Ministry agreement that remuneration is open to arbitration and it is reasonable to assume that in the event of serious disagreement neither the Minister of Health nor the medical profession would in practice fail to seek the obvious and fair method of resolving a dispute—arbitration or a committee of inquiry."

Having therefore secured agreement to arbitration concerning remuneration it is difficult to appreciate the opinion expressed in paragraph 6 of the bulletin that "From the time these Terms of Service came into effect our conditions of service ceased to be 'interim' and we ceased to have any legal claims to modification in our remuneration based on the recommendations of the Spens Committee." Either we are being "led up the garden path" today, or alternatively the Joint Committee at that time failed in their duty by not warning consultants that they would be signing away their "birthright" and abandoning Spens. At this point the members of the South West Metropolitan (Western) Regional Committee saw fit to send a signed letter to the *British Medical Journal* as follows: "It has been noted also that the Joint Committee has omitted to report regularly its proceeding to the Central Committee and finally acted without authority in agreeing with the Ministry to recommend the terms for the permanent contracts of hospital staffs . . ." This would appear to have created a, by now, well established precedent.

Paragraph 10 informs us that the terms and conditions of service "compared very favourably with preceding consultant standards of remuneration"; but these had been carefully determined by the Spens Committee as being £1500-2500 in 1939, so that it is not easy to see how £1700-2750 compares "very favourably" in view of the Government's own admission in 1946 that the increase in cost of living at that time was 45%.

Paragraph 12 is misleading when it states that the "general practitioners and the Government by mutual agreement submitted the matter to arbitration by a High Court Judge in 1952." The facts are that the general practitioners had failed to get the Minister, in spite of previous promises, to agree to arbitration; Mr. Aneurin Bevan¹ being reported

to the effect that "The Minister is clear that in the light of these figures no reasonable case can be made for any increase in the total remuneration of general practitioners, nor any argument substantiated to show that general practitioners as a group are inadequately paid. Nor, in his view, could any claim be justified that any future alteration of remuneration at any later date should be made retrospective, either to July, 1948, or to the present day." This statement has a familiar ring to it, and shows that the "mutual agreement" may perhaps have been brought about by some other factor. This of course was the action taken by the general practitioners when they threatened to withdraw completely from the service. This speedily brought about a "mutual agreement" which possessed all the sweet romantic charm of a "shotgun" wedding, and was as embarrassing to the Minister as a baby at the church.

In view of the many occasions when it had been made quite clear that remuneration, whatever the basis, was a subject suitable for arbitration, it is difficult to comprehend why any committee of inquiry on this subject "would not have discussed increases in remuneration but only improvements in methods of calculating part-time consultants' contracts," and also "might, for example, have brought the principle of 'clocking-in' nearer." Some further light on this curious attitude may perhaps be gleaned by Sir Russell Brain's statement² that an inquiry into the remuneration of hospital medical staff "would not have concerned itself with cost-of-living betterment but would have looked into the earnings of part-time consultants," going on to imply that this might have had unfortunate results. He concluded in a recent letter³: "Can we not continue to put unity before sectional interest?"

It would seem reasonable to assume that unity might be fostered better by adopting the view that inquiries into the remuneration of hospital medical staff would primarily be concerned with the remuneration of hospital medical staff, even though some adjustment to the obviously unfair relationship between the incomes of part-time and whole-time staff might result.

Paragraph 15 is most confusing but possibly, though improbably, offers a weak ray of hope in the sentence: "It was made clear that the maximum that the Government could grant at present towards this end was an annual increase in the neighbourhood of £3,000,000 . . ." This obviously needs some clarification.

Paragraph 17 remarks: "To prevent misunderstanding (and the chief purpose in life of some people seems to be to try to create and perpetuate misunderstanding) we must again repeat—no price has been paid which limits our power to press whatever claims we like, such as our moral rights under Spens or on any other grounds." Whilst few would disagree with the most appropriate comment in parentheses, few will be able to reconcile "our moral rights under Spens" with the statement in para. 6 that from the time the terms of service came into effect "we ceased to have any legal claims to modification in our remuneration based on the recommendations of the Spens Committee." Possibly it all depends, as the late Professor Joad would have said, on what you mean by "moral," which seems to be a curious word to be using at this juncture.

In appendix I, Sir Russell Brain remarks: "If we take the whole-time consultants we find that there can be few, if any, who, even when they reach the maximum salary on the basic scale, are not earning substantially more than they were before the Health Service was introduced, and in some instances the increase is very great." This, I submit, with respect, is complete and utter rubbish. There can be few people in any walk of life who are not earning substantially more today than they did in 1948, but this is quite beside the point. The essential fact is that the whole-time consultant today is earning very substantially less than he was offered as an inducement to enter the National Health Service in preference to seeking a reward for the long years of preparation in private practice, or part-time hospital practice reinforced with private practice. Deprived of the just allowances recommended in the Spens report, he has been obliged to live for six years in the forlorn hope that the Government would honour their bond, and that his representatives in the profession would not fail him in insisting that this was done

1. *Brit. med. J. suppl.* 1950, i, 180.

2. *Brit. med. J. suppl.* May 8, 1954, p. 228.
3. *Lancet*, April 10, 1954, p. 769.

whilst at the same time preserving the terms laid down in the Spens Charter to the last iota.

Sir Russell Brain continues in the appendix to say: "I have been asked why the agreement was not retrospective, but this question seems to imply some confusion of thought. An agreement based upon cost of living betterment would clearly have had to be retrospective . . ." When the whole-time medical staffs of this country, from house-surgeons to consultants, who have contributed the greater part of the work in the service, reflect that in so doing they have been forced to sell their insurance policies, exhaust their savings, buy their clothes upon hire purchase, send their wives out to work, and generally subsist at a level which, as a senior registrar's wife remarked in *The Lancet* recently, caused a lay person to inquire whether her husband had succeeded in qualifying—and then find themselves reading such a statement, they are within their rights in rising in their wrath to demand why this has not been done. The staff side of Whitley Council "B," consisting of fourteen part-time and two whole-time consultants, should realise that when they are negotiating for hospital medical staff, they are primarily negotiating for the underpaid and underprivileged whole-time hospital staff and not for part-time consultants, who may be concerned with inquiries by committees "into the earnings of part-time consultants."

The melancholy tale which has been unfolded to us as a justification for past events does nothing to lighten the burden of our days, beset as they are by constant financial anxiety, and the threat to our future brought about by the jettisoning of the Spens "sheet-anchor." We are adrift in treacherous waters, and we require a firm hand at the helm to avoid the rocks of internecine strife which bestrew our apparently uncharted course. The time has come for a careful check on our position, all hands on deck, and a determined tack to a port that offers something more substantial to the weary traveller than "moral rights."

Andover, Hants.

N. L. ROWE.

PREVENTION OF MENTAL ILLNESS

SIR.—A good deal of attention has been focused on the urgent need for more hospital beds, but little thought or encouragement has been given to the coördination of the curative and preventive services in this field. Coördination of these services must result in considerable financial economy, but primarily it is in the best interest of the patient.

Since December, 1950, following the appointment of a consultant psychiatrist to the Oldham Hospital Group, there has been complete coördination of these services in the area of the Oldham County Borough. The social workers employed in the mental health department undertake all the social work in connection with the Psychiatric Unit of the Boundary Park General Hospital Annexe and act under the direction of the medical officer of health and the consultant psychiatrist who has been appointed to the staff of the health department. The team includes a psychologist, and mental health visitors who also act as duly authorised officers.

Every encouragement is given to home care and outpatient treatment. Patients are admitted to hospital only as the last resort; and only in exceptional circumstances is a patient admitted without prior consultation with the consultant psychiatrist. The hospital management committee has gradually developed and extended the psychiatric outpatient department, and a limited number of selected patients are admitted for day care.

This progressive policy has borne fruit; the number of cases admitted to mental hospitals has fallen, and no problem exists with regards to urgent admissions.

The following figures show the number of Oldham residents admitted to mental hospitals during the years 1951–53 and the percentage of the population admitted annually:

	1951	1952	1953
Number of patients admitted ..	169	184	126
Percentage of population ..	0.142	0.154	0.106

This scheme embodies some of the Amsterdam principles as described by Dr. Ling (May 29), and it is interesting that the percentage of the population admitted in 1953 compares favourably with the figure for Amsterdam.

Public Health Department, J. T. CHALMERS KEDDIE
Oldham. Medical officer of health.

PORPHYRIA TREATED WITH NEOSTIGMINE

SIR.—As Professor Rimington and Dr. Goldberg pointed out last week, Dr. Gillhespy and Mr. Smith (May 1) are not the first to have administered neostigmine in cases of porphyria. Among earlier relevant references cited by us¹ it is worth recalling that Gordin² favoured this drug and recommended its further trial. This in no way detracts from the demonstration by Gillhespy and Smith that neostigmine was promptly, repeatedly, and unequivocally (control injection) effective in their patient with profound myasthenia. La Tona and Foe³ had previously found this drug valuable for the relief of abdominal cramps in porphyria. Less eulogistic reports on its efficacy in the related peripheral neuropathy preceded⁴ and have followed^{5,6} the report by Gillhespy and Smith.

We assessed, but for the sake of brevity did not report,¹ the results of a comparative evaluation of neostigmine and pethidine for the relief of the intestinal colic in porphyria. Our patient's crude but vivid description of his colic was "a feeling as if a fish-hook was being drawn through my guts." Using heavier dosage of neostigmine than other workers referred to here, it was shown that pethidine (100 mg.) was reliable while neostigmine (1.5 mg.) failed when each was given four-hourly by intramuscular injection. Atropine or its synthetic analogues were not tried, to avoid the risk of adding undesirable side-effects to his deranged physical and mental state. We, like other workers,^{7,8} concluded that pethidine is valuable in controlling the extreme intestinal colic of porphyria. Indeed, pethidine may be superior to opiates because of its antispasmodic and analgesic actions.⁹ Favourable results have also been reported with an intravenous procaine drip⁹; the cholinergic substance, urecholine¹⁰; and the injection of tetraethylammonium chloride (T.E.A.C.).¹¹

Whipps Cross Hospital,
London, E.11.

R. J. CALVERT.

NON-THROMBOTIC PHLEBITIS AND PERIPHLEBITIS

SIR.—Since my publication in your issue of Jan. 16 (p. 131) there have been several communications in *The Lancet* and *British Medical Journal* bearing on the subject. But unfortunately none of them throw any real light on the case of my original patient, Mrs. A.B., who developed the remarkable travelling nodules, unless Sir Henry Tidy's cases were really of the same nature. Mrs. A.B.'s "travelling nodules" must therefore be accepted as the account of an extremely rare condition, possibly almost unique. They resembled the Mondor malady in one particular only—namely, that they completely disappeared, at least temporarily.

Most of the communications concerned the whiplash-like lines across the chest, &c., now known as the Mondor malady, a typical example of which I recorded in my paper (Mr. C.D.) and which terminated as usual without

1. Calvert, R. J., Rimington, C. *Brit. med. J.* 1953, ii, 1131.
2. Gordin, R. *Nord. Med.* 1948, 37, 480.
3. La Tona, S. R., Foe, A. *Cleveland Clin. Quart.* 1951, 18, 227.
4. Ashby, D. W., Bulmer, E. *Brit. med. J.* 1950, ii, 248.
5. Fawcett, J. W. *Lancet*, May 22, 1954, p. 1079.
6. Wilson, J. A. C. *Ibid.* May 29, 1954, p. 1134.
7. Calvy, G. L. *Surg. Gynec. Obstet.* 1950, 90, 716.
8. Watson, C. J. *Textbook of Medicine*. Edited by R. L. Cecil and R. F. Loeb. Philadelphia, 1951; p. 665.
9. Grubbschmidt, H. A. *California Med.* 1950, 72, 243.
10. Robinson, C., Harbour, J. H., Plummer, K. *Gastroenterology*, 1952, 20, 662.
11. Wehrmacher, W. H. *Arch. intern. Med.* 1952, 89, 111.

any important therapeutic aid. By this time the English reading public ought to be almost as familiar as the French with the symptoms which constitute the Mondor malady. But who deserves the credit of first describing an undoubted case in the English language—that is quite another matter.

London, N.W.1.

F. PARKES WEBER.

A NOVELTY IN SPURS

SIR.—Your review of *Pulmonary Tuberculosis* (May 8) expects too much of surgical methods. Even the knight in *Alice Through the Looking-Glass* did not own “long-term spurs”!

Buxton.

F. A. BEARN.

POLYURIA

SIR.—In your leader of May 15 you state that “change in glomerular filtration-rate is little concerned in the regulation of urine flow in the adult” and you give no consideration to the factor of glomerular intervention in such regulation. From the evidence I intend to adduce, it is apparent that glomerular change is unmistakably reflected in the amount of the urine produced; that it serves as an index of the renal haemodynamics; and that it offers a guide to the understanding and treatment of certain diseases, including the toxæmias of pregnancy.

In the polyuria accompanying diabetes insipidus, you emphasise the defect of tubular function and its treatment, but you fail to mention that such polyuria can be controlled by the glomeruli. For Bykov¹ has shown that the intact kidney of dogs conditioned to antidiuresis can still display such conditioning even after hypophysectomy has produced in them diabetes insipidus, thereby indicating a renal control independent of the antidiuretic hormone (A.D.H.) and the tubular regulation it imposes. Denervation of the kidney abolishes this response and therefore it is apparent the antidiuretic effect is due to the only remaining mechanism that could produce it—namely, a glomerular shut-down which reduces the glomerular filtration-rate. Glomerular shut-down can be effected by the influence of the cerebral cortex, so it may be presumed that with such stimuli constantly at work the glomerular state must considerably affect the urine flow.

In this connection, Hoff² has shown experimentally that when the cortex of the brain is stimulated electrically there follows a considerable ischaemia of the renal cortex, which, if oft repeated, can result in “nephron nephrosis.” Then again, the dependence of urine flow on glomerular filtration-rates has been demonstrated by Lawson,³ who observed an immediate rise of water and salt excretion after the injection of albumin in a nephrotic patient; this was too immediate a change to be ascribed to any cause other than the raised glomerular filtration-rate that accompanied it.

Urine flow depends on glomerular change even when the extracellular space is contracted, for Shannon⁴ has shown that serious dehydration, produced by deprivation of water, caused dogs with diabetes insipidus to excrete less urine—the result of reduced glomerular filtration. In fact, on occasion hormone effects on variations of urine flow can be completely excluded as in the preliminary experiments of Harvey L. White.⁵ By moderate constriction of the lumen of one renal artery in dogs with an exteriorised bladder base, he demonstrated that that kidney excreted only half the water and half the salt it normally did, while the excretion of the intact kidney showed a corresponding increase. This could not be ascribed to a circulating hormone, which would have produced a similar and equal effect on each side. Confidence in biochemical determinations to interpret renal haemodynamics must be considerably shaken by the fact that they failed herein to reveal any alteration in glomerular filtration-rates or in renal plasma-flow as underlying the changes. Yet the occurrence of glomerular spasm or diversion of renal blood-flow from cortex to medulla is challenged by such determinations.

1. Bykov, K. M. *The Cerebral Cortex and the Internal Organs. (In Russian.)* 1947.
2. Hoff, E. C., Kell, J. F. jun., Hastings, N., Sholes, D. M., Gray, E. H. *J. Neurophysiol.* 1951, 14, 317.
3. Lawson, H. D. *Transactions of the 2nd Josiah Macy Conference on Renal Function.* New York, 1950; p. 40.
4. Shannon, J. A. *Ibid.* p. 35.
5. White, H. L. *Ibid.* p. 128.

Renal ischaemia can often determine antidiuresis. Indirect evidence of its occurrence and of its responsibility for oliguria is provided by the new hypotensive drugs. And the relief of ischaemia in the presence of an expanded extracellular space can be a cause of polyuria.

Rothlin⁶ has shown that experimental renal ischaemia can be overcome by dihydroergocornine (D.H.O. 180)—a drug which produces diuresis in toxæmia or even in anuria, indicating that it has been effective in overcoming the underlying glomerular spasm. Whitney⁷ has shown that renin has an antidiuretic action in dogs, even those with diabetes insipidus. By its use in normal animals or in animals with diabetes insipidus the glomerular filtration-rate was diminished by 33·4% and the renal plasma-flow by 40·8%. The accompanying antidiuresis must have been influenced by the diminished rate of filtration.

Basing his work on the original experiments of Masson,⁸ Gaunt⁹ has demonstrated that the relief of glomerular spasm in the presence of an expanded extracellular space can cause polyuria. He “primed” unilaterally nephrectomised rats with deoxycortone acetate and a fluid intake of nothing but normal saline for 30 days. “This caused a marked increase in the daily water exchange, the fluid intake at the end ranging from 105–284 ml./day. Blood pressure was elevated mildly from an initial mean of 119 to a terminal mean of 139 mm.” Subsequently a renin preparation was injected for 24–48 hours into one of a paired series. Over half these cases developed massive œdema, while oliguria and convulsions and death occurred in nearly all. It was apparent that the glomerular shut-down produced by renin aggravated the “sensitivity” provoked by deoxycortone and sodium chloride. The kidneys of these animals showed “severe damage consisting of hydronephrosis, distension of the tubules with plasma, tubular necrosis, hyaline changes in some glomeruli, and diffuse nephritis in others.” It was considered that ‘Apresoline,’ which Schroeder¹⁰ thought blocked the effects of angiotonin, should be studied for its effects at this stage. Consequently the second of the pair in the series had apresoline injected 24 hours after the renin. Death from renal failure no longer resulted, nor did convulsions supervene. Such treatment reduced the hypertension, and the œdema rapidly vanished and was accompanied by a phenomenal diuresis, while the kidneys showed only slight abnormalities, probably the result of the “priming” treatment alone. To quote the authors,¹¹ “as a working hypothesis it might be suggested that renin caused a fatal renal ischaemia and the apresoline prevented this action of renin.” If this assessment is acceptable, then renal ischaemia may be responsible for the oliguria/anuria, while its abolition may lead to diuresis.

Finally, Selkurt¹² has published an extensive review of the literature on renal sodium excretion, and he has added his own results. He challenges the orthodox reabsorption theory: “the evidence preponderantly favours the view . . . that excretion is a changing fraction of the amount filtered, rather than a constant fraction (proximal segment) plus a constant amount (distal segment) as postulated by Wesson, Anslow, and Smith.”¹³

He also criticises biochemical findings: “The possibility remains open that small alterations in glomerular filtration-rate, undetectable by present techniques, may account for changes in the urinary excretion of sodium ($U_{Na}V$) often considered significant in certain experiments of an acute nature. As a corollary it seems unwarranted to conclude that whenever an alteration in $U_{Na}V$ occurs in the absence of detectable changes in glomerular filtration-rate a change in endocrine regulation (pituitary, adrenal) is the necessary alternative without more intensive investigation to prove the claim.” This supports my argument that far too much reliance is being placed on biochemical data. It should be realised that “a deviation of as little as 1% from

6. Rothlin, E., Cerletti, A. *J. Mt Sinai Hosp.* 1952, 19, 138.
7. Whitney, J., Smith, S., Marmotson, J., Goodman, H., Sellers, A. *Amer. J. Physiol.* 1954, 176, 419.
8. Masson, G. M., Corcoran, A. C., Page, I. H. *J. Lab. clin. Med.* 1951, 38, 213.
9. Gaunt, R., Renzi, A. A. *Ciba Clinical Symposium*, 1954, vol. 6, no. 1, p. 29.
10. Schroeder, H. A. *Circulation*, 1952, 5, 28.
11. Gaunt, R., Renzi, A. A. *Amer. J. Physiol.* 1953, 175, 313.
12. Selkurt, E. E. *Physiol. Rev.* 1954, 34, 287.
13. Wesson, L. G. J., Anslow, W. P. jun., Smith, H. W. *Bull. N.Y. Acad. Med.* 1948, 24, 586.

the amount of sodium normally filtered and reabsorbed would mean the gain or loss of 11 g. of sodium and attendant anions per day—a not insignificant amount."

Selkurt concluded: "It has become obvious that sodium excretion by the mammalian kidney during varied physiological circumstances is regulated by changes in glomerular filtration-rate or by alteration in tubular absorption. Frequently it is difficult to decide which is the dominant mechanism particularly when they are simultaneously involved. Often when alterations in filtration-rate are undetectable or small, investigators are prone to conclude that tubular reactivity towards sodium has been altered."

The importance of glomerular spasm is gradually becoming evident. On its appreciation depends the rational treatment of pre-eclampsia, revealed in the use of drugs such as dihydroergocornine, 'Veratrone,' and apresoline. An imperfect understanding of renal physiology, especially of the part played by the Trueta or Oxford mechanism, and a too ready acceptance of biochemical data are obscuring the significance of renal ischaemia in oedema, in hypertension, in albuminuria, and in convulsions—especially when these conditions are combined, as in eclampsia.

London, W.1.

JOHN SOPHIAN.

BACKACHE AND THE DISC

SIR.—May I congratulate Mr. Rose on his paper last week on this much-cannassed matter: not only is it objective and well based, it is extremely helpful to the practising surgeon.

May I also thank you for the retention of the spelling of the word "disc"; it may be theoretically right to replace the "c" with a "k" but I believe we should discard (or should I say "diskard") the office boy's mentality.

London, W.1.

W. GRANT WAUGH.

THE PLIGHT OF SENIOR REGISTRARS

SIR.—I agree entirely with the views expressed by "A Senior Registrar's Wife" (May 8).

When my husband was demobilised we decided, after much consideration, that he should embark upon the long and arduous training required to become a consultant. Every encouragement was given by the authorities. Let me make it quite clear that we did not imagine that an appointment would be easily attained; we expected great financial hardship and gruelling work for a number of years, and this we have had in full measure. However, we did believe there would be a reasonable number of consultant vacancies at the end. But now we find these hopelessly inadequate, and no effort is being made to create more.

We entered the National Health Service with a promise of a wide expansion of the consultant services, and remuneration according to the recommendations of the Spens Committee. What has happened to these promises?

Our contemporaries who entered general practice are financially secure: they have the benefit of the "betterment factor" and back pay. Is this not unfair? Let anyone who would accuse me of being mercenary attempt to sustain a decent standard of living and educate two children on a senior registrar's salary.

The newly qualified doctor sees the hazards and wisely steers clear. In a few years there will be a great shortage of hospital staff; but where shall we be then?

A large number of senior registrars find that, through no fault of their own, they are redundant. How tragic that young men who started out with such high ideals should become disillusioned and frustrated. Our husbands have not been lazy, or they would not have stayed the course; they are not stupid, or they would never have passed the higher examinations. Who cares about their plight? Apparently nobody.

ANOTHER REGISTRAR'S WIFE.

ARTIFICIAL RESPIRATION BY INTERMITTENT POSITIVE PRESSURE

SIR.—Dr. Crampton Smith and his colleagues are to be congratulated on a valuable paper (May 8), but their remarks on neck seals in tracheotomised patients in tank respirators call for some comment.

An efficient neck seal under these conditions does not involve such "great difficulty" as their remarks suggest, and such a seal has been used in the U.S.A. for a good many years.

U-shaped metal "tracheotomy bars," of which there are several designs, are attached by adjustable fittings to the head of the tank or to the collar surround, and push the collar inwards in the midline of the neck, allowing the seal to be made below the tracheostomy. Collars need to be of yielding foam rubber and over-size, the type supplied with the Nuffield-Both respirator being unsuitable for this purpose; the ingenious plastic "spiral twist" collars¹ are particularly suitable for use with tracheostomies.

In view of the importance of planning for a possible large epidemic of respiratory poliomyelitis, it should be known that tracheotomised patients with bulbar paralysis can be treated in a tank respirator. The difficult choice between this older-established method and the newer one of intermittent positive endotracheal respiration depends on many factors.

Galway, Eire.

BRIAN McNICHOLL.

GRADUATE WIVES

SIR.—With reference to Dr. Lycett's letter (May 29) I quite agree that part-time sessional work is most unsatisfactory both to the patients, who meet a succession of doctors who know nothing of their background, and to the doctors who see no continuity in their work.

However, I see no reason why married women should not be employed full-time in the public-health service. Most authorities have a maternity-leave scheme whereby they can have adequate time off for each confinement; and, if the salary is large enough, they can employ good domestic help: there is no reason why the family or the work should suffer. Indeed, most women with sufficient intelligence to obtain a medical degree find full-time domesticity frustrating and irritating.

I can assure Dr. Lycett that in maternity and child-welfare work personal experience of raising one's own family is of equal if not greater value than the D.P.H. or D.C.H. From the point of view of the family, public-health work has the great advantage of regular hours.

I regard a woman doctor living among and bringing up a family as the ideal health educator.

Wednesbury, Staffs.

HAZEL B. BAKER.

SIR.—I would like to reply to a few remarks by correspondents in your issues of May 22 and 29.

I regret that Dr. Gillie and Dr. Beard should have supposed that I suggested that married women doctors should attempt to undercut the market as a method of obtaining employment: this would obviously be unethical, to say the least of it. I did mean, however, that it might be possible to evolve a system in our public-health clinics whereby there were some specialised supervisory staff, who would be paid at a higher salary, and some part-time doctors (less specialised) working for a lower salary, thereby relieving the specialists of some of the donkey-work. After all, the house-surgeon is not accused of undercutting the market because he works for a lower salary than the consultant.

I am glad to be assured by Dr. Gillie that the anomaly between full and part-time workers (or those working on a sessional basis) has been at any rate partly reduced, though this does not altogether seem to be the case in the blood-transfusion service where a part-time worker

1. Made by the Iron Lung Company of America and by the J. H. Emerson Company, both of Boston, Mass.

receives up to 3 guineas a session and the full-time worker a salary of £700 per annum. Here of course the hours are more irregular, and therefore it is more difficult to reckon the part-time worker's annual salary.

Far be it from me to put personal experience before that gained in obtaining a postgraduate degree, but I would like to see the ordinary knowledge gained in bringing up one's family used, instead of being counted as so many years wasted. The aim of the child-welfare clinics is surely to give advice and to supervise normal children (though of course the abnormal must be recognised). Many psychiatrists would probably be the better of a little personal experience of psychiatric patients in their own families, though I would not wish this on them, even to refute Dr. Beard.

It seems to me a sorry state when, after six years' specialised training plus house-jobs, many of the younger married women doctors are barred from obtaining part-time employment—though we would be welcomed if we chose to go out charring. It is a hard struggle for many who had to set up house after the war and are now struggling to educate their children, and it seems especially hard when we cannot utilise our training to help financially and to satisfy our continuing interest in medicine.

London, S.W.15.

MARY E. LENNOX.

A WORD WANTED

SIR.—In his letter of April 10, Dr. Apley is wanting a word. Perhaps he will agree that the Greeks still have it, should he ponder the word *zegetic*, the anglicised derivation, now rare, which has been defined as "proceeding by inquiry." There is no hint of retrospection attached to this word but on the contrary it is all forward-looking. Its use in the way Dr. Apley wishes might do much to retain it in the English language.

Pinelands,
Cape of Good Hope.

THEODORE JAMES.

THE PATHOGENESIS OF RHEUMATIC FEVER

SIR.—In his Milroy lectures published in your issue of March 13 Dr. D. A. Long concludes that in the guineapig, as in man, the so-called antiphlogistic hormones (A.C.T.H., cortisone, hydrocortisone) inhibit only the delayed tuberculin-type of inflammatory reactions. He questions the relevance, for human beings, of experiments performed on rats, and sharply attacks the views of Byron H. Waksman and Hans Selye on the possible derailment of adaptation in rheumatic and allied diseases.

It happens that my Ph.D. thesis¹ was largely concerned with this topic. I had occasion to note that an entirely non-specific type of inflammation, such as that obtained by injection of mustard powder into the joint region, is very effectively inhibited by A.C.T.H. (corticotrophin) in the guineapig. After reading Dr. Long's lecture I perused the literature of the last few years to see whether others have made similar observations. Since the alleged cortisone-resistance of the guineapig plays a cardinal part in his speculations, I feel that he and your readers will be interested in the following annotated references:

- Abernathy, R., Spink, W. W. *J. clin. Invest.* 1952, 31, 947. (Cortisone suppressed dermal hypersensitivity to brucella antigen in the guineapig.)
- Asboe-Hansen, G. *Proc. Soc. exp. Biol. N.Y.* 1952, 80, 677. (Cortisone and A.C.T.H. decrease the number and alter the morphology of mast cells in the connective tissue of the guineapig. This is considered to play a fundamental rôle in the anti-inflammatory effects of these hormones.)
- Baggi, G. F., Favilli, G. *Rev. path. gen.* 1953, 652, 1331. (Cortisone inhibits the development of peritonitis following intraperitoneal injection of croton oil in the guineapig.)
- Ballabio, C. B., Bonomo, E. *Boll. Ist. sieroter. Milano.* 1951, 30, 1. (Cortisone inhibits skin sensitivity to tuberculin while desoxy-corticosterone increases it in the guineapig.)
- Criep, I. H., Weigler, R. R., Mayer, L. D. *J. Allergy*, 1952, 23, 541. (Cortisone decreases inflammatory reactions accompanying Arthur's phenomenon.)

1. Contribution à l'étude de l'arthrite expérimentale. University of Montreal, 1952.

- De Brux, J., Du Boistesselin, R. *Pr. méd.* 1953, 61, 600. (Cortisone inhibits inflammatory response to subcutaneously injected turpentine in the guineapig.)
- Elberg, S. S., Schneider, P. *J. infect. Dis.* 1953, 93, 36. (Cortisone affects the migration of leucocytes in response to infection and other stimuli in guineapigs.)
- Fischel, E. E., Kabat, E. A., Stoerk, H. C., Skolnick, M., Bezer, A. E. *Fed. Proc.* 1953, 12, 442. (Cortisone inhibits granuloma formation in guineapigs receiving egg-albumin with Freund's adjuvants.)
- Grifa, P., Lenzi, E., Rossi, E., Zaca, F. *Atti 6° Congr. Naz. Soc. Ital. Reumatol. Taormina, Maggio*, 1952. (A.C.T.H. inhibits the spreading effect of intradermally injected hyaluronidase and this effect is considered to play an important part in its anti-inflammatory action.)
- Hoene, R., Coutu, L., Horava, A., Procopio, J., Robert, A., Salgado, E. *J. Allergy*, 1952, 23, 343. (A.C.T.H. inhibits the experimental arthritis produced by the injection of a mustard-powder suspension into the joint region of the guineapig.)
- Lichlitz, A., De Sézé, S., Thiery, G., Hioco, D., Delaville, M. *Sém. Hôp. Paris*, 1951, 27, 3337. (Cortisone inhibits while desoxycorticosterone aggravates, inflammatory reactions to tuberculin in the guineapig.)
- Lovell, R. R. H., Scott, G. B. D., Hudson, B., Osborne, J. A. *Brit. J. exp. Path.* 1953, 34, 535. (Cortisone and A.C.T.H. diminish inflammatory reactions and spreading of blood after experimental skin bruises in the guineapig.)
- Lyall, A. *Glasg. med. J.* 1953, 34, 208. (Cortisone prevents the formation of inflammatory adhesions following intra-peritoneal administration of talcum suspensions or mandarin black, &c., in the guineapig.)
- Marchin, P. de. *Acta clin. belg.* 1952, 7, 165. (A.C.T.H. inhibits the experimental arthritis which can be normally produced by repeated injections of anti-diphtheria serum into the knee-joint of the guineapig.)
- Moon, V. H., Terschakovec, G. A. *Proc. Soc. exp. Biol. N.Y.* 1952, 79, 63. (Cortisone inhibits inflammatory reactions to burns or freezing in the guineapig.)
- Nilzen, A. *J. Invest. Derm.* 1952, 18, 7. (Cortisone decreases inflammatory reactions of the skin to croton oil, cantharidin, colchicine, and 2,4-dinitrochlorobenzene.)
- Schilling, J. A., Radakovitch, M., Favata, B. V., Filer, L. J. Jun., Jescherson, H. W. *Surg. Gynec. Obstet.* 1953, 97, 434. (A.C.T.H. inhibits inflammatory fibroblast proliferation following traumatic injuries in guineapigs.)
- Ungar, G. *Amer. J. Physiol.* 1951, 167, 833. (Cortisone inhibits allergic arthritis in guineapigs.)
- Ungar, G., Damgaard, E., Weinstein, H. G. *Fed. Proc.* 1951, 10, 422. (Cortisone inhibits the "anaphylactic arthritis," which can be produced by egg white in the guineapig.)
- Ungar, G., Damgaard, E., Weinstein, H. G. *Amer. J. Physiol.* 1951, 166, 340. (Anaphylactic arthritis normally produced by intra-articular injection of egg-albumin in sensitised guineapigs.)
- Weimer, H. E., Boak, R. A. *Fed. Proc.* 1953, 12, 465. (Cortisone and A.C.T.H. suppress inflammatory reactions to brucellergen in the guineapig.)
- Weinstein, H. G. *Ibid.* 1951, 10, 144. (Cortisone inhibits the dermal inflammation normally produced by topical application of xylene in the guineapig.)
- Hôtel-Dieu de Montréal, Montreal, Canada.
- LUCIEN L. COUTU.

REMPLOY

SIR.—I am a benchman in a Remploy furniture factory. To supplement your article of April 24, may I offer the views of the disabled who are employed by the Remploy organisation? The Piercy inquiry, the knowledge that Remploy is in the red to the tune of £2½ million, and the fact that it costs £399 per annum to keep every one of us employed, cause much discussion and fear among us. We naturally dread possible closure of Remploy.

The Piercy inquiry will doubtless be conducted at a very high level. Officials will meet and discuss profit and loss accounts, the improvement of factory layout, particular types of Government contracts, the need for economy, and the problem of passing trained personnel from Remploy factories into open industry; but we doubt whether any account will be taken of the mood and ideas of the men at the bench. We fear that decisions and recommendations will be made without anyone consulting the disabled employees. Very likely the instructors, clerical staff, and managerial and divisional officers will be consulted; but these, almost without exception, are able-bodied.

Among the employees at the bench there is a widely held belief that the training and employment of the severely disabled leads to the establishment of a core of able-bodied, whose main interest is in maintaining their own status and conditions, sometimes at the expense of the disabled. Promotion of the disabled within the organisation is not usual. There is a progress-slip used in Remploy (noting the time spent on a job) on which is printed: "These times must on no account be discussed

with a disabled employee." This seems to imply an undesirable attitude to the disabled. We also feel it to be an anomaly that—in an organisation for the severely disabled—only the able-bodied have a pension or superannuation scheme.

Do not imagine that we are ungrateful. Far from it : I have heard Remploy described as "a God's blessing." But I have also heard it called the new Marxism : "from each according to his ability ; to the most productive, 80% of the district rate."

This is a reference to the fact that after two years' training a man can ask to be considered for the full district rate. This application is discussed by the manager and a full-time trade-union official ; and according to the man's proficiency he is granted all or part of the full rate. In practice, however, he is usually kept at his old rate of 75-80%, on the grounds that he is not proficient, or "not worth a penny more"—even though his work may be quantitatively and qualitatively better than that of others in the factory receiving the same rate.

In these circumstances incentive is stifled, and some of the men go sour and say "We're here only to cut down National Assistance costs. Don't work too hard. You'll be paid just the same as the mugs."

When production falls and wastages and costs rise, it is very often the fault of the workers, as they will admit. But it is not always their fault. The situation is often shrugged away with the comment, "Poor souls, they really can't be expected to do very much"—an excuse which can be used to cover bad planning and buying, lack of skill, and lack of method.

The mounting costs of Remploy, if not checked, must lead inevitably to the end of the experiment. The able-bodied would then find other employment ; but for almost all the disabled it would mean life-long unemployment. They would go down with the ship.

FRANK CARR.

TEXTBOOK ILLUSTRATIONS

SIR.—I quite agree with the opinions and suggestions of Mr. Engel, expressed in his letter of May 8. It may interest your readers to know that the same problem was discussed at the First World Conference on Medical Education in London last August. Since the Proceedings of the Congress have not yet appeared, I should like to repeat here a few words of criticism, as an addition to Dr. Engel's ideas :

"It must be regretted that latest editions of several good textbooks published in various countries still contain illustrations—e.g. of exanthemata, bacteria, blood and bone-marrow cells, &c.—which were skilfully drawn by an artist decades ago but are no longer in keeping with the eminent progresses of colour photography. I think that some authors should be more anxious to replace the out-of-date pictures by modern ones."

First Medical Department,
University Hospital,
Hamburg, Germany.

H. WENDEROTH.

ISAMBARD KINGDOM BRUNEL

SIR.—Your peripatetic correspondent's remarks (May 29) on Isambard Kingdom Brunel as hospital architect demand enlargement. According to Dugan,¹ Brunel's portable fifteen-hundred-bed military hospital used by the War Office was prefabricated in this country and erected by eighteen men in ten weeks at Renkioi, Turkey, no part of the structure being too heavy to be carried by two men. Plumbing was included, together with an "air-conditioned system" pumping 1300 cubic feet per minute of cooled humidified air around each bed.

The apparatus Brunel designed for rapidly inverting himself and thus ejecting the sovereign lodged in his right bronchus has been likened by Dugan to the old-fashioned looking-glass on a horizontal pivot. Your correspondent states : "the manoeuvre was successful, and the coin was immediately coughed out." Lest this apparatus be thought unduly efficient and a sine

1. Dugan, J. *The Great Iron Ship.* London, 1953.

qua non of hospital equipment, it should be pointed out that after six weeks of intermittent torture on the "rack" Brunel's medical advisers forbade him to continue. Tracheotomy was advocated, Brunel himself sketching the special forceps to be used for reaching the coin. This instrument is now known as the Brodie forceps² after Sir Benjamin Brodie, Brunel's brother-in-law, who carried out tracheotomy without anaesthesia ; the operation was not successful. However, three days later Brunel, with the wound still open, took a further turn on his machine, at last coughing up the sovereign into his mouth.

National Institute for Research in Dairying, Shinfield, near Reading. C. A. E. BRIGGS.

COXSACKIE INFECTIONS

SIR.—After the discovery of Coxsackie viruses,^{3,4} many papers reported the isolation of these viruses in a number of different conditions⁴ : epidemic pleurodynia (Bornholm disease),⁵ herpangina,⁴ "minor illnesses,"⁶ and diseases of the nervous system—aseptic meningitis,⁵ encephalitis,⁷ meningo-encephalitis,⁸ and Guillain-Barré syndrome.^{9,10} Coxsackie viruses were also isolated from cases of poliomyelitis, but the significance of these findings was not established.¹¹ It has been shown that in some of these diseases the strains isolated belong to a definite group—e.g., in cases of Bornholm disease, Dalldorf's group-B strains are present, and in cases of herpangina the group-A strains are isolated.⁴

We have adopted the term *coxsackioses* for these conditions. This name is in line with those used in other infections where the organisms produce a variety of clinical manifestations—e.g., brucellosis, salmonellosis, rickettsiosis, &c. A tentative classification of the Coxsackie infections is as follows :

- (1) Indefinite febrile forms.
- (2) Typical forms : epidemic pleurodynia (Bornholm disease), herpangina.
- (3) Nervous forms : "aseptic meningitis," encephalitis, meningo-encephalitis, Guillain-Barré syndrome.

Department of Microbiology,
School of Pharmacy,
University of Brazil,
Rio de Janeiro.

PAULO DE GÓES
J. TRAVASSOS.

RISKS OF LEUCOTOMY

SIR.—I have read with interest your account (May 22) of the address by Dr. Radzan and Dr. Cook, of Bexley Hospital. This reveals the overcrowding of hospital wards, which, I understand, prevails elsewhere, and the urgent need of removing the obstacle to individual care and continuous observation of patients under treatment, without which hardly any successful result can reasonably be expected.

Dr. Cook is also reported as saying that sedation itself, if prolonged, produces more serious mental deterioration than electroconvulsion therapy combined with pre-frontal leucotomy. This may be so, but I know of 2 cases in which the results of leucotomy are nothing short of tragic. In suicidal and homicidal maniacs, such rapid deterioration may be beneficial, in that leucotomy renders the patient more docile and more easily managed, even if at the same time he is turned

- 2. Dalldorf, G., Sickles, G. M. *Science*, 1948, 108, 61.
- 3. Dalldorf, G. *Ibid.* 1949, 110, 594.
- 4. Huebner, J. R., Beeman, E. A., Cole, R. M., Beigelman, P. M., Bell, J. A. *New Engl. J. Med.* 1952, 247, 249.
- 5. Curran, E. C. 2nd International Poliomyelitis Conference, Copenhagen, 1952.
- 6. Melnick, J. L., Walton, M., Myers, I. L. *Publ. Hlth Rep., Wash.* 1953, 68, 1178.
- 7. Stanley, N. F., Dorman, D. C., Ponsford, J. *Aust. J. exp. Biol. med. Sci.* 1953, 31, 31.
- 8. Galpine, J. F., Macrae, A. D. *Lancet*, 1953, i, 372.
- 9. Forrester, R. M., Tobin, J. O'H. *Ibid.* 1951, ii, 663.
- 10. Menut, G. *Arch. franc. Pédiat.* 1952, 9, 978.
- 11. De Góes, P., Travassos, J., Pinheiro-Campos, O., Bruno-Lobo, M., Vasconcellos, J. V. *An. Microbiol.* 1952-53, 2, 101.

into a semi-idiot, without initiative, mental alertness, and responsiveness. Hastiness of action or faulty selection of cases for leucotomy may cause deep regret to all concerned—to the psychiatrist that it had ever entered his mind to recommend the operation, and to the relative whose consent was sought. It is my unalterable opinion that no such operation should ever be contemplated, and consent obtained, without telling all whom it may concern, everything about the grave risks involved therein.

Greenhithe, Kent.

D. W. STANDLEY.

CAROTENÆMIA

SIR.—Dr. McConaghey's excellent article¹ gave a complete bibliography of this subject and a description of two cases. He did not mention oranges as a cause, so I thought a report of this case might be interesting.

A girl of 17, who was putting on weight, thought of slimming herself by eating little but oranges. She used to eat from 25 to 30 oranges a day. After about six months, she and her parents noticed that she had become yellow in colour, and she was thought to have jaundice.

She looked very healthy, and her temperature, pulse, and blood-pressure were normal. Her skin was yellow, especially on the palms and soles. The conjunctivæ were not coloured. No other abnormality was found on physical examination. Hæmoglobin, red and white cell-counts, and the urine and stools were normal. So we thought that this might be a case of carotenæmia caused by a surfeit of oranges. When she returned to a normal diet, she gradually improved and the yellow colour disappeared in a few weeks.

Oranges contain β-carotene, lycopene, cryptoxanthine, lutein, violaxanthin, zeaxanthin, β-citraurin, and citroxanthin.²⁻⁵

Faculty of Medicine,
Alexandria University,
Egypt.

H. BARSOUM.

TREATMENT OF DEAFNESS

SIR.—May I add an account of my personal experience?

Forty-two years ago I was a woman medical student. I consulted a leading otologist because of slight difference of acuity in hearing of my two ears. He told me I had otosclerosis and would be hopelessly deaf in two or three years, and advised me to give up medicine, which I did. Ten years later my deafness was no worse and I went to another otologist who said there was very little amiss and advised me to resume my studies. I did so, but, for personal reasons, did not subsequently qualify. In the next fifteen years I visited four or five otologists to keep the deafness under review. I was not noticeably any deafener.

Eleven years ago I had a severe shock, being told that I was liable to die suddenly. I woke the next morning very deaf and have remained so. I have been treated by four otologists and three psychiatrists, all leading men, and derived no benefit from treatment including electroconvulsive therapy.

During the past two years I have had treatment by two spiritual healers, and for short periods after this treatment I have been able to hear quite well, which shows that some part, at least, of the hearing mechanism is in fair working order.

Other deaf people have given me similar accounts of inconsistent though firm opinions from experts; and I would suggest to Mr. Robin and other otologists that dogmatic condemnation of any method of helping deaf people should be avoided. The impression I have formed is that hearing depends partly on factors which are not yet measurable, and may improve under treatment which appears incapable of affecting the physical lesions on which attention is usually concentrated.

A DEAF PATIENT.

1. McConaghey, R. M. S. *Lancet*, 1952, II, 714.

2. Zechmeister, L., Tuzson, P. *Naturwissenschaften*, 1931, 19, 307.

3. Vermast, P. G. F. *Ibid*, p. 442.

4. Zechmeister, L., Tuzson, P. *Ber. dtsch. chem. Ges.* 1936, 69, 1878.

5. Karrer, P., Jucker, E. *Helv. chim. acta*, 1944, 27, 1695; *Ibid*,

1947, 30, 536.

OBITUARY

Obituary

ANDREW OLIVER FERGUSSON ROSS

M.D. Edin., D.P.H.

Dr. A. O. Fergusson Ross, director of venereal-diseases clinics in the city and port of Liverpool, died on June 3 at Birkenhead.

He was born at Scone in 1895 and he was educated in Edinburgh at George Watson's School and at the university. During the first world war he served as a surgeon probationer in the Royal Navy. He returned to Edinburgh to take his M.B. in 1917, and later he became a specialist in genito-urinary surgery and in venereal diseases at the Royal Naval Hospital at Haslar.

After he was demobilised he spent some years in consultant practice in Glasgow before he moved to Liverpool in the late '20s. He was appointed v.d.c. consultant to the Royal Liverpool United Hospitals and the Liverpool Seamen's Dispensary, and later he became the regional adviser in venereology and lecturer to the university.

R. J. M. writes: "Though a man of world-wide repute, Fergusson Ross always retained the humility of the true student, and in the art and practice of his profession his own interest and comfort were matters of least moment. In his last illness his sense of duty led him to prepare and deliver six brilliant lectures for the World Health Organisation in Rotterdam. Indeed he never lost the urge to question, to seek, and to verify, and all his teaching bore these hallmarks. Everyone who met him was impressed by his deep love of humanity, by his unfailing courtesy, and by his forgetfulness of self. No man ever loved the quiet things of life more than he did: his family, his friends, his garden, the way of the countryside; the thrust and parry of good conversation, and the story that was apposite."

He leaves his wife with three sons and a daughter.

ANDREW JAMES MOYES BUTTER

M.M., M.A., M.D. Edin.

Dr. A. J. M. Butter died on June 3 at his home in North London, where he had been in general practice for some 30 years.

He was born in Perth 59 years ago, and at the outbreak of the first world war he was studying arts at Edinburgh University. He immediately volunteered and was soon in France, where, as a sergeant, he won the Military Medal with the special gas company of the Royal Engineers, in which regiment he was later commissioned. At the end of the war he returned to Edinburgh, and after completing his M.A. began to study medicine. He graduated M.B. in 1923, and he held house-appointments at the Royal Infirmary and the Royal Hospital for Sick Children, Edinburgh. He came to London as house-physician in Queen Mary's Hospital for the East End, Stratford, and later entered general practice in North London. He graduated M.D. with commendation in 1925. Despite the demands of a large private practice he found time to join the staff of Wood Green and Southgate Cottage Hospital, and to act as medical officer in charge of St. David's Hospital for Epilepsy. In recent years he had published a number of valuable papers on the treatment of this disease. For many years he was also secretary of the local medical society—the Ganglion Club.

J. A. B. Y., a contemporary of his Edinburgh years, writes: "Butter played a leading part in the social life of the university. A member of the Students' Representative Council and the debating society, he was also president of the Philomathic Society and of the University Union. When Mr. Lloyd George was installed as Lord Rector in 1923, at the luncheon in the union speeches were made by several great men of the time, but many who heard Butter speak that day felt that he outshone everyone. At heart he was rather a shy person, and he would rise to speak with a diffidence that enhanced the wit of his remarks."

"Andrew Butter became a gifted physician whose presence in the sickroom never failed to comfort his patient—he was so kind, so gentle, and so patient. Many of his colleagues and their families had reason to be grate-

ful to him. Although he had been in poor health for three years, he preserved a remarkably youthful appearance. With characteristic courage he remained hard at work, and the end came in the midst of a full day's work. Kind and unassuming at all times, he was incapable of any action that was not a generous one, and he will not be forgotten in the medical community of North London."

Dr. Butter married Miss Ena Laing, who survives him with two sons.

ROBERT WILLIAM LOCKE
M.D. Durh.

Dr. R. W. Locke, deputy school medical officer for the county of Durham, died on May 23 at the age of 58.

He qualified with honours from the University of Durham in 1922, proceeding to the degree of M.D. two years later. He held resident appointments in Newcastle upon Tyne at the Royal Victoria Infirmary, the Maternity Hospital, and the Dispensary before he joined the staff of the Durham county education committee as an assistant school medical officer. Later he was promoted to be deputy principal school medical officer. He was especially interested in the welfare of handicapped children and he was a member of the advisory selection committee of the Percy Hedley School for Spastics.

G. H. S. writes: "The outstanding feature of Dr. Locke's private and professional life was his broad and humane outlook. Every new entrant to the service was made aware that the paramount consideration was always to ensure and safeguard the interests of the child. He was a most approachable man and his advice and help were sought by many outside his own service. It was his dearest wish that he should see the completion of the county development plan, particularly the provision of the several special schools. Unhappily this has been denied him, but the work he has done still lives and his influence will long be appreciated in the service."

JAMES BASIL BUXTON
M.A. Camb., F.R.C.V.S., D.V.H.

Prof. J. B. Buxton, principal and dean of the Royal Veterinary College since 1936, died on May 25 at the age of 66. Through his work on tuberculin tests in cattle and on other aspects of bovine tuberculosis he was often called to share in the researches and studies of his medical colleagues, and he was long associated both with the Medical Research Council and the Ministry of Health.

He was educated at Highgate School, the Royal Veterinary College in London, and Liverpool University. He took the M.R.C.V.S. in 1909, and in 1912 he was appointed veterinary superintendent at the Wellcome Physiological Research Laboratories. In 1922 he became director of the farm laboratories of the Medical Research Council, but he gave up this post the following year to accept the chair of animal pathology at Cambridge. During 1932-33 he served the Royal College of Veterinary Surgeons as president, and in 1936 he succeeded Sir Frederick Hobday as its principal.

Sir Arthur MacNalty, recalling how Buxton was first drawn into the work of the M.R.C., writes: "In 1921 several wealthy owners of dairy herds who were anxious to free their herds from infected animals, were in despair at the imperfections of the diagnostic methods then in use. They made urgent representations to the council and the Ministry of Health of the grave need for scientific inquiry. With the co-operation of the Ministry the council accordingly undertook to investigate the modes of detecting tuberculosis in cattle, and the inquiry was entrusted to the tuberculin committee of the council, of which S. R. Douglas was chairman and I was the secretary. Hitherto, the committee had been studying tuberculin reactions of interest in medical work, and it was obvious that for these further investigations it must be strengthened by those with expert knowledge of veterinary practice and dairy conditions. Buxton joined our committee and at once reinforced our work with his experience. After four years of work in the laboratory and the field the committee reported that the 'subcutaneous' tuberculin test, hitherto almost universally used, was inconvenient, often fallacious, and

always open to difficulties of interpretation. They recommended instead the 'double intradermal' test as simple and convenient, trustworthy and unambiguous, even under ordinary farm conditions. To confirm the evidence gained in field inquiries post-mortem investigations, including thorough microscopical examinations and inoculation experiments, were made at the Metropolitan Market under Buxton's supervision, and he spared neither time nor skill in doing them. In 1927 the committee entrusted Buxton and me with an inquiry into the results of the test in representative practical experience; we collected reports from nearly 80 experienced veterinary surgeons in different parts of the country, and analysed the data and the opinions given. Our report (1928) showed that the test was regarded as much more trustworthy than the old, and much easier to perform.

"While he was in Cambridge Professor Buxton also did work for our committee, with Stanley Griffith, on B.C.G., and in many other ways increased our knowledge of tuberculosis. At the Ministry of Health we often sought his advice on problems in which medicine and veterinary medicine are concerned, and on these occasions he was the most helpful of colleagues. He was delightful as a friend, stimulating to work with, ever ready to promote knowledge. He is gone from us but his works remain."

Sir JAMES SPENCE

THE following are extracts from personal recollections by members of Sir James Spence's department at Newcastle :

Teaching that the fundamental purpose of a university department is to advance knowledge of its subject, James Spence recognised that a child health department in the faculty of medicine has other responsibilities—to care for sick children; to teach undergraduates; to transmit changing knowledge to family doctors; and to undertake research with or on behalf of local health authorities. These were the objects of his department. The instrument to achieve these ends was a group of friends, with a similar basic philosophy of medicine and able to work and think together, who, sharing all the activities of teaching, clinical responsibility, and research would gradually build a common body of knowledge and experience for the service of others. Such a group is not quickly formed; but slowly, as it increased, James Spence was always at the centre, accessible, stimulating, guiding, helping, sharing his wisdom generously.

He knew that students could not be taught paediatrics in three months, but he did think they could be sensitised to the needs of children and parents; that they could see parents and children treated with courtesy and understanding; that they could be shown an approach to the difficulties of helping sick children to build upon in later experience. For these things he regarded as the centre of the art of medicine, whether the student was later to work in family practice or in hospital.

Clinical work in the children's wards of the department and in the Babies' Hospital has largely been concerned with the "common problems" of paediatrics—acute medical and surgical emergencies, appendicitis, intussusception, osteitis, trauma, tuberculosis, burns and scalds—and these problems have been worked out jointly by surgical and medical colleagues. Problems have been defined, classified, and simplified as far as possible, and the results added to departmental teaching and practice and conveyed to family doctors in letter and conversation. He would never allow "special clinics." If anybody was engaged in active study of a problem or undertaking a specific piece of research, then others in the department would help him with cases; after the research was finished and the lessons learnt had been communicated to the whole department, the care of the children would revert to the different clinicians. In the wards emphasis has been upon clinical study and history-taking. He always frowned on unthinking laboratory investigation, whereas he delighted in the minutiae of clinical observation.

The third responsibility of the department is the advancement of the subject; and here too, James Spence's methods were highly individual: he would throw off a stream of ideas, and when a member of the depart-

ment became really interested in one of them he would be encouraged but allowed to develop the interest along his own line. Thus, all members of the department have their special interests and can pursue them freely; no-one is engaged wholly on investigation, everyone has some clinical responsibility.

His conception of a department of friends working together for a common end was achieved for these few brief and happy years; it brought order and a sense of firm and corporate spirit to the work—an order not perhaps apparent to all those inside the department, for it was never irksome, but seemingly obvious to many of our frequent visitors, who amused us by admiring what they called "the organisation." He has left a department of devoted people bound to him and to each other by years of comradeship.

F. J. W. M.

The decisive impact of the department on the mind of a very inexperienced would-be paediatrician who visited it only four years after its formation was something quite unique. The decision which it forced upon me, there and then, was that I must somehow contrive to become a member of it, no matter in what capacity or at what cost to my family. The Professor's own personality was, of course, the dominant factor in the situation: but almost as compelling was the way in which his personality and ideas so obviously permeated all the separate units of which the department was composed. The interests which he fostered were those which concerned the common, simple, important problems, and he was always encouraging us to develop accuracy of planned clinical observation as the basic tool for the advancement of knowledge in our subject. In his contacts with students he was always more concerned with the broad educational value of what he taught, and how he taught it, than with its direct practical applications: the man who was interested primarily in passing his examinations was likely to profit little, but the best enjoyed a dramatic intellectual experience which could alter their whole outlook in their chosen profession.

G. A. N.

The first impression made by James Spence on visitor and colleague alike came from his charm. In his own home, taking tea with sisters and residents on the wards, in the meetings of his department, or as president of the local medical society, he was always the gracious and charming host. But to remain here would be to miss the measure and the nature of his greatness. He was a fine clinician; yet he made no outstanding discoveries in clinical medicine. He started his career as a biochemist, and almost his last communication was entitled the Methodology of Clinical Science; yet he was not essentially a medical scientist. Perhaps a friend came near to the heart of the matter in describing him as "an artist who had survived a scientific training."

If this estimate is true then the first and maybe the greatest expression of his sensitive insight into the nature of family life was the creation of the Babies' Hospital where the mothers were admitted to nurse their own children. The second was the binding together in mutual inquiry of the university department and the local health authority. But it was in the conception and creation of the university department that his sensitivity and strength found their fullest expression.

The simple but profound conviction which guided his thinking in this field I first learnt from the postscript to a card telling me the arrangements for my coming to Newcastle: it ran as follows. "The first aim of my department is comradeship not achievement." Friendship between all concerned with the care of children in Newcastle was the catalyst which brought into being the combined medical and surgical units, the clear definition of the aims and instruments of undergraduate teaching, and the varied pattern of clinical and social investigation which he developed in the last years of his life.

He was a great teacher of the gifted student; those who were seeking a main road to the final examination often found his exacting standard of clinical accuracy and his unpredictable questions too much for them. They recognised that "despite the manner of a kindly patrician he was a dangerous man." He was at his best when faced with the swift and calamitous illness in the ward, or painting a vivid picture of disease in the

20 minutes of a clinical lecture, and above all in sensing and handling the hidden fear of a mother in consultation.

Those of us who owe so much to this generosity find it difficult at this time to speak of his faults. His loyalty, which was often less critical than was good for us, made us all temporarily a little larger than life size. His quick intuitive mind had a distrust of the typewriter, the memorandum, and all the wordy planning of modern administration. In consequence our first awareness of the visit of a distinguished visitor would often be their appearance in the ward or outpatient clinic with the introductory greeting from James Spence "this is Professor — who will be with us for the next fortnight and I know I can leave him in your care."

He had too a love of the novel and the unexpected—new faces, new stories, and new ideas—and a capacity for distilling their essence and adding it quickly to his current counsel which, though refreshing, sometimes led to a superficiality of judgment. Yet even when you felt most sure he was wrong, you always emerged wiser from the encounter. James Spence, artist and scientist, romantic and realist, conservative and rebel, was always a leader.

D. C.

Public Health

Infectious Diseases in England and Wales

Disease	Week ended May				
	1	8	15	22	*29
Diphtheria	12	9	9	22	13
Dysentery	761	949	1031	1104	1136
Encephalitis:					
Infective	—	—	2	3	2
Postinfectious	3	5	3	2	4
Food-poisoning	112	231	240	195	173
Measles, excluding rubella	1973	1735	1706	1940	2046
Meningococcal infection	29	32	35	27	32
Ophthalmia neonatorum	38	32	29	37	50
Paratyphoid fever	3	13	7	4	2
Pneumonia, primary or influenzal	530	506	463	520	428
Poliomyelitis:					
Paralytic	15	15	14	17	10
Non-paralytic	5	8	5	9	6
Puerperal pyrexia	222	244	258	208	229
Scarlet fever	627	721	899	834	911
Smallpox	—	—	—	—	—
Tuberculosis:					
Respiratory	811	934	816	935	862
Meninges and C.N.S.	20	24	19	19	18
Other	109	125	99	131	110
Typhoid fever	3	2	3	3	1
Whooping-cough	2252	2337	2660	2428	2207

* Not including late returns.

Births, Marriages, and Deaths

BIRTHS

DAVIES.—On June 1, in London, to Dr. Celia Marjorie Davies (formerly Rapport), wife of Dr. D. L. Davies—a son.

PYKE.—On June 6, at the Radcliffe Infirmary, Oxford, to Janet, wife of Dr. David Pyke—a daughter.

Appointments

GLENNIE, R. E., M.D. Aberd., D.C.H., D.P.M.: consultant child psychiatrist, Cambridge area.

JACKSON, RUBY M., M.B. Sheff., D.O.BST.: asst. county m.o., North East Kent.

MCLEWAN, J. M., M.B. Glasg., D.P.H.: executive m.o., west area Northumberland, M.O.H., urban districts of Hexham and rural districts of Bellingham, Haltwhistle, and Hexham.

MACRAE, A. K. M., M.B. Edin., M.R.C.P., DIP. PSYCH.: physician-superintendent, Bangour Mental Hospital, West Lothian.

PATERSON, WILLIAM, M.B. Glasg., D.P.H.: m.o., Cornwall, school m.o. and M.O.H. area 6.

SMITHAM, J. HILLIER, M.B. Lond., F.F.R., D.M.R.E.: part-time diagnostic radiologist (consultant status), Chelsea Hospital for Women, London.

WILSON, H. B., M.B. Aberd., F.F.A. R.C.S., D.P.H., D.A.: senior anaesthetist, University of Aberdeen.

Manchester Regional Hospital Board:

HARVEY, P. W., M.B. Manx., DIP. PATH.: consultant pathologist, group laboratory, Victoria Hospital, Blackpool.

SHANNON, T. E., M.B. N.U.I., D.O.M.S.: consultant ophthalmologist, Bolton and district hospitals.

WILSON, T. MCs., M.C., M.B. Edin., M.R.C.P.: consultant chest physician and physician-superintendent, Baguley Hospital.

Notes and News

AT HOME IN THE HOSPITAL

DREAD of hospitals, though less common than it was, is still severe enough among the few to deserve a place with the other phobias. We recommend to those who suffer from it a good prophylactic in the form of a book¹ just published on behalf of the Middlesex Hospital. Here nearly all the activities of a hospital are shown, in really splendid photographs, and explained in a minimum of text. Mr. Derek Adkins, the photographer, followed individual patients with typical diseases through every stage of their treatment, beginning at the moment when they were first seen as outpatients. He attended operations, watched fractures reduced, saw the pathology department examine slides for tubercle bacilli, watched X-ray diagnosis and treatment, and photographed these and many other medical and surgical procedures. He also visited the kitchens, the laundry, the storerooms, the engineers' department, and the dispensary; he arrived for the milk delivery, and went to Covent Garden with the hospital florist; he attended an evening meeting in the boardroom, and a Sunday morning service in the chapel. From his 850 photographs 150 were chosen to appear in this book, and these present the daily work of a great hospital in a way that has not been done before.

The patients' histories are perhaps the most telling part of this persuasive work. The boy who fractured his ankle in a motor-bicycle accident is seen, at the end of his stay in hospital, riding confidently away on the same machine; the medical student whose miniature radiograph showed tuberculosis is eventually passed fit to return to his career; the diabetic settles down at home to his régime, under the guidance of a social worker who is herself a diabetic; the blue baby tricycles triumphantly round the ward. Perhaps the most reassuring case of all is that of the gastric ulcer patient who came in looking an old sick man, and went back to work, after partial gastrectomy, apparently twenty years younger.

As Colonel Astor, the chairman of the Middlesex, notes in his introduction, a far larger book would be needed to outline the work of every part of the complex organisation which is a hospital. The purpose of this small work is, first, to give an impression of the way a modern hospital staff go about their duties, and how numerous and varied are their callings: and this it does to perfection. Its second aim is to add to the confidence of the patient in those who are looking after him, for this, as Colonel Astor says, is a factor of unchanging importance in his recovery. This book should do much to establish such confidence.

DOCTOR AND ENGINEER IN PUBLIC HEALTH

ADDRESSING the Institution of Sanitary Engineers, on April 3, Dr. R. F. Guymer, Rockefeller tutor in public-health engineering at the London School of Hygiene and Tropical Medicine, said that if any good is to come of the liaison between doctors, engineers, and others, we must guard against adopting a too local and a too parochial attitude. Such labels as preventive medicine, social medicine, and environmental sanitation are unimportant: the basic principles are what matter.

In his "Report of a general plan for the promotion of public and personal health in the State of Massachusetts," published in 1850, Lemuel Shattuck, the Boston bookseller, proposed that a general board of health should be created, consisting of two physicians, one counsellor-at-law, one civil engineer, one chemist, and two persons of other professions or occupations. His reasons for giving the board this constitution were, first, that many questions would arise requiring knowledge possessed by different professions, and secondly that the promotion of public health is a matter that concerns every profession and every person. This was perhaps the first mention of a great basic principle: that the promotion and maintenance of health is not the prerogative of any one section of the population or of any one profession; it is the concern of everyone to a greater or less extent.

Today, said Dr. Guymer, the creation and maintenance of good health depend upon team-work, and he drew examples from Ceylon, Egypt, and America. Many years ago Ceylon possessed a good irrigation scheme which was largely responsible for the prosperity of the island; but it was seriously upset by invasions in the 14th and 15th centuries, and malaria became a scourge of the population. In this century, besides

installing new irrigation it has been necessary to try to stamp out malaria, and such progress has been made that there is no reason why the island should not regain its former prosperity. In Egypt in modern times irrigation improved to such an extent that two or even three crops were grown in a year; but unfortunately the new system produced ideal conditions for the water-snail which harbours bilharzia. The consequent advance of bilharziasis illustrates how, in the absence of team-work and foresight, improvement in one environmental factor may increase an already existing endemic disease. The American example was of the Tennessee Valley project where, up to 1933, an area of more than 60,000 square miles was for all practical purposes derelict, largely because of malaria. Such persons as lived in the area were so diseased that they possessed neither the physique nor the morale to remedy their plight. To develop this area the Tennessee Valley Authority employed nearly 40,000 persons, including engineers, doctors, chemists, entomologists, agriculturists, architects, and veterinary surgeons. A length of the Tennessee River, over 600 miles in extent, was divided into a series of lakes or reservoirs by the building of dams, and to remove mosquito breeding-places a strip of the river bank between the highest water level and the top of the bank was cleared of vegetation. By operating the sluice-gates of the dams, the water level is raised in winter above its highest normal, in order to strand floating debris; this level is maintained during early spring (the mosquito breeding-season) so that the water shall never be stagnant; and in late spring and summer the level is raised and lowered weekly so as to strand the mosquitoes on the dry sun-baked earth where they cannot live. Other problems solved included the supply of water and electricity, the restoration of fertility to the land, with lessening of soil erosion, and the provision of seed and fertilisers. Gradually this desert area began to blossom as a rose.

Such enterprises, said Dr. Guymer, are of great importance; for the world population is increasing, and it is imperative that places which are at present barren and useless should be developed and transformed into places where man can live healthily and happily. By such work, he believed, we shall make a very real contribution to the establishment of a lasting peace; for people who are housed, fed, and clothed adequately, and who can work and relax in congenial surroundings, free from disease, are probably less likely to resort to war to settle their disputes.

MASSON ET CIE

Masson, the well-known French medical publishers, celebrate their 150th year with a handsomely printed and illustrated monograph.¹ The firm began life as the Librairie Médicale et Scientifique in 1804, in an era when, under the First Empire, many educational reforms were being made in France and the growing importance of the natural sciences was creating a need for better textbooks and journals. Victor Masson (1807-79) joined Nicolas Crochard, the founder, in 1838 and became sole owner eight years later. He brought original ideas to scientific publishing; he improved the format of textbooks and introduced the use of illustrations both in the text and by engraved plates. He also realised the importance of exporting medical and scientific books, both for trade and as a means of maintaining the prestige of French culture. He was succeeded in 1859 by his son Georges Masson; and the present Georges Masson, his great-grandson, who is one of three co-directors, carries on the family connection with the firm. Since 1904 Masson et Cie have published the *Presse Médicale*. This firm's publishing programme since the war show that venerable age has not impaired its vigour.

POSTS IN NIGERIA

IN an advertisement in this issue the Colonial Office invite applications for posts in the medical department of the Northern Region of Nigeria. But the Colonial Office feel that British doctors may hesitate to join the service without formal reassurance as to their future prospects, and they have accordingly sent us a statement issued in Lagos last January by the heads of Nigerian delegations on the future employment of overseas officers in their public services.

The heads state: "We are determined to press forward with the Nigerianisation of the Civil Service; but we are aware that the efficient administrative machinery which the country

1. 1804-1954: Masson et Cie. 120, Boulevard Saint-Germain, Paris 6^e.

must have cannot, as yet, be provided unless a sufficient number of experienced and qualified overseas officers continue to be available." They go on to declare their intention to safeguard the interest of overseas officers and to "assure them that future terms and conditions of service will be fair and reasonable and no less favourable than those obtaining today." They also state that they support the principle that all public-service questions—including appointments, promotions, transfers, postings, dismissal and other disciplinary matters—should be kept independent of political control, and that they hope that the traditional principle of promotion according to qualifications, experience, merit, without regard to race, will be maintained.

University of Cambridge

On May 29 the following degrees were conferred :

M.D.—J. D. Lever.
M.B., B.Chir.—A. E. Gibbs, *J. H. H. Webster.
M.B.—J. D. Salmon.

* By proxy.

Faculty of Anæsthetists

At a meeting of the board of the faculty, held on June 2, at the Royal College of Surgeons of England, Dr. Bernard Johnson was re-elected dean, and Dr. R. F. Woolmer was elected vice-dean for the ensuing year.

Scottish National Health Service Tribunal

Mr. I. H. Shearer, Q.C., has been appointed chairman of the tribunal in succession to Mr. William Grant, Q.C., who has resigned.

La Semaine Médicale de Paris

This year the meeting will be held in Paris from Oct. 3 to 10. As last year, most of the meetings will be held at the Salpêtrière.

London Medical Orchestra

A section of this orchestra will play music by Purcell, Bach, and Mozart at a meeting of the London Association of the Medical Women's Federation at the Royal Free Hospital School of Medicine, on Friday, June 18, at 8.15 P.M.

Military Appointments

Sir Arthur Porritt has been appointed honorary consulting surgeon to the Army at home, in succession to Sir Heneage Ogilvie; Mr. J. B. Blaikley has been appointed honorary consultant in gynaecology to the Queen Alexandra Military Hospital, Millbank, in succession to Mr. Frank Cook.

The Physician and Traffic Safety

The International Union of Associations of Doctor Motorists has chosen this subject as the main topic of its first post-war congress, which is to be held in Vienna from September 8 to 11. Further particulars may be had from the Secretariat of the Ärztliche Kraftfahrvereinigung Österreichs, Vienna 1, Weihburggasse 10-12, Austria.

Hospital Research Prizes

The board of governors of Queen Charlotte's and Chelsea Hospitals have awarded a prize of £200 to Mr. J. H. Gibson for his paper (written with Dr. R. M. Calman) on Pyrexia in the Puerperium with particular reference to Uterine Infections, and a prize of £50 to Dr. W. E. Hunt for his paper on Acute Oesophagitis in the Newborn Infant.

International Award

An international award is planned to honour outstanding workers in the field of the venereal diseases and non-venereal treponematoses. If sufficient funds are collected the award will be administered by W.H.O. In the United Kingdom cheques, payable to the International Treponematosis Award Fund, should be sent to Dr. R. R. Willcox, St. Mary's Hospital London, W.2.

Electronics Exhibition

This exhibition, which is to be held at the Manchester College of Technology from July 14 to 20, will include several medical exhibits. The Christie Hospital and Holt Radium Institute is showing a scintillation dose-rate meter, a dose-rate comparator, and a dose-rate and integrating dose monitor for use with an X-ray tube; the Institute of Cancer Research of the Royal Cancer Hospital, ultrasonic echo locating equipment; and the Burden Neurological Institute a portable 12-channel toposcope. Further particulars may be had from the secretary, Mr. W. Birtwistle, 78, Shaw Road, Thornham, Rochdale.

Medical Insurance Agency

The annual meeting of this agency was held on June 3, with Dr. James Fenton in the chair. The committee of management reported that in 1953 the net profit was greater than ever before: this is distributable solely to the medical and dental charities. The total of rebates of premiums granted to clients also reached a new peak. Dr. Fenton was re-elected chairman, and Dr. Henry Robinson hon. secretary. The following retiring members of the committee were re-elected: Dr. J. A. Brown, Dr. J. T. Ingram, Dr. G. Roche Lynch, Sir Henry Souttar, and Prof. R. J. Willan. New members elected were: Prof. Alan Kekwick and Prof. G. A. Wishart.

Lord Webb-Johnson has been appointed consulting surgeon to the Royal Dental Hospital of London and School of Dental Surgery.

The second edition of the *Directory of International Scientific Organizations* has been published by UNESCO. Copies may be had from H.M. Stationery Office (13s. 6d.).

Diary of the Week

JUNE 13 TO 19

Monday, 14th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. H. E. Holling: Ballistocardiography.
INSTITUTE OF NEUROLOGY, The National Hospital, Queen Square, W.C.1

5 P.M. Dr. E. H. Botterell (Toronto): Management of Spinal-cord Injuries and Studies on Spinal Man.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY
3 P.M. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Prof. J. Louw (Cape Town): Abortions.

4.30 P.M. Prof. Bruce Mayes (Sydney): Infertility.

Tuesday, 15th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. J. L. Livingstone: Treatment of Pulmonary Tuberculosis at the Present Time. (Mitchell lecture.)

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. M. F. Lucas Keene: Embryological Background of Some Common Abnormalities. (Arnott demonstration.)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8 P.M. Section of Psychiatry. Dr. V. E. Frankl (Vienna): The Concept of Man in Psychotherapy.

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. A. M. Cooke: On Writing for a Medical Journal.

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. W. N. Goldsmith: Tuberculosis.

Wednesday, 16th

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. C. D. Calman: Ringworm Infections and Their Treatment.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY
NOON (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Professor Mayes: Could the Chapter on Eclampsia Disappear?

Thursday, 17th

ROYAL COLLEGE OF SURGEONS
5 P.M. Sir Stanford Cade: Adrenalectomy. (Hunterian lecture.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. Cooke: Medical Writing from MS. to Reprint.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. H. Haber: Specific Granulomas.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Professor Mayes: The Pregnant Diabetic.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. C. C. Chesterman: Training and Employment of African Auxiliary Medical Personnel.

Friday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr. J. Ellsworth Laing: General Principles of Plastic Repair.

4 P.M. Dr. Douglas Hubble: Investigation of Endocrine Syndromes.

MEDICAL RESEARCH SOCIETY
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. G. W. Thorn (Harvard): Adrenal Cortical Response to Stress in Man.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. M. B. MacKenna: Tuberculosis and Sarcoid.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY
2 P.M. (Queen Charlotte's Hospital.) Professor Louw: Rupture of Uterus.

Saturday, 19th

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY
11 A.M. (Chelsea Hospital for Women.) Mr. C. Kimbell: Subtotal, Total, and Vaginal Hysterectomy.

BIOCHEMICAL SOCIETY
11 A.M. (Department of Biochemistry, University of Cambridge.) Scientific papers.

THE ABUSE OF REST*

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THE Concise Oxford Dictionary defines rest clearly enough as "repose or sleep especially in bed at night; abstinence or freedom from or absence of exertion or activity or movement or care or molestation." But there are few terms in the English language which possess such a complex superstructure of special meaning and oblique implication as this simple monosyllable. Take for instance its use in relation to gainful employment, of which it is the antithesis. No less an authority than George Schwartz, writing in the *Sunday Times* of Sept. 6, 1953, states (as usual, with his tongue in his cheek) that "if there is one thing that justifies man's claim to be only a little lower than the angels it is that the human race is not fond of work for work's sake."

Rest has an aura of desirability because work includes, or has included, an element of exploitation. Everybody would agree that a week of 70-80 hours toiling in the "dark satanic mills" of the Industrial Revolution was intrinsically harmful, but when a claim is made that to work for more than 40 hours per week in a modern engineering works is unhealthy one is not really expected to believe that it is the toil itself that hurts. Such a claim is merely a move in the complex adjustment of remuneration—the setting of the dividing line between normal and overtime rates.

Consider further the widespread belief that hard work, with its mental and physical activity, plays an important part in the causation of disease. This belief has little rational basis; it does not rest on a critical analysis of the physiology of activity; and it is not attached to any demonstration of damage by repeated muscular contraction, by the elevated metabolism of effort, or by concentrated thought. Indeed there is abundant evidence that none of the known effects of work can harm healthy tissues. On the contrary all these effects are, in a different context, regarded as beneficial in the sense that they develop and extend the range of adaptation of physiological mechanisms.

The evil reputation of work as a cause of disease springs from two rather disreputable and quite illogical traits in human character. The first is the widespread reluctance of medical men to admit frankly that they are ignorant of the cause of disease—that they do not know why a particular person has fallen victim to an infection or why another person's blood-pressure has risen or a clot formed in his coronary artery. The second is the very understandable but really quite indecent avidity with which a patient accepts the explanation that his illness is due to overwork and insufficient rest. It is a belief which nourishes his amour-propre; it enrols him in the noble army of martyrs; he has fallen fighting the good fight. Believing this, he can relax with a clear conscience and enjoy to the full the provisions of a Welfare State, the bondage of a possessive wife, and the plaudits of an admiring family. In brief the general implication is that work is hell and rest is heaven as implied in the words of the lovely hymn which refers to "the saints who from their labours rest."

I am sure then we should all agree that work—even hard work—which involves no avoidable hazard, does not interfere with sleep or nutrition, which is remunerated sufficiently to remove any sense of exploitation, and which allows of enough recreation to counteract tedium, is harmless. Indeed, it is beneficial. One cynic has said that the chief aim of life is to fill in the time between

birth and death—which is perhaps why medicine is so popular a profession, for we can all at least be sure that our work will fill our thoughts and direct our activities from when we wake in the morning until late at night we go wearily to bed.

* * *

Now if rest in general were as blameless a state as work there would be no question of abusing it. If the possibility of abuse was merely negative—in that at worst the prescription of rest could do no more than exclude other more useful measures—it would hardly deserve comment. But the truth is that in overdose rest is very toxic and even lethal, and should be classed as one of the most powerful of the "drugs of addiction." Indeed, like morphine, cocaine, and the others, it should be included in the scope of the Dangerous Drugs Act and be prescribable only in clearly defined doses not to be repeated without a further prescription. Of course in a sense this is so, since certificates of incapacity have to be repeated at regular intervals; but all too often repetition is the rule rather than the exception.

Using the term as indicating certified incapacity for normal gainful occupation there are degrees of rest ranging from immobilisation in a plaster cast to a régime of rehabilitatory exercise which make the patient's ordinary occupation a rest-cure by comparison. Rest in bed has come to occupy a large place in current therapeutics: in fact it is widely regarded as normal for the sick person to be in bed. The attitude is such that the burden of proof is on the physician who says the patient should not be in bed, rather than the reverse which I believe is the only logical position. Surely it is normal for a person to be mobile and absurd for him to spend all or most of his time in bed. Once that is accepted—and it is irrefutable—then it becomes illogical to allow or encourage confinement to bed without good and sufficient evidence of its beneficial effect. The difference between the doctor who practises intelligently and with judgment and one whose activities consist in some rather simple conditioned reflexes is that the latter sees nothing incongruous in ordering bed rest without proof of its beneficial value, just as he prescribes iron, vitamin B₁₂, and folic-acid pills in unspecified anaemia or puts all his patients on multiple vitamin pills despite the overwhelming evidence of the rarity of vitamin deficiency in this country. To treat without reason is to ape the witch-doctor and to defend such action by pleading that the patient expects it is a contemptible retreat from reason.

There is abundant evidence that the mere act of immobilising a man produces profound changes in metabolic function. Deitrick, Whedon, and Shorr¹ reported a well-controlled study of the effects of immobilising young healthy men for periods of six or seven weeks. Among the changes observed were (1) negative nitrogen balance to an average extent of 54 g.; (2) a total calcium loss of 9-24 g. This excretion of calcium, combined with unchanged urinary volume, a slight rise in urinary pH and a failure of urinary citric acid to rise, all favour the precipitation of calcium phosphate in the urinary tract. Normal calcium metabolism was not resumed until six weeks after the rest period. Circulatory changes brought about by immobilisation were a decline in total blood volume and a deterioration in the mechanisms essential for adequate circulation in the erect position as indicated by an increased tendency to faint in tilt-table tests. The legs seemed to be the principal site of changes responsible for this deterioration—changes such as venous engorgement, capillary fragility, and impaired muscle tone. Exercise tolerance, leg girth, and pulse-rate took approximately six weeks to return to normal.

1. Deitrick, J. E., Whedon, G. O., Shorr, E. Amer. J. Med. 1948, 4, 3.

* From an address to the Section of Medicine, Royal Society of Medicine, Nov. 24, 1953.

This work shows that, even in the healthy young adult, immobilisation causes profound metabolic changes. However, it has long been evident to clinicians that a long sojourn in bed has harmful results, particularly if the patient be elderly. Skeletal changes, such as muscular contraction and wasting, joint malposition, and ligamentous stretching, are common. Urinary calculi can be caused by immobilisation in the horizontal position, while confinement to bed is an important factor in the all too common incontinence of the elderly—a defect which can often be terminated by getting the patient up. Probably the most disastrous complication of bed rest is the bedsore, which can be prevented only by continual attention to the pressure areas, demanding an amount of nursing care which is very hard to provide. Satisfactory alimentary function is very difficult to secure in the bedridden; anorexia and constipation are common. A welcome development in this respect is the increasing realisation that the efficient use of a bedpan is an athletic feat demanding a degree of training, coöordination, and endurance which would do credit to the young and healthy. Except in cases of extreme paralysis and major fractures it is usually far better to help the patient on to a commode.

To summarise the harmful effects of bed rest I cannot do better than quote the vivid crescendos of Dr. R. A. J. Asher,² who in describing the evils of an overdose says:

"even those evils I have outlined may help to show that rest in bed is anatomically, physiologically, and psychologically unsound. Look at a patient lying long in bed. What a pathetic picture he makes! The blood clotting in his veins, the lime draining from his bones, the scybala stacking up in his colon, the flesh rotting from his seat, the urine leaking from his distended bladder, and the spirit evaporating from his soul."

In the face of this damning indictment it is remarkable that bed rest should be used at all, and still more remarkable that it should be used to the extent implied in the threadbare joke "stay in bed till I come back."

* * *

I cannot claim to have made anything more than a very superficial attempt to trace the history of bed rest as a therapeutic measure. It has, of course always been recognised that rest is essential for the acutely ill person, for no more profound reason than that bodily function is so disturbed that activity is distressing or even impossible. But there is little mention of bed rest in the 18th and early 19th century by such authors as Withering, Heberden, and Stokes. The medical history of John Hunter shows that he spent little time in bed during his various illnesses—though one must not deduce much from that, for he was the sort of rugged individualist who would ignore bodily distress and medical advice. The mid-19th century saw the impact of Hilton's *Rest and Pain*; and as I turned over its pages again there was borne in on me afresh the utter irrationality of therapeutics unrelated to the scientific study of disease. In case after case Hilton scored success, after all sorts of fantastic treatments had failed, because he recognised the value of rest in inflammation—particularly in osteomyelitis and bone and joint tuberculosis which was then so prevalent. As so often happens, opinion swung to the opposite extreme, and rest came to be regarded as the universal healer.

Another reason for undue emphasis on bed rest may be the tendency, since the 19th century, to treat illness in hospital rather than at home. In most hospitals, even today, the patient is expected to be in bed: the whole organisation is geared to such a state, and there is little provision for the up patient. Often, when the patient is admitted, the relatives take his clothes away, bringing them back only when discharge is imminent; for only a minority of hospitals have lockers or stores for the

retention of patients' clothing. Furthermore, the routine of the bed bath and the bedpan is firmly established in nursing care. Indeed, many of our older hospitals—especially those for the chronic sick, with large inadequately heated wards and too few nurses—enforce bed rest as the only modus operandi. The visitor to Continental clinics and to tropical hospitals cannot fail to be impressed by the extent to which patients get up and stroll around without any apparent harm—indeed much advantage.

* * *

Finally let me return to the wider question of rest in the sense of absence from employment.

In advising a patient not to work, the doctor assumes responsibility for (1) reducing the patient's income, (2) withdrawing several pounds per week from the Public Purse, and (3) reducing the efficiency of a factory or business: moreover at the same time he enforces on the patient an impression of the gravity of the illness. As these results of the certification of incapacity are obvious, such a costly prescription should never be written without a reasoned belief in its necessity, and the dose should be the minimum calculated to get the desired result. Yet nobody can for a moment suppose that such critical care is universal or even usual in either general or consulting practice.

One hears much of the inalienable right of a doctor to prescribe what he thinks is best for the patient but not enough of the inescapable duty of the doctor to reconcile the good of the patient with the good of the community of which the patient is a part. The vital importance of the welfare of the community as an extension of the welfare of the individual was brought forcibly home to me during the war, when for a time I was the medical specialist of a hospital in a beleaguered garrison. It required little imagination to see that every patient in hospital was one man less on the perimeter—rest was dispensed with rigid economy. If the same spirit pervaded the practice of medicine in present-day Britain there would be substantial advantage both material and moral. Excess prescribing of rest, and excess prescribing of drugs, are millstones around the neck of the health service and the nation—extravagances we cannot afford. Before he advises rest, let every doctor ask himself whether his prescription is really necessary, and, if it is, how little will suffice.

ACUTE APPENDICITIS IN LATE PREGNANCY *

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WHEN acute appendicitis develops in a pregnant woman, a prompt diagnosis may be unusually difficult; for the abdominal pain and vomiting may be attributed to the pregnancy, and the physical signs are altered by the progressive enlargement of the uterus and by the corresponding displacement of the appendix towards the right flank. The difficulty in diagnosis is greatest in the later months of pregnancy, and not all workers are agreed on what is the correct treatment at that time. All previous papers on the subject in English have come from America, except individual cases. Fahmy (1944), for example, described a difficult case at the eighth month.

* The substance of this paper was presented at a joint meeting of the Birmingham and Midland and South-Western Obstetrical and Gynaecological Societies at Birmingham on May 7.

The following case-records refer to patients admitted to the Birmingham Maternity Hospital in 1950-53 with acute appendicitis in the last trimester. The cases range from early to late or neglected admissions and are presented with the object of assessing the criteria of diagnosis and recording the results of treatment by appendicectomy with conservative management of the pregnancy.

Case-records

Case 1.—A woman, aged 31, was admitted as an emergency in the thirty-eighth week of her second pregnancy. Fifteen hours before admission pain came on in the centre of the abdomen, and after five hours it moved to the right iliac fossa. The pain was continuous and moderately severe, and the patient vomited soon after its onset. There was a history of occasional bouts of subacute appendicitis in the previous eighteen years, and on one occasion she had been admitted to hospital for observation but had no operation.

On examination her temperature was 99°F, pulse-rate 86, and tongue coated but moist. There were some guarding and tenderness on pressure in the right iliac fossa. The pregnancy appeared to be normal. On rectal examination no tenderness was elicited. Acute appendicitis was diagnosed.

Laparotomy was undertaken through a right paramedian incision eighteen hours after the onset of pain. Free turbid fluid was found in the peritoneal cavity. The appendix, lying alongside the cæcum, was acutely inflamed but not perforated. Appendicectomy was done, the stump was buried, and the abdomen was closed in layers. The patient received morphine and streptomycin.

Labour.—Twenty-four hours after operation labour began, and after five hours, when the cervix was fully dilated, forceps were applied under general anaesthesia. A healthy child was delivered. The patient made a good recovery, being apyrexial from the second day. There was no distension of the gut, and the wound healed by first intention.

Case 2.—A primigravida, aged 33, was admitted as an emergency, when thirty-nine weeks pregnant, with a history of sudden severe pain in the right iliac fossa coming on six hours before admission. The pain developed into a generalised ache across the lower abdomen. The patient had not vomited.

On examination the temperature was 100°F, the pulse-rate 98, and the tongue slightly furred but moist. The abdomen was a little tense; there was no true guarding or rigidity, but there was tenderness on deep pressure in the right iliac fossa. It was impossible to say whether the source of this tenderness was uterine or extra-uterine, because the pregnancy was filling the abdomen. There was no "release tenderness" or renal tenderness, and rectal examination revealed no abnormality. The foetal heart was heard. A catheter specimen of urine showed a moderate number of pus cells. The diagnosis rested between urinary infection, appendicitis, and accidental haemorrhage. In view of the early stage of the condition it was considered proper to allow a short period of observation. Eight hours later the temperature was 98.4°F, and the pulse-rate 92; there was no vomiting and no alteration in physical signs. A further specimen of urine showed only an occasional pus cell. A further period of four hours' observation was undertaken, during which the patient had a sudden sharp attack of abdominal pain like the initial attack but felt in the midline above the pubis. The temperature was 99.2°F, and a white-cell count showed 18,200 leucocytes per c.mm. (76% polymorphs).

Laparotomy was therefore done twenty-one hours after the onset of symptoms. A McBurney incision was made and extended by cutting the muscle towards the loin. The appendix was found grossly inflamed but not ruptured, with fibrinous adhesions to the bowel. Appendicectomy was done, the stump was carbolised but not buried, and the abdomen was closed in layers. The patient received morphine and penicillin. Next day her condition was satisfactory and her temperature normal, but the foetal heart was not heard; it had last been detected four hours before laparotomy.

Labour.—Four days after the operation labour began spontaneously. After a first stage lasting eight hours a forceps delivery was undertaken under general anaesthesia, and a macerated baby was delivered. There was no evidence of accidental haemorrhage or of any other reason for the intra-uterine death. The patient's progress continued to be

uneventful, and the wound healed by first intention. Nine months later she again became pregnant.

Case 3.—A primigravida, aged 29, was admitted, when thirty-seven weeks pregnant, with twenty-four hours' history of pain beginning in the epigastrium and settling in the right iliac fossa. She had vomited all food taken during this time. A record of her temperature taken before admission showed readings of 98.8° and 99°F.

On examination her temperature was 99°F, pulse-rate 90, tongue coated and dry, and the abdomen tender on pressure in both iliac fossæ, more notably on the right. There was no rigidity or guarding and no tenderness in the loins. "Release tenderness" was classed as doubtful. The uterus was of normal size for a pregnancy near term, and the foetal heart was heard. Rectal examination showed no abnormality. A catheter specimen of urine showed no pus cells but much acetone. The patient's doctor stated in his letter that she had a previous history of "indigestion" which could have been appendicitis; but on admission it was not felt that the diagnosis could be substantiated, and a period of observation was allowed during which 500 ml. of 10% dextrose solution was given intravenously. Six hours later the patient's temperature was 98.8°F and pulse-rate 84. There was no other significant alteration; but, since the tenderness in the right iliac fossa persisted the patient was operated on.

Laparotomy was performed twelve hours after admission. A McBurney incision was made and extended by cutting the muscle upwards. When the peritoneum was opened, a little free pus was found. The appendix was in an advanced stage of inflammation but had not ruptured; it was lying in the pelvic position. Appendicectomy was done, the stump was buried, and the abdomen was closed in layers without drainage.

Postoperatively morphine was given and the patient's condition was good for the first day. After forty-eight hours she became distended and began to vomit, and paralytic ileus developed. Streptomycin was given, and gastric suction and intravenous therapy without bowel stimulation was continued for four days before peristalsis started again satisfactorily. Thereafter the patient's recovery was uninterrupted.

Labour began spontaneously thirteen days after the operation. The uterine action was somewhat inert, but the patient delivered herself, with the aid of an episiotomy, of a baby weighing 8 lb. 3 oz. The wound healed satisfactorily.

Case 4.—A primigravida, aged 29, was admitted to hospital, when twenty-nine weeks pregnant, with two weeks' history of a "cold" in the course of which she developed pain in the right loin, made worse by walking, and this pain persisted after the cold had disappeared. Four days before admission she complained of sharp pain in the right groin which made her vomit, and this continued up to the time of admission. No record was available of her temperature during this time.

On examination her temperature was 96.8°F, pulse-rate 110, and tongue dry and furred. Tenderness was greatest in the right iliac fossa. A catheter specimen of urine showed no abnormality, and acute appendicitis with peritonitis was diagnosed.

Laparotomy was undertaken through an extended gridiron incision. Much pus was found in the peritoneal cavity. The appendix was retrocæcal and acutely inflamed but not ruptured. Appendicectomy was done, the stump was oversewn, a stab drain was inserted laterally, and the abdomen was closed in layers. Penicillin powder was dusted into the wound, and therapy with systemic penicillin and soluble sulphathiazole was begun immediately. Intravenous therapy was also begun at once, no fluid being given by mouth.

Labour.—Thirty-two hours after the operation labour began spontaneously, and after four hours low-forceps delivery was done under local infiltration anaesthesia; the baby was alive but premature and died soon after birth. No flatus was passed, and no gut sounds were heard for two days after the operation; but on the third day, when intravenous fluids were still being given, peristalsis began and the patient began to pass large liquid stools. She continued to have several loose motions daily for a few days. On the fourth day after operation her haemoglobin was 36% and red cells 2,430,000 per c.mm. Altogether two pints of blood was therefore given on the fifth and sixth days, with considerable symptomatic improvement. The wound healed well, and the following year the patient had a normal pregnancy and delivery.

Case 5.—A woman, aged 31, was admitted at the thirty-sixth week of her fourth pregnancy. Throughout the pregnancy

she had not felt well. Six weeks before admission she complained of right-sided abdominal pain, shivering, sickness, and frequency of micturition. She was confined to bed for three weeks and was attended by her doctor; after this the pain became intermittent and less severe. Thirty-six hours before admission she had acute right-sided abdominal pain and vomited once. The pain persisted during the next day, and she vomited again. She began to want to pass water every few minutes and felt feverish. She was then admitted to hospital.

On examination she looked toxic, and her temperature was 99.8°F, pulse-rate 120, and tongue furred and dry. Her uterus was enlarged to the size of a full-term pregnancy, contracting strongly but relaxing normally between contractions. The foetal heart was heard. There was tenderness on pressure over the right side at the level of the umbilicus, and the patient noticed similar pain when the fetus moved. There was neither rigidity nor release tenderness, but there was slight tenderness on pressure over the right costovertebral angle. On vaginal examination no tenderness was felt and the cervix was not dilated. A catheter specimen of urine showed only an occasional pus cell but much acetone. The diagnosis seemed to rest between acute appendicitis and a relapsing pyelitis. It was decided to wait for a short time during which intravenous fluids and morphine were to be given. Four hours later the pulse-rate was 92, and after a further five hours the patient was feeling better and the pain was less. Her temperature was then 99°F and pulse-rate 112. Twelve hours after admission her temperature was 98.4°F and pulse-rate 100. She had had 2 litres of dextrose, 1 containing saline solution, and there was no acetone in her urine. She had vomited a few ounces of clear fluid, however, and there was tenderness on the right side of her abdomen at the level of the umbilicus.

Laparotomy was therefore undertaken, forty-eight hours after the onset of symptoms, through a McBurney incision extended by cutting the muscle. Free purulent fluid was present in the peritoneal cavity, and the inflamed appendix was found crossing the pelvic brim and burying its tip in the back of the broad ligament. The tip was firmly adherent and was separated only with difficulty. The fallopian tube and ovary were drawn down to this inflammatory zone. Appendicectomy was done, and the stump was buried. Penicillin powder 5 g. was placed in the peritoneal cavity, and the pelvis was drained through a rubber tube brought out through the lower end of the wound. The abdomen was closed in layers.

Postoperatively the patient became cyanosed whenever the administration of oxygen was stopped; so it was necessary to continue giving oxygen on her return to the ward. Treatment with intravenous fluids and large doses of penicillin and streptomycin was begun. Next morning the patient still tended to be cyanosed and was dyspneic at rest, though the lung bases were clear. That day routine investigation of her blood chemistry revealed considerable methemoglobinemia. An intravenous injection of 10 ml. of methylene-blue solution improved her colour without entirely relieving her cyanosis. Occasional bowel sounds were heard; but there was considerable distension, and the stomach contents were therefore aspirated with a Ryle's tube left in situ. She received a mixture of Darrow's solution, Hartmann's solution, and 5% dextrose intravenously; and her general condition improved next day, although the ileus remained.

Labour.—Forty-eight hours after operation, with very little warning, she delivered herself of a healthy baby weighing 6 lb. 9 oz. Thereafter her pulse-rate improved, dyspnea ceased, and tendency to cyanosis disappeared. The ileus was suddenly relieved on the third day, and she began to pass a large amount of liquid stools, after which the bowel returned to normal. The peritoneal drain allowed a large volume of serous fluid to escape, and this continued for some days after its removal. An alarm was raised that this contained a gas-forming organism, and anti-gas-gangrene serum was given; but her convalescence proceeded satisfactorily, and she was discharged after sixteen days. When she was seen as an outpatient, her wound had healed well and the baby was progressing satisfactorily.

This patient's breathing was considerably embarrassed by the combination of ileus secondary to peritonitis and a full-term uterus inhibiting movement of the diaphragm. If she had not gone into labour spontaneously, rupture of the membranes might have been justified to provide relief. The improvement after delivery was dramatic.

Case 6.—A woman, aged 25, was admitted, in the thirty-ninth week of her second pregnancy, with seven days' history of epigastric pain continuing until eighteen hours before her arrival in hospital, when it shifted to the right side and became spasmoid and severe. She had been vomiting for five days, and shoulder pain had arisen twelve hours before her admission. She was unmarried and had neglected to inform her doctor of her pregnancy and her illness alike.

On examination her temperature was 98.8°F, pulse-rate 110, and tongue dry and coated. Her abdomen showed generalised tenderness, maximal on the right side. Her abdominal wall was tense but not rigid. There was no release tenderness. The uterus was enlarged to the size of a full-term pregnancy, and the foetal heart was heard. On rectal examination there was no undue tenderness. A catheter specimen of urine showed no pus cells. Acute appendicitis was diagnosed.

Laparotomy was done through a right paramedian incision. Pus was found in the right paracolic gutter, and free fluid in the abdominal cavity. The appendix was found perforated, lying coiled behind the ascending colon. On dissection it broke off at its base, and the base could not be ligated. The patient's condition was then very poor. A stab-drain was made in the loin and the wound was closed, but she died undelivered six hours after operation. Cæsarean section post mortem produced a stillbirth.

Necropsy Findings.—Fibrinous exudate was present in the peritoneal cavity, causing adhesions between loops of bowel and occasional pockets of pus on the right side; the fibrinous exudate extended to the liver and diaphragm. In the cæcum there was a ragged abscess cavity, mostly retrocecal and confined to the exterior of the bowel.

Diagnosis

HISTORY

2 patients gave a history of previous bouts of pain in which appendicitis was suspected, and this may be a valuable hint, as noted by Kerr and Moir (1949). The pain was typical of appendicitis (starting in the midline and soon settling in the right iliac fossa) in only 2 cases. In the other cases it could not be well localised by the patient and was described as "right-sided" or "lower abdominal." 1 patient noted pain on foetal movement. Vomiting at, or soon after, the onset of the pain occurred in all but 1 case (case 2), in which the history was deceptively trivial. *Rigors* did not occur in any case, but 2 patients (cases 4 and 6) described symptoms lasting two and six weeks and suggesting infection of the urinary tract, and it was particularly difficult on first examination to reach a correct diagnosis in these cases.

EXAMINATION

The temperature on admission ranged from 96.8° to 100°F and bore no relationship to the severity of the condition within the abdomen. The pulse-rate provided a better indicator, being less than 100 in patients with less than twenty-four hours' symptoms. The tongue also proved to be a reliable index of the patient's general condition, being coated in all the cases and moist only in the early admission. The abdomen is never easy to examine in these cases with a pregnancy near term. Krieg (1949) states that examination often shows an "interesting lack of findings." I prefer to emphasise the uncertainty of the physical signs compared with the clear-cut clinical findings of typical appendicitis in the non-pregnant patient.

Tenderness was present in all the cases, sometimes extending to the right hypochondrium and across to the left iliac fossa, but always maximal in the right iliac fossa or in the right para-umbilical area. It was never confined to a "point," and a confirmatory examination after an interval was often necessary to make certain that the right iliac fossa was the main source of trouble. In seeking to localise the site of abdominal tenderness, it should be recalled that the appendix is displaced upwards and outwards towards the flank as pregnancy advances (Baer et al. 1932). On occasion it was difficult to decide whether the source of the tenderness was

uterine or extra-uterine—e.g., in case 2. Only twice was guarding or rigidity noted, and release tenderness was not certainly defined in any case. *Vaginal* and *rectal* examinations were not helpful. This is what might be expected, because the depth of the pouch of Douglas is reduced in late pregnancy, and its contents are displaced upwards by the foetal head.

Auxiliary investigations have not been widely used in these cases. Krieg (1949) points out that a white-cell count is never pathognomonic and may be misleading—a third of his patients had counts of less than 14,000 per c.mm.—but a high count may confirm a presumptive diagnosis of appendicitis. A catheter specimen of urine should always be examined; but, since a clear specimen does not exclude pyelitis in pregnancy, and a small number of pus cells does not inculpate the renal pelvis, the only positive help comes from specimens which show a massive urinary infection.

DIFFERENTIAL DIAGNOSIS

Only two conditions were considered as alternative diagnoses in these cases. In case 2, where the tenderness was at first thought to be referred to the uterine wall, a small concealed accidental haemorrhage was considered, but subsequent examination suggested an extra-uterine source of inflammatory nature, a suspicion which was supported by a slight rise in temperature and a raised white-cell count. In cases 2, 3, and 5 pyelitis was considered as a possible or probable diagnosis on first examination, but in all the cases appendicitis was suspected. In these cases delays of twelve hours occurred before laparotomy; in each case rest in bed and the use of sedatives produced a dangerously misleading improvement within four hours, and further periods of observation were allowed. In the absence of *positive* evidence of pyelitis after four hours this was probably an error of judgment. In case 4 the general practitioner was similarly misled to believe in a urinary cause for pain, and a rather longer delay resulted. Baird (1935) holds that in such cases a ureteric catheter should be passed, since this would relieve pain of renal origin. Other and rarer conditions may easily be confused with appendicitis. Child and Douglas (1944) and Priddle and Hesseltine (1951) list several such sources of error in their series (degenerating myoma, salpingitis, torsion of cyst, &c.).

Thus the early diagnosis of appendicitis in pregnancy must be made on relatively few clinical findings. The history may simply be that of abdominal pain, usually accompanied by vomiting and without rigors. On examination the patient is pyrexial but the temperature is commonly not much raised (100°F or less), the tongue is coated, and there is right-sided abdominal tenderness not well localised. There are no other reliable signs, and auxiliary investigations are disappointing. The condition most commonly confused with it is acute pyelitis. Probably in most cases of pyelitis severe enough to cause pain and vomiting a high temperature and pulse-rate will be recorded, whereas patients with low-grade pyrexia will rarely complain of abdominal pain. Unless there is a temperature of 101°F or more, with a history of rigors and with frank pus in the urine, it is dangerous to ascribe right-sided tenderness to pyelitis; for, as emphasised by all writers since Babler (1908), delay in the treatment of appendicitis in pregnancy is a most serious mistake.

Treatment

On studying the *management* of these 6 cases the most striking fact which emerges is the difference between the cases subjected to appendicectomy early (cases 1 and 2) and those (cases 4, 5, and 6) in whom operation was delayed forty-eight hours or more after the onset of symptoms. The former made a smooth recovery, whereas the latter had a stormy and worrying postoperative

course due to peritonitis and ileus. At laparotomy the best exposure in late pregnancy has been obtained through a high McBurney incision, starting in the plane of the anterior superior iliac spines and extending it upwards by cutting the muscle in the direction of the right loin.

In no case was the appendiceal infection localised. Many previous workers have commented on this and offered explanations—e.g., Warfield (1950). The main responsible factors appear to be the upward displacement which the appendix undergoes in pregnancy, the barrier placed in the way of the protecting omentum by the enlarged uterus, and the mobility of the inflamed zone due to the large contractile organ in close relation to it. In all the cases the general peritoneal cavity contained free fluid, fibrinous adhesions, or free pus. The appendix was not found in any constant position. A stab or wound drain was used in those cases where the appendix was ruptured, or where free purulent fluid was present in considerable amount. Antibiotics were used in all the cases, though it may be unnecessary in the early cases. It is a recurring fear of previous workers that the effect of labour will be to disseminate intra-peritoneal infection—indeed caesarean section has been advocated to avoid this (Crossen and Crossen 1948)—therefore every patient received antibiotics. In this series there was no evidence that *labour* following appendicectomy caused any such deterioration. 3 of the 5 patients who survived went into labour within forty-eight hours of operation. In all of these cases labour was uneventful; forceps delivery was undertaken when practicable to prevent maternal distress and to relieve strain upon the abdominal wound, but in all the cases healing of the wound was satisfactory, and any anxieties we felt were, in retrospect, largely unwarranted. Other workers—e.g., Meiling (1947)—have commented on the onset of premature labour following appendicectomy, and it seems that the onset of labour may be expected within forty-eight hours of operation in a good number of these patients near term.

The *baby* was unaffected by the mother's illness except in case 2, where the stillbirth remains unexplained. De Voe et al. (1947), discussing a similar intra-uterine death, suggest severe maternal acidosis as a factor, but in the present case the patient's general condition was good.

The *postoperative* course was uneventful in cases 1 and 2. In the cases subjected to laparotomy after a

TABLE I—HISTORY

Case no. and year of operation	Age (yr.)	Gravida	Gestation (weeks)	Symptoms			Duration on admission (hr.)
				Location of pain	Vomiting	Other	
1 (1953)	31	2	37	Midline→right iliac fossa	+	None	15
2 (1952)	33	1	39	Right iliac fossa→lower abdomen	..	None	6
3 (1951)	29	1	37	Midline→right iliac fossa	+	None	20
4 (1950)	29	1	29	Right groin→"right side," and midline	+	Previous (2 weeks) right loin pain on walking	96
5 (1953)	31	4	36	" Right side "	+	Frequency of micturition; previous 6 weeks' history suggesting pyelitis; tenderness on movement of fetus	36
6 (1950)	25	2	39	Epigastrium→"right side"→ shoulder	+	..	ca. 170

TABLE II—EXAMINATION

Case no.	Clinical findings on admission						Investigations	
	Temperature (°F)	Pulse-rate	Tongue	Abdominal tenderness	Abdominal rigidity	Release tenderness	Urine (catheter specimen)	White-cell count (per c.m.m.)
1	99.0	86	Coated, moist	+ Right iliac fossa	"Guarding"	Nil	Not done	Not done
2	100.0	98	Coated, moist	+ Right iliac fossa	Nil	Nil	Pus cells + (moderate number)	18,200 (polymorphs 76%)
3	99.0	90	Coated, dry	+ Both iliac fossae right > left	Nil	Doubtful	No pus	Not done
4	96.8	110	Coated, dry	+ Maximal in right iliac fossa	+	Not noted	No pus	Not done
5	99.8	120	Coated, dry	+ Right side	Nil	Nil	Pus cell occasional	Not done
6	98.8	110	Coated, dry	+ Maximal in right iliac fossa	Nil	Nil	No pus	Not done

delay of more than twenty-four hours ileus secondary to peritonitis caused anxiety but responded finally to antibiotics, gastric aspiration, and intravenous replacement therapy biochemically controlled.

The clinical findings are summarised in tables I-III.

Discussion

The incidence of acute appendicitis in pregnancy is estimated to be about 1 in 1000-2000 cases (Baer et al. 1932, Child and Douglas 1944, Priddle and Hesseltine 1951), but it is probably higher than some workers suggest whose figures are taken from institutions dealing with obstetrics and gynaecology only. There seems to be no good reason to believe that the occurrence of appendicitis should be altered by the existence of a pregnancy (Johnson 1944). On the other hand, it is widely held that a patient subject to recurrent attacks of appendicitis is more liable to have an exacerbation during a pregnancy. The incidence of appendicitis in the different trimesters of pregnancy is assessed variously by different workers. The incidence is the same in the different trimesters in the series of Priddle and Hesseltine (1951) and Hoffman and Suzuki (1949); but most of the recent writers suggest that acute appendicitis is rarer in the last trimester (Child and Douglas 1944, Krieg 1949, Meiling 1947). No really satisfactory explanation for this has yet been offered. The most telling comment is that of Child and Douglas, who, noting the difficulty of diagnosis in a patient near term and the "natural hesitancy of obstetricians and surgeons to complicate a term pregnancy by an operation," suggest that appendicitis may be no less common in late pregnancy, but that an undue number may be given the opportunity of subsiding spontaneously. Thus, they infer, some patients will remain at home with their pain attributed to degeneration in a fibroid or to a small accidental haemorrhage, and will recover spontaneously. Others, diagnosed as having pyelitis, may receive chemotherapy and have their appendicitis cured. But some such patients will develop true obstructive appendicitis and require subsequent admission to hospital. If this be true, one would expect fewer admissions in the last trimester but a higher mortality-rate because of the inclusion of these late or neglected cases. Reference to table IV appears to confirm this deduction.

In the present series, in relation to the question of misdiagnosis, it is reasonable to speculate whether the history of pyelitis preceding the acute phase of symptoms in cases 4 and 5 might not have been confused with that of subacute non-obstructive appendicitis. In fact I consider that many cases of appendicitis in pregnancy may be treated (sometimes successfully) as pyelitis with sulpha drugs and antibiotics, especially in the later months; and I believe that a reasonable suspicion of acute appendicitis at any stage of pregnancy should lead to laparotomy without delay. It will be seen that our

TABLE IV—PUBLISHED CASES OF ACUTE APPENDICITIS IN PREGNANCY

Reference	Total no. of cases		Cases in first 6 mos. of pregnancy		Cases in last 3 mos. of pregnancy	
	No. in series	No. of deaths	No. of cases	No. of deaths	No. of cases	No. of deaths
Child and Douglas (1944)	25	2	21	0	4	2
Cogswell (1937)	18	1	9	0	9	1
*Krieg (1949)	51	3	42	1	9	1
Meiling (1947)	25	2	21	1	4	1
†Priddle and Hesseltine (1951)	28	1
Priest (1936)	6	0	5	0	1	0
†Smith and Bartlett (1940)	20	3
†Twyman et al. (1940)	28	0
Warfield (1950)	5	0	3	0	2	0
Total	206	12 (5.8%)	101 (2.0%)	29 (20.7%)	29	6

* 1 fatal case is omitted from the series because the period of gestation at death is unknown.

† No further analysis possible, because the period of gestation is not stated.

own practice has fallen short of this precept (cases 2, 3, and 5), yet a delay of more than four hours has seldom given any valuable information, and in retrospect I feel that further hesitation was unjustifiable in these cases (except perhaps in the very early admission, case 2).

At laparotomy, if appendicitis is confirmed, appendicectomy should be done without further interference. Though this opinion is now held by most workers, some (Meiling 1947, Potter and Sadugor 1949, Renn et al. 1951) have reported cases in the last trimester in which

TABLE III—TREATMENT

Case no.	Operation			Result			
	Time after onset of symptoms	Condition of appendix	Drain	Onset of labour after operation	Ileus	Mother	Child
1	18 hr.	Acutely inflamed	Nil	24 hr. 4 days	Nil Nil	Recovered	Alive and well
2	20 hr.	Acutely inflamed	Nil	13 days	+from 2 to 7 days after operation	Recovered	Stillborn
3	30 hr.	Acutely inflamed	Nil			Recovered	Alive and well
4	100 hr.	Acutely inflamed	Stab rubber tube in loin	32 hr.	+from 2 to 7 days after operation	Recovered	Born alive, premature; neonatal death
5	48 hr.	Acutely inflamed, probably ruptured at tip	Tube drain in wound	48 hr.	+from 2 to 7 days after operation	Recovered	Alive and well
6	7 days	Necrotic at base, abscess around	Stab drain in loin	..	++	Died	Stillborn

appendicectomy was successfully combined with caesarean section. I suspect that the danger of peritonitis spreading after appendicectomy, owing to the presence of a contractile uterus, is a theoretical risk not borne out in practice today, and it certainly does not warrant routine opening of the uterus in the presence of known peritoneal sepsis. Where labour is imminent or in progress at the time of appendicectomy, and where an absolute barrier to vaginal delivery exists, the combined procedure will be necessary; it is in such cases that Kerr and Moir (1949) suggest that appendicectomy might be combined with caesarean section followed by total hysterectomy to provide drainage. In these circumstances, I think, hysterectomy should not be necessary, provided that antibacterial agents are freely available, but experience of such cases must obviously be very limited.

The objection may rightly be made that unnecessary laparotomies will be done as a result of these recommendations. In both the series of cases recorded by Child and Douglas (1944) and Priddle and Hesseltinge (1951) 41 patients were subjected to laparotomy with a diagnosis of acute appendicitis. The diagnosis proved correct in only 25 and 28 cases respectively, but other conditions warranting laparotomy (ectopic pregnancy, twisted ovarian cyst, &c.) were found, and in only 5 cases in each series (of pyelitis or gastro-enteritis) was the laparotomy a mistake. In the four years during which the 6 cases reported here were treated at the Birmingham Maternity Hospital, 1 laparotomy was done in a case of pyelitis because appendicitis was suspected. It is admitted that, if appendicitis is to be treated early, as it must be in pregnancy, an occasional laparotomy will be done in error, but this seems a small price to pay for a handsome reward.

In assessing the results of the treatment of appendicitis in pregnancy today it is difficult to arrive at a figure representative of an over-all mortality. Meiling (1947) cites a maternal mortality-rate of 0·71% when disease is limited to the appendix, rising to 30% when peritonitis develops, and 50% after rupture of the appendix, and it is said that the rate is about 25% during the last trimester. These figures are probably dated, and in an effort to make an estimate in keeping with modern conditions table IV was compiled from series of 5 or more cases published in America in the last twenty years. Cases of true acute appendicitis only are included, and I believe that there is no overlapping between the series. Although no statistical reliance should be placed on figures from these obviously selected cases, an over-all mortality-rate of 5% may not be unfair for present-day conditions, and I submit that a mortality-rate for the last trimester ten times as high as that in the first six months proves conclusively the danger of the condition reported here.

Summary

6 cases of acute appendicitis complicating late pregnancy are described. 1 mother and 3 babies were lost.

The criteria of diagnosis are discussed with the object of minimising the delay in doing a laparotomy; in late pregnancy abdominal pain and vomiting with poorly localised right-sided tenderness and low-grade pyrexia means appendicitis until proved otherwise.

Appendicectomy without interference with the pregnancy through a high McBurney incision is advocated.

Labour tends to follow soon after operation, but no ill effects of this have been observed.

The mortality of appendicitis in late pregnancy is believed to be ten times as great as that in the early months, and possible reasons for this are discussed.

I wish to thank members of the consultant staff of the Birmingham Maternity Hospital for permission to publish case-records; especially Prof. H. C. McLaren, under whose care cases 2 and 5 (whom I treated) were admitted, and

Mr. A. L. Deacon, F.R.C.S.E., who operated on cases 3 and 4 and gave me much valuable advice in the preparation of this paper.

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PROTECTIVE ANTIGEN OF HÆMOPHILUS PERTUSSIS

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In a preliminary report (Pillemer 1950) it was shown that an antigen (P.A.) could be extracted from *Hæmophilus pertussis* by sonic disintegration, and that it combined irreversibly under special conditions with human red-cell stromata. The stromata-protective antigen complex (S.P.A.) was shown to be a highly protective agent, judged by its ability to protect mice against intracerebral infection with *H. pertussis*, to be free from pertussis toxin, and to represent only a minute proportion of the organism.

We describe here investigations of the factors which influence the liberation of P.A. from *H. pertussis*, and of the conditions required for the interaction of P.A. with stromata. As a result of these investigations a method was devised for the large-scale preparation of S.P.A. for use in clinical trials.

Materials and Methods

H. pertussis Suspensions

A strain of *H. pertussis* designated 134 was used. The strain had been maintained in the vacuum-dried state. Other strains have also proved satisfactory, but most of the present work was done with no. 134, which proved amenable to sonic disintegration and produced little or no haemagglutinin. Moreover, whole bacterial vaccines prepared from strain 134 protected mice against experimental intracerebral infection with *H. pertussis*.

In preparing suspensions for sonic treatment the following procedure was adopted:

The strain was cultured at 34°–36°C on Bordet-Gengou medium containing 30% sheep blood, and the 24–48 hr. growth was inoculated into flasks of modified Cohen and Wheeler (1946) medium made with a specially prepared human peptone (supplied by Lederle Laboratories). The flasks were incubated at 34°–36°C for about 40 hr. with gentle agitation, during which time the total bacterial count increased from

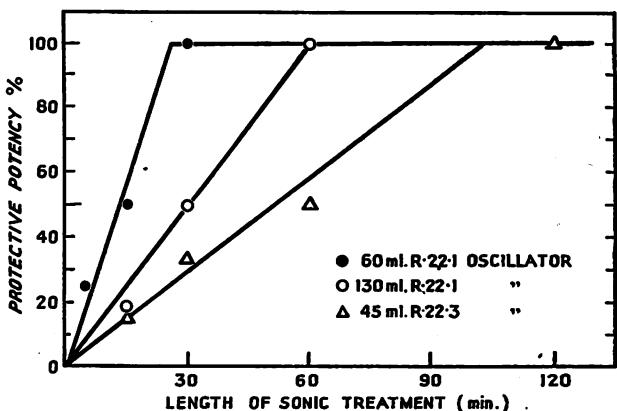


Fig. 1.—Protective potency of S.P.A. prepared from 500×10^9 organisms per ml. subjected to sonic treatment for different lengths of time. In figs. 1-5 the protective potency is given as a percentage of the potency of the parent bacterial suspension.

about 1×10^9 per ml. to about 50×10^9 organisms per ml. (U.S. National Institutes of Health opacity standard). The bacteria were separated from the culture and washed with distilled water at 1°C and then stored at $2^\circ\text{--}5^\circ\text{C}$ for no longer than 24 hr. before resuspension and sonic disintegration. The deposit was suspended in distilled water to give a concentration of about 500×10^9 organisms per ml. Throughout these operations sterile precautions were observed, since it was impossible to sterilise S.P.A. by filtration.

Stromata

Group-O Rh-negative erythrocytes were washed four times with 5 volumes of 0.15 M sodium chloride at 1°C and then lysed by adding 10 volumes of cold distilled water to 1 volume of packed cells, adjusting the pH value of the mixture to 5.2-5.4 with acetic acid, and allowing it to stand overnight at 1°C . The stromata were then centrifuged at 1°C for 1 hr. at 4000 r.p.m. and washed three times with 20 volumes of cold distilled water. A 50% suspension was prepared from the deposited stromata by suspending them in water to twice the volume which the washed packed cells originally occupied. This suspension was autoclaved at 15 lb. for 30 min.

Sonic Oscillators

Two types of sonic oscillator, manufactured by the Raytheon Manufacturing Company, Waltham, Massachusetts, U.S.A., were used: type R-22-1 (10 kilocycles, 200 watts) and type R-22-3 (9 kilocycles, 60 watts). The former type proved the more successful since it could deal with larger volumes and was more efficient in liberating P.A. The vibrator-cup assembly was autoclaved at 15 lb. for 30 min. and then filled with the bacterial suspension, which was maintained at 1°C during sonic treatment.

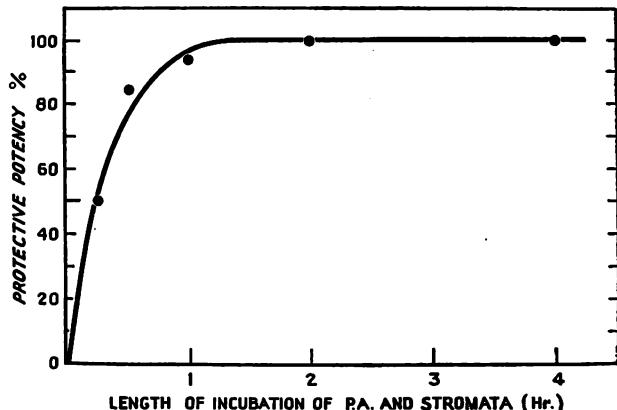


Fig. 2.—Protective potency of S.P.A. prepared by interaction of P.A. and stromata for different lengths of time; other conditions constant.

Assessment of Protective Potency

The protective potency of the various preparations was tested by immunising mice and determining the level of immunity by intracerebral challenge of virulent *H. pertussis* (Kendrick et al. 1947). All the preparations were diluted before testing so that they contained the equivalent of 10×10^9 organisms per ml. It was thus possible to compare their protective action directly with that of the parent bacterial suspension made up to a concentration of 10×10^9 organisms per ml. and to express their potency as a percentage of the potency of the bacterial suspension (figs. 1-5).

In assessing the potency of S.P.A. prepared for clinical trials at least three tests were made on samples from each batch by the method suggested by the United States National Institutes of Health (1952) using their reference pertussis vaccine.

Experimental

PREPARATION OF SONIC EXTRACTS

It was found that the amount of P.A. liberated from the organisms depended on the volume of the suspension, the type of oscillator, the temperature, and the time of sonic treatment. Optimal conditions were obtained with Raytheon oscillator type R-22-1, when 60 ml. of an aqueous bacterial suspension containing 500×10^9

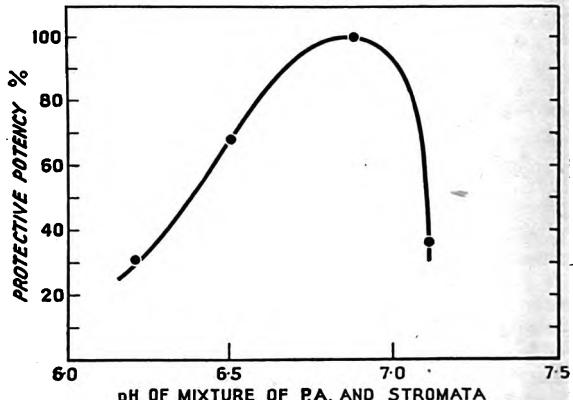


Fig. 3.—Protective potency of S.P.A. prepared by interaction of P.A. and stromata at different pH values; other conditions constant.

organisms per ml. was subjected to sonic disintegration at 1°C for 30 min., or 130 ml. for 2 hr. The Raytheon type R-22-3 was not so effective (fig. 1). These optimal conditions for the production of P.A. relate entirely to strain 134; if other strains are used, the optimal conditions may be different.

After sonic treatment 1 part of Eagle's solution (sodium chloride 17.0 g., potassium dihydrogen phosphate 1.36 g., sodium hydroxide 0.35 g., distilled water 100 ml.; pH 7.35 ± 0.05) was added to 19 parts of the disintegrated suspension maintained at 1°C , giving an ionic strength of 0.15 and a pH value of 7.05 ± 0.05 . The suspension was left at 1°C for 12-24 hr., and the insoluble residue was removed by centrifugation at 1°C for 2 hr. at 4000 r.p.m. The precise control of pH at this stage was important because a reduction of the pH value below 6.8 led to the precipitation of P.A. with the insoluble residue.

INTERACTION OF P.A. WITH STROMATA

Experiments were made to determine the ideal conditions for the combination of P.A. with stromata. Clarified sonic extract was mixed with 50% autoclaved stromata in different proportions at different ionic concentrations, pH values, and periods of incubation of the mixture. Incubation was at 37°C because experiments showed that at this temperature the combination of P.A. and stromata was complete in about 1 hr. (fig. 2). After incubation the mixtures were centrifuged at 4000 r.p.m.

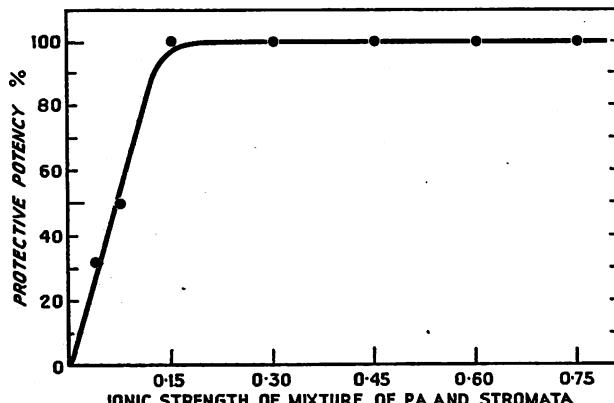


Fig. 4—Protective potency of S.P.A. prepared by interaction of P.A. and stromata at different ionic strengths; other conditions constant.

at 1°C for 1-2 hr. The supernatant fluids were discarded, and the residues were suspended uniformly to the desired concentration in glycine-phosphate buffer at pH 7.4 (9 parts of 0.3 M glycine and 1 part of M/15 phosphate buffer) containing 1/10,000 thiomersalate.

The results of some of the experiments are summarised in figs. 3-5, from which the following conclusions were drawn:

(1) P.A. combined with stromata at pH 6.85 ± 0.05 and slight deviations from this pH produced a less potent preparation of S.P.A. (fig. 3).

(2) P.A. combined with stromata at an ionic strength of 0.15 or more, and ionic strengths less than 0.15 retarded combination (fig. 4).

(3) The most active preparations of S.P.A. were obtained when 30 parts or less of P.A. were added to 1 part of 50% stromata suspension (fig. 5).

LARGE-SCALE PREPARATION OF S.P.A.

As a result of these experiments the following procedure was decided on for the large-scale preparation of S.P.A. We consider that this procedure should be rigidly followed to obtain reproducible results, since slight deviations, which may seem insignificant, cause a decrease in the yield, purity, and antigenic potency of the final product.

(1) The growth of *H. pertussis* in modified Cohen and Wheeler medium was centrifuged at 4000 r.p.m. for 1 hr. at 1°C.

(2) The deposit was washed five times with large volumes of distilled water at 1°C.

(3) The washed bacteria were suspended to 500×10^9 organisms per ml. in distilled water at 1°C.

(4) The suspension in 60 ml. amounts was subjected to disintegration at 1° ± 1°C in the Raytheon type R-22-1 sonic oscillator for 40 min., or in 130 ml. amounts for 2 hr.

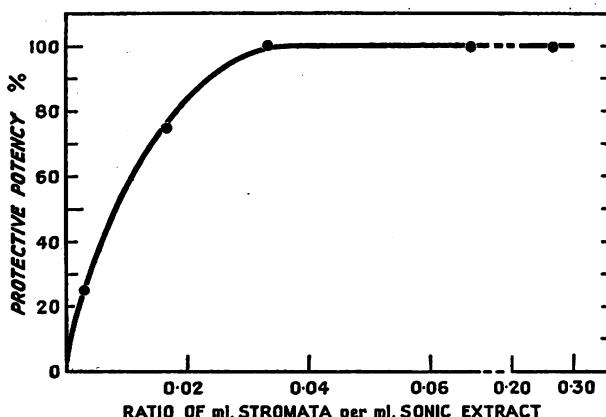


Fig. 5—Protective potency of S.P.A. prepared by interaction of different proportions of stromata and extract; other conditions constant.

(5) To 19 parts of sonic disintegrated suspension 1 part of Eagle's buffer solution was added, and the final pH was adjusted, if necessary, to 7.05 ± 0.05.

(6) The buffered disintegrated suspension was allowed to stand overnight at 1°C and then centrifuged at 1°C for 2 hr. at 4000 r.p.m. The deposit was discarded.

(7) To 30 parts of clear extract at pH 6.85 ± 0.05, 1 part of 50% autoclaved stromata suspension was added, and the mixture was incubated in a water-bath at 37°C for 2 hr.

(8) The stromata-extract mixture was centrifuged at 1°C for 2 hr. at 4000 r.p.m. The supernatant fluid was discarded.

(9) The deposited S.P.A. was suspended in glycine-phosphate buffer at pH 7.4 containing 1/10,000 thiomersalate.

(10) The suspended S.P.A. in 100 ml. amounts was subjected to sonic vibration at 1° ± 1°C in the Raytheon type R-22-1 sonic oscillator for 30 min. to produce a homogeneous suspension.

PROPERTIES OF LARGE-SCALE PREPARATIONS OF S.P.A.

This procedure yielded stable and sterile preparations of S.P.A. which protected mice against intracerebral infection with *H. pertussis*. Typical protocols are given in the accompanying table of tests made on two different

COMPARISON OF PROTECTIVE ACTION OF 2 BATCHES OF S.P.A. WITH U.S. NATIONAL INSTITUTE OF HEALTH REFERENCE VACCINE N.I.H.4

Preparation	Dose inoculated (ml.)	Proportion of mice surviving after challenge
S.P.A. (batch 51200-35)*	1/21	54/63
	1/105	29/64
	1/525	15/64
N.I.H.4	1/6.7	41/63
	1/33.5	19/62
	1/167.5	6/64
S.P.A. (batch 7-1175-11)*	1/21	28/32
	1/105	18/32
	1/525	5/32
N.I.H.4	1/6.7	24/32
	1/33.5	8/32
	1/167.5	5/32

* Equivalent to 100×10^9 organisms per ml.

batches of S.P.A. in comparison with the National Institutes of Health reference vaccine. These batches were made up equivalent to 100×10^9 organisms per ml., and the results indicated that each batch was from four to six times as potent as the reference vaccine.

Tests made with S.P.A. heated at 56°C for 1 hr. indicated that such treatment did not reduce the protective potency. Other experiments showed that S.P.A. remained stable for fifteen months at 1°C and for six months at 37°C, although it was readily inactivated at 100°C.

S.P.A. was shown to be non-toxic. The intravenous injection of 1 ml. of S.P.A. made up equivalent to 250×10^9 bacteria was tolerated by mice and by guinea-pigs, and 5 ml. by rabbits, without showing any harmful effects.

No attempts were made to characterise S.P.A. completely. Electrophoretic analyses of extracts before and after addition of stromata showed no alteration in the distribution or mobilities of the electrophoretic components, and no difference was detected in the nitrogen content of extracts before and after addition of stromata. These observations indicate that P.A. represented only a minute proportion of the organism, probably less than 1% of the nitrogenous material in the extract.

Discussion

Although the nature of P.A. is not yet known, certain information about its properties is evident. It appears to be firmly associated with the bacterial cell and not loosely attached to the cell surface. Bacteria which were washed many times before they were subjected to sonic disintegration yielded high concentrations of P.A. The

extraction of P.A. from the cell by sonic disintegration and separation from the extract by stromata was largely quantitative; for under optimal conditions the protective potency of S.P.A. was very similar to that of the parent bacterial suspension. P.A. is probably not associated with pertussis haemagglutinin (Keogh and North 1948), since this latter antigen does not protect mice against intracerebral infection (Masry 1952). Moreover the strain used produced only small amounts of haemagglutinin, and this antigen has not been detected in preparations of S.P.A. It is also evident that P.A. is not associated with pertussis toxin (Evans and Maitland 1937); preparations of S.P.A. were unable to kill mice on intravenous injection or to produce dermonecrosis in rabbits. Finally, P.A. is not associated with pertussis agglutinogen. D. G. Evans and F. T. Perkins (private communication) have recently shown that S.P.A., tested by the agglutinin-production method (Evans and Perkins 1953), produced little or no agglutinin in mice. Although there is little or no evidence of an association between P.A. and the other known antigens of *H. pertussis*, there is some evidence that P.A. may be concerned with the ability of the organism to sensitise mice to histamine. Margaret Pittman (private communication) has recently shown that S.P.A. produced in mice a sensitisation to histamine similar to that produced by whole bacterial vaccines. This is interesting because the power to render tissues sensitive to histamine and the protective potency of bacterial vaccines have been shown to be very closely correlated (Pittman 1951).

The question of the efficacy of S.P.A. as a prophylactic against whooping-cough can only be answered by controlled trials, which are now in progress. If such trials prove that S.P.A. is effective, a more extensive investigation of the nature of the antigen is undoubtedly justified.

Summary

An investigation was made of the factors which influence the liberation of a protective antigen (P.A.) from *H. pertussis*, and of the conditions required for the formation of a stromata-protective antigen complex (S.P.A.).

A method is outlined for the large-scale production of S.P.A. The method involves the extraction of P.A. from *H. pertussis* by sonic disintegration and the removal of P.A. from the extract by the addition, in suitable proportions, of autoclaved stromata under controlled conditions of temperature, pH, and ionic strength.

Preparations of S.P.A. prepared for clinical trials have been tested in comparison with the U.S. National Institutes of Health reference pertussis vaccine and shown to be effective in protecting mice against intracerebral infection with *H. pertussis*.

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CHRONIC SUBDURAL HAEMATOMA MENTAL CHANGE AS THE PRINCIPAL CLINICAL FEATURE

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It is well known that mental changes are often produced by a subdural haematoma, but when such changes occur in the absence of a history of trauma to the head, and when there are no abnormal neurological signs initially, the diagnosis of subdural haematoma is difficult.

Case-report

A publican, aged 59, was admitted to Hammersmith Hospital on Aug. 7, 1952, under the care of Dr. Purdon Martin. In the past he had suffered many minor ailments and had attended the hospital on several occasions for numerous vague symptoms. During the first world war, 34 years before admission, he had "shell shock" and as a result spent a year in hospital. During this time he complained of incessant headaches but made a satisfactory recovery. No further details of this illness could be obtained. Since then he had occasionally experienced headaches that were neither persistent nor severe. His wife said that, apart from being abnormally preoccupied with the state of his health, there had been no mental change in the past. He did not usually drink heavily, but recently he had been drinking more than usual. The family history contained no relevant information. Five weeks before admission he began to have headaches, and at first thought these were the same as he had experienced previously. A bifrontal ache with a sensation of pressure on the vertex was constantly present, occasionally disturbing sleep. Stooping sometimes aggravated it, but there was no nausea, vomiting, vertigo, or visual disturbance. A change of glasses gave no relief, and analgesics eased the pain only temporarily.

On examination his general condition was good, and despite his pale skin the blood picture was normal. He lay in bed with his eyes closed and gently rocked his head from side to side, giving an impression of intense suffering. He gained a great deal of sympathy from his fellow patients and he obviously enjoyed and sought this. He was alert and able to give an adequate history as well as co-operate in all the tests used. There was no defect of intellect or of memory, and his personality was unimpaired. The central nervous system was entirely normal. The blood-pressure was 140/90 mm. Hg, and his cardiovascular and other systems showed no abnormalities.

Investigations.—Radiographs of the skull and of the chest were normal. Cerebrospinal fluid (c.s.f.) under a pressure of 100 mm. of water contained 2 lymphocytes per c.mm., and protein 30 mg per 100 ml. The Lange reaction was normal, and the Wassermann reaction was negative. The Wassermann reaction of the blood was also negative.

Progress.—In view of the complete lack of abnormal physical signs, the normal results of the investigations, and the patient's previous history, it was thought that his state was not due to an organic lesion of the nervous system. His wife was not unduly surprised at this conclusion, feeling that his present illness was "all in his mind" and probably related to recent business difficulties. He was therefore encouraged to get up, and for a few days the headaches seemed to subside. This, however, was only temporary, and soon he could not be coaxed from his bed. It was now evident that his mental state was changing. He became drowsy but could always readily be roused to co-operate fully. At times he was confused and disoriented. He talked incoherently and in a rambling fashion, with a tendency to perseverate. He exhibited amnesia and mild euphoria, at times displaying a childlike and fatuousness hitherto foreign to him. He would make bizarre facial grimaces and often muttered to himself. The headache was still present but did not seem to have become worse. At this time, and throughout the nineteen days that had elapsed since his admission, no abnormal signs were

detected in the central nervous system, despite careful and regular observation. A psychiatric opinion was then sought, and it was considered that he presented an organic syndrome characteristic of progressive cerebral deterioration. The diagnosis seemed to lie between a type of presenile dementia and chronic alcoholic deterioration. Admission to an observation ward was advised, and arrangements for this were being made when, on Aug. 29, 1952 (three weeks after admission), the patient suddenly developed an acute pulmonary infection. Three days later, while his chest condition was responding to treatment, his mental state had deteriorated further. He had periods of great restlessness, and satisfactory contact with him was impossible. He still complained of headache, but his speech was mostly incoherent and often incomprehensible. At times he was very drowsy but he could always be aroused without difficulty and he was never comatose nor incontinent. The c.s.f. pressure was so low that it could not be recorded; it was normal in content. Four days later, on Sept. 5 (thirty days after admission), abnormal neurological signs were detected for the first time. There was definite falling away of the right arm when both were outstretched, the reflexes were slightly increased on the right side, and both plantar reflexes were weakly extensor. Since he might have had a frontal neoplasm or possibly a subdural haematoma, he was transferred to a neurosurgical unit (Mr. Geoffrey Knight) where, on the same day, 30 ml. of old blood was evacuated from the subdural space on each side. It was thought that it had probably been present less than six months. He made a very rapid and gratifying recovery: a week after the operation he was free from all headache, bright and alert, and no longer confused or disorientated. In fact he was an entirely different person; instead of being dull and complaining he was now likeable and jovial. He now said that during his work he frequently had to pass beneath a low-beamed door and often knocked his head against the lintel. At no time, however, had he been rendered unconscious, and he did not recall any particularly severe blow before the onset of his headaches. Intellectual testing and assessment of his personality, as well as examination of his nervous system, revealed no abnormalities, and he was discharged on Oct. 13, 1952. When seen a year later, he had returned to his work and had no complaints at all.

Initially there was no history of head injury, and even on direct questioning after operation there was only a vague story of repeated trivial blows, reminiscent of Trotter's (1914) second patient in whom there was the same type of trauma to the head. Many years previously our patient had had a psychiatric illness which included severe headaches, and in the ensuing years had experienced many illnesses, some of which were without an organic basis. He was known to be anxious and hypochondriacal, and when headaches returned as the first manifestation of the subdural haematoma it was thought that they were functional. Despite repeated and careful examination no clinical abnormalities were found in the central nervous system, and the appropriate special investigations gave normal results. Only late in the illness did signs of focal cerebral involvement develop, and at no time was there any indication of increased intracranial pressure. After the subdural clots had been removed, the patient recovered completely.

Discussion

All writers agree that mental disturbances are among the most common manifestation of chronic subdural haematomas, yet this fact is rarely mentioned in textbooks on psychiatry. Admittedly, in most cases the symptoms and signs are sufficient to warrant a tentative diagnosis, but rarely is the clinical picture mainly psychiatric.

INCIDENCE OF MENTAL CHANGES

The incidence of mental changes has been assessed very differently by different writers, the more reliable figures being 21.2% of 48 cases (Kunkel and Dandy 1939), 75% of 50 cases (Krayenbühl and Noto 1949), 86% of 44 cases (Jelsma 1930), and in all of 50 cases (Wortis et al. 1945). Trotter (1914) emphasised the mental changes and believed that they occurred in many, if not all, cases of subdural haematoma. This notion was corroborated by Coleman (1935), who said that, in cases of

subdural clot, changes in mental state are found "perhaps oftener than in any space-occupying lesion of the brain."

The figures given by different authors depend partly on their conception of the term "mental changes" and partly on the thoroughness with which they are sought. Wortis et al. (1945) examined their cases very carefully and found mental changes in all of them. On the other hand, although we agree with Abbott et al. (1943) that psychiatric estimation is important in all cases of chronic subdural haematoma it is, in our view, by no means the major aspect of the clinical problem, as these workers would have us believe.

It is well known that there is a high incidence of subdural haematoma among inmates of mental institutions coming to necropsy. Allen et al. (1940) found 245 (7.9%) in 3100 consecutive necropsies on psychotics, exactly the percentage recorded by Lewis (1889). In only 35 of the cases of Allen et al. (1940), however, was the subdural haematoma the primary cause of death, and it was impossible to say in how many patients the psychosis was due to the subdural clot. That epileptics and alcoholics have a greater liability to head injuries, and that cerebral changes in arteriosclerosis and neurosyphilis may predispose to subdural haematoma, is admitted by Allen et al., and such conditions are probably all-important in these cases.

Another cause to be considered is the form of therapy used. The schizophrenic reaction in Singh's (1950) patient may have been produced by a subdural haematoma precipitated by electroconvulsive therapy; and Furlow (1939) blames insulin-shock therapy in his case 2. These forms of therapy, however, seem to be less likely causes of subdural haematoma, which has not so far been reported as a complication of these widely used procedures. The reason why only certain patients with subdural haematomas manifest prominent mental changes is explained best by Lewis (1946): any disturbance of the brain, whether it be head injury, anaemia, toxic agents, or focal lesion, if severe enough, will interfere with the mental state and so produce a type of mental reaction typical of an organic lesion. But some people are more loosely integrated in their personality, being "oriented toward psychosis" (Lewis 1946); their past history may readily illustrate this; they break down mentally more readily and much more extensively under stress than the more intact person, and psychiatric features dominate the clinical picture.

TYPES OF MENTAL CHANGES

Wortis et al. (1945) have carefully analysed the mental disturbances in patients with acute or chronic subdural haematomas. They recognised that it was difficult to exclude other coexisting traumatic cerebral lesions that would complicate the clinical picture. However, in a series of 50 cases, they divided the preoperative mental changes into groups which included changes in the state of consciousness and in mood and disturbance of the sensorium and of thinking. They found that in each of their patients there was some mental abnormality. Like other workers, they included disordered states of consciousness which are present in all cases at one time or another and should perhaps be considered separately. The high incidence (86%) of mental changes in Jelsma's (1930) collected series, for example, is probably explained by the inclusion of drowsiness and the various stages of coma.

The commonest psychological findings of Wortis et al. (1945) were progressive confusion and disorientation (present in two-thirds of cases), emotional dullness, irritability, and uncooperativeness (in a quarter of cases), and a general reduction in mentation. de Morsier (1937) mentioned a similar rather non-specific constellation of mental changes, which are often included in the term "dementia." Depression, euphoria, delirium, hallucina-

CASES OF CHRONIC SUBDURAL HÆMATOMA WITH MENTAL CHANGE AS PRINCIPAL CLINICAL FEATURE

Reference	Sex	Age (yr.)	Presenting symptoms	Mental features	Duration to operation or death	Findings at operation	Outcome
Trotter (1914) case 2	M	41	"Strange manner"	Absent-minded; lack of initiative Vague; poor memory; repetitive	?	Left-sided hæmatoma	Complete recovery
Martin (1931) ..	M	52	Headaches		5-6 mos.	..	Death; hæmatoma not described in detail
Furlow (1936) case 8	M	45	Irritability, with suicidal tendencies	Poor memory; disoriented	10 mos.	..	Death; right-sided hæmatoma
Olkon (1938) ..	M	37	Acute confusional state	Paranoia; hallucinations and delusions	11 days (see text)	Dark subdural blood	Complete recovery
Furlow (1939) case 1	M	63	Mental changes	Dementia with sexual aberrations; irritable	3 yr.	Right-sided hæmatoma	Complete recovery
Furlow (1939) case 3	M	48	Headache and vomiting	Hallucinations	4 mos.	Right-sided chronic hæmatoma	Slow but complete recovery
Fleiss (1945) ..	M	56	Manic-depressive psychosis	..	2 mos. (see text)	Left-sided hæmatoma	Several relapses but eventual recovery
Whitfield (1946) case 1	M	32	"Peculiar behaviour"	Transient amnesia	1 7 yr. (see text)	Left frontal hæmatoma	Complete recovery
Clarke and Cooper	M	59	Headache	Confusion; disorientation; mental deterioration	2 mos.	Bilateral hæmatoma	Complete recovery

tions, and delusions, on the other hand, were rare. Confusion tends to be more severe in the older patients; and alterations in personality, particularly in the patient's attitude to his work and family, are important. Wortis et al. (1945) emphasised the diagnostic importance of the steady progression of mental deterioration—an event that was witnessed in the present case. Krayenbühl and Noto (1949) mentioned disorders of affect, lack of initiative and critical judgment, weakness, and apathy as common mental disturbances. Homburger (1905) described a patient with a Korsakoff type of psychosis produced by a subdural hæmatoma, and Kasemeyer's (1911) patient was thought to have a post-traumatic neurosis. Among the 50 cases of Krayenbühl and Noto (1949) there were 2 (cases 4 and 46) displaying features of a frontal-lobe lesion. There were also physical abnormalities present, and the cases reported by Petit-Dutaillis et al. (1953) were similar. The case of Micheels (1953) is the only one in which a catatonic state was a prominent feature.

Thus, just as many neurological syndromes may be produced by a subdural collection of blood, so the psychiatric disorders are likewise variable, within the organic reaction pattern.

MENTAL CHANGES AS PRINCIPAL CLINICAL FEATURE

We are particularly concerned with cases of subdural hæmatoma in which mental disturbances and headache are the sole features of the early stages of the illness, there is no evidence of head injury, and the nervous system is normal.

Trotter (1914) stated: "These mental symptoms may be perceptible even to uneducated observers, when no physical signs of interference with the brain can be detected." Ample confirmation of this statement has been produced by different workers, particularly Wortis et al. (1945), who occasionally found patients in whom the mental abnormalities far outweighed the neurological abnormalities. At least 8 cases similar to ours have been published in which the principal clinical feature at the onset was an abnormal mental state, and the nervous system and special investigations were all normal. These cases are summarised in the accompanying table.

Other cases with predominant mental changes have been recorded, but in all of them a history of trauma was readily elicited or examination revealed neurological abnormalities indicating a focal cerebral lesion (Homburger 1905; Kasemeyer 1911; Furlow 1936, case 10; Linell 1940, cases 4 and 5; Abbott et al. 1943, case 7; Matera et al. 1948, 2 cases; Krayenbühl and Noto 1949, cases 4 and 46). It is important to remember these cases when dealing with postconcussional psychotic or neurotic

states, for if a subdural hæmatoma is left untreated it will almost always prove fatal; but if it is removed the results can be excellent. As mentioned already, however, the picture may be complicated by additional intracranial damage. This may have been so in case 4 of Linell (1940), where operation did not dispel the patient's mental symptoms.

Of the cases in the table mention must be made of 3. The patient of Fleiss (1945) had several manic and depressive episodes that usually coincided with the appearance of a subdural accumulation; but they did not always do so, and one cannot subscribe to Fleiss's suggestion that the clot may at times have been absorbed spontaneously. In Whitfield's (1946) first patient mental changes had been present seven years, but it is doubtful if the subdural clot was of a similar age; although recovery was complete after the removal of the hæmatoma, only further observation will determine the actual rôle of the mental features. The patient described by Singh (1950) presented with a schizophrenic reaction, and a subdural hæmatoma was found at necropsy. It was difficult, however, to correlate these two findings; as mentioned already, the possibility of the clot being a product of electroconvulsive therapy, although unlikely, could not be entirely excluded. Because of the uncertainty this case will not be considered further.

In summarising the clinical picture in the selected group of cases shown in the table, it is seen that all the patients were men. Since subdural hæmatoma occurs more often in males, this finding is of little significance in a small series. The ages varied from 32 to 63, the average being 49; if anything, there was grouping in middle and late adult life. So far as was known initially, there had been no injury to the head, although it transpired later that Trotter's (1914) second patient and ours had repeatedly sustained minor trauma. In case 8 of Furlow (1936) there was no history of head injury, but the patient was a chronic alcoholic, and radiographs and necropsy revealed skull fractures. Similarly, in Whitfield's (1946) patient, radiographs showed a fracture, although there had been no indication of trauma. The mental changes mentioned in the series were of considerable variety, no constant syndrome being observed. They usually began insidiously. In Olkon's (1938) patient the onset seemed to be acute, but it was later revealed that personality changes had preceded the acute exacerbation; the clot was found to be of long standing and therefore must have antedated the presenting confusional state. All the patients had headache, which usually began after the mental changes, and disturbances of consciousness were invariably present. The characteristic waxing and waning of consciousness was not

regularly seen but, if present, is a most helpful sign of subdural haematooma. The length of history varied from a few weeks to three years. Abnormal neurological signs were absent initially but appeared later in all the cases, usually accompanying the increasing drowsiness, as often happens in this condition. Apart from the drowsiness, signs of increased intracranial pressure were rare. Special investigations were of little diagnostic value. The c.s.f. was examined in 6 of the patients, and the pressure was either normal or less than normal in all of them; only 1 patient had xanthochromia, and he and another patient had an increased amount of protein in the c.s.f. Skull radiography was done in 6 cases, and, apart from the 2 patients with fractures mentioned already, they were always normal.

The preoperative diagnoses in these cases were acute psychosis, war neurosis, frontal tumour, cerebral degeneration, presenile dementia, and manic-depressive psychosis. All but 2 patients were operated on, and subdural haematomas of various sizes and in various positions were successfully removed. There seemed to be no correlation between the location and size of the lesion and the clinical picture, but full details of the clot were rarely available. Of the 9 cases in which mental change was the principal feature the haematoma was bilateral in the present case only.

Although the follow-up on most of these cases was limited and the end-results are thus unknown, the immediate postoperative recovery, both mental and physical, was rapid and usually complete. This fact emphasises the importance of being aware of this small group of cases. In any patient with severe headache who manifests progressive non-specific mental changes accompanied by increasing drowsiness, which may or may not fluctuate, a subdural haematoma should be considered, even in the absence of known trauma, increased intracranial tension, and abnormal neurological signs. If the drowsiness leads to coma, and abnormalities of the central nervous system appear, special diagnostic procedures and the help of a neurosurgeon are called for immediately.

Summary

A case of chronic subdural haematoma is described in which the major clinical feature was mental change without any history of head injury. The central nervous system appeared to be normal, as were skull radiographs and the c.s.f. Removal of the clot led to complete recovery.

The mental changes observed with subdural haematoma are described, and previously published cases are discussed.

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HEPATIC COMA *

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A NEUROLOGICAL syndrome termed "episodic stupor" has been observed in patients who have undergone portacaval anastomosis. This syndrome has been shown to be caused by ammonia intoxication (McDermott and Adams 1954). The similarity of "episodic stupor" to hepatic coma is striking, since the neurological disturbances are similar to, and the electroencephalographic changes identical with, those observed in patients with liver disease who are in a state of stupor or coma (Adams and Foley 1949, Foley et al. 1950).

Because of this similarity between episodic stupor resulting from a portacaval anastomosis and the syndrome of hepatic coma, we have investigated the ammonia metabolism of patients with liver disease. Other investigators have reported changes of the blood-ammonia level in liver disease (Burchi 1927, Caulaert et al. 1932, Fuld 1933, Kirk 1936, Gaustad 1949), but the results of their studies have been inconclusive and have not established ammonia as an aetiological factor in hepatic coma.

A syndrome indistinguishable from hepatic coma has been reported to follow the administration of an ammonium-containing cation-exchange resin to patients with cirrhosis of the liver (Gabuzda et al. 1952). Later Phillips et al. (1952) reported their findings in a group

of 9 alcoholics with advanced cirrhosis who were given various nitrogenous substances. Five substances were given by mouth: ammonium chloride, diammonium citrate, an ammonium-potassium exchange resin, urea, and a high-protein diet. A condition resembling the onset of hepatic coma occurred in 5 of the 9 patients studied. The blood-ammonia levels were estimated, but the correlation between the blood-ammonia level and the abnormal signs was not consistent enough to establish a direct relationship.

Walshe (1951, 1953) suggests that hepatic coma may be due to an intracellular disturbance of ammonia metabolism, and that in hepatic coma the normal ammonia-binding mechanism of the brain-cell, the combination of glutamic acid with ammonia to form glutamine (Weil-Malherbe 1950), is disturbed. This theory is supported by the observation that glutamic-acid therapy led to the recovery of 3 patients who between them had five episodes of hepatic coma (Walshe 1953).

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In our investigation the peripheral blood-ammonia levels were determined in patients with hepatic coma, and the effect of glutamic acid on both clinical symptoms and blood-ammonia levels was studied.

Methods

The patients were under observation in the wards of the Massachusetts General Hospital. They were seen daily, often more frequently, when their neurological status was assessed and their peripheral blood-ammonia levels were determined. None of the patients had undergone portacaval anastomosis.

To correlate the mental state and the biochemical findings, the degrees of alertness and reactivity were graded on a scale from 0 to 4. Normal mental function was recorded as 0, coma as 4, the slightest alteration of mental function as 1, severe mental confusion or disorientation as 2, and stupor and semicomma as 3.

The electro-encephalographic changes were graded from 0 to 3, zero meaning normal. This scheme of reporting the neurological and electro-encephalographic changes has already been published in detail (McDermott and Adams 1954).

Blood-ammonia levels were determined by a modification (McDermott and Adams 1954) of the Conway (1950) microdiffusion technique which shows the ammonia level in the peripheral venous blood of normal people to be 55.6 (44.0-71.0) µg. of ammonia nitrogen per 100 ml. There is evidence that abnormally high levels of ammonia nitrogen in the blood reflect changes in the actual free ammonia level in the blood (McDermott and Riddell 1954).

The sodium glutamate for intravenous use was prepared by the method of Mayer-Gross and Walker (1949) and given in doses of 25 g. A few patients were treated with intravenous sodium succinate in doses of 10 g.

Results

The results of studies made on 29 patients with hepatic coma or pre-coma are summarised in the accompanying table. Patients with hepatic coma have a high blood-ammonia level related to the severity of their symptoms. The pattern of the blood-ammonia levels varies, but two predominant types are illustrated by the following case-histories:

Case 1.—A chronic alcoholic woman, aged 47, vomited a pint of blood on the eve of admission to hospital. Next

SUMMARY OF STUDIES ON PATIENTS WITH HEPATIC COMA

Case no.	Age (yr.)	Sex	Diagnosis	Days under observation, and outcome	Neurological state	Blood-ammonia levels (µg. per 100 ml.)	Comments
1	47	F	Alcoholic cirrhosis; bleeding oesophageal varices	3 Died	Within 12 hr. of onset progressed to deep coma with convulsions	518-115	Treatment with intravenous sodium glutamate was followed by fall of blood-ammonia level, but patient did not improve
2	39	M	Alcoholic cirrhosis	8 Died	Admitted in gross confusion, progressed to coma and death	463-189-235	Died in hepatic coma after temporary fall in blood-ammonia level accompanied by transient clinical improvement
3	62	M	Alcoholic cirrhosis; bleeding oesophageal varices	1 Died	Drowsy and confused	451	Died of massive hemorrhage within 12 hr. of onset
4	52	M	Alcoholic cirrhosis; bleeding oesophageal varices	48 Recovery	Admitted in coma precipitated by haemorrhage	412-53	Treatment with intravenous sodium succinate was followed by recovery for four days, but patient died of postoperative sepsis
5	49	M	Alcoholic cirrhosis; pulmonary tuberculosis	9 Died	Increasing drowsiness progressing to coma and death	76-408	Died of hepatic coma with rising blood-ammonia level
6	71	M	Alcoholic cirrhosis	18 Died	Recurrent attacks of stupor; improved temporarily and later died in coma	146-396	Terminal episode despite restriction of protein
7	49	M	Alcoholic cirrhosis	32 Recovery	Recurrent attacks of drowsiness and confusion with development of flapping tremor	393-142	Attacks related to high-protein intake associated with rise in blood-ammonia level
8	42	M	Alcoholic cirrhosis; bleeding oesophageal varices	16 Recovery	Admitted in coma which had lasted 12 hr.	385-94	Blood-ammonia level fell off rapidly
9	24	F	Acute virus hepatitis	4 Died	Stuporous when first seen, progressive deterioration	232-383	Treated with intravenous sodium glutamate
10	54	F	Hæmochromatosis	11 Died	Became progressively worse during study and died in coma	92-380	Progressive deterioration with rising blood-ammonia level despite sodium glutamate and succinate
11	55	M	Alcoholic cirrhosis	6 Died	In deep coma throughout study	272-374	Coma probably induced by high-protein diet
12	38	F	Alcoholic cirrhosis	3 Died	Admitted in deep coma and continued in this state until death	300-355	On one day treatment with sodium glutamate 25 g. was followed by fall of blood-ammonia level to 155 µg. per 100 ml. without clinical improvement
13	41	M	Alcoholic cirrhosis; bleeding oesophageal varices	95 (2 admissions) Died	Normal except for one episode of semicomma lasting 3 days	(1) 75-106 (2) 219-59-343-76-275-122	219 at onset semicomma, 343 no symptoms; probably related to high-protein diet; died from postoperative sepsis
14	62	F	Portal cirrhosis	15 Died	Progressive deterioration ending in coma and death	51-333	On high-protein diet
15	47	M	Alcoholic cirrhosis; bleeding oesophageal varices	8 Died	Varied between semicomma and deep coma during study	147-312	Progressive deterioration with rising blood-ammonia level

morning, Oct. 25, 1953, her husband noticed that she was drowsy and arranged for her admission. During the next six hours she became increasingly worse until she was maniacal and finally lapsed into deep coma.

On admission in the maniacal stage her blood-ammonia level was 518 µg. of ammonia nitrogen per 100 ml. She was treated with intravenous dextrose, aureomycin, and sodium glutamate but in spite of this therapy remained in deep coma until death (fig. 1), although her blood-ammonia level fell to a relatively low figure—115 µg. of ammonia nitrogen per 100 ml.

Comment.—There are several interesting features in this case. If the patient's blood-ammonia level had not been determined before the second day, no relationship between her neurological condition and blood-ammonia level would have been apparent. This pattern of blood-ammonia levels has been observed also in cases 4, 7, 8, 21, and 24, who all recovered from their coma, but none had such a high initial blood-ammonia level.

Case 1 appears to have had a syndrome comparable to that seen in dogs and humans with Eck fistulae, where it has been shown that a rise of blood-ammonia level induces symptoms which persist after the blood-ammonia level has fallen to nearly normal (McDermott and Adams 1954, Riddell et al. 1954).

Case 5.—A chronic alcoholic man, aged 49, was admitted to hospital on Sept. 23, 1953, with two months' history of abdominal swelling. A year earlier he had been treated in another hospital for portal cirrhosis with ascites.

On examination he was wasted and jaundiced; his abdomen was grossly distended with fluid, his liver was enlarged, and he had severe bilateral pulmonary tuberculosis, with tubercle bacilli in his sputum. Liver-function tests on Sept. 24 showed total serum-protein 5.3 g. per 100 ml. (albumin 1.1 g. per 100 ml.); and total serum-bilirubin 3.3 mg. per 100 ml. There was no neurological abnormality on admission, but on Oct. 2 the patient became drowsy. His condition became progressively worse, and on Oct. 7 he went into deep coma and remained in this state until he died on Oct. 10 (fig. 2).

Comment.—The pattern of a progressive rise in blood-ammonia level (fig. 2) is that seen in patients with terminal hepatic failure (see table). The blood-ammonia level rose from an initial reading of 76 µg. of ammonia nitrogen per 100 ml. on Oct. 2 to 408 µg. per 100 ml. on Oct. 7, then fell on Oct. 8, but rose again next day, and on the day of his death (Oct. 10) was 313 µg. per 100 ml. The administration of relatively large amounts of protein may have contributed to his death. The rise in the blood-ammonia level followed an oral intake of

SUMMARY OF STUDIES ON PATIENTS WITH HEPATIC COMA—continued

Case no.	Age (yr.)	Sex	Diagnosis	Days under observation, and outcome	Neurological state	Blood-ammonia levels (µg. per 100 ml.)	Comments
16	26	M	Cirrhosis with ulcerative colitis	9 Died	Drowsy on admission, died in coma	103-311	Temporary improvement on intravenous sodium glutamate, with fall in blood-ammonia level
17	66	M	Alcoholic cirrhosis	9 Died	Drowsy, confused about place and time	131-300	Precipitated by ammonium chloride; temporary lowering of blood-ammonia level to 73 µg. per 100 ml. after treatment with intravenous sodium glutamate, with improvement; died of coronary thrombosis
18	44	M	Cirrhosis; haemochromatosis; bleeding oesophageal varices	40 Recovery	Became comatosed after haemorrhage; recovered rapidly	88-291-146	Highest blood-ammonia level preceding coma 203 µg. per 100 ml.; died of recurrent haemorrhage from varices
19	43	F	Alcoholic cirrhosis	22 Recovery	Drowsy and confused with flapping tremor	290-134	Recovery with fall in blood-ammonia level after therapy with intravenous sodium glutamate
20	43	M	Alcoholic cirrhosis; bleeding oesophageal varices	5 Died	Increasing drowsiness progressing to semicomma	138-285	Died from haemorrhage on fifth day
21	65	F	Alcoholic cirrhosis	3 Died	In semicomma, responding to painful stimuli only	253-131	Coma precipitated by course of ammonium chloride; given intravenous sodium glutamate on admission; this was followed by improvement with fall in blood-ammonia level; patient died suddenly of brain-stem hemorrhage; no necropsy
22	52	F	Postnecrotic scarring; bleeding oesophageal varices	11 Recovery	First seen in deep coma; recovery	252-82	Treated with intravenous sodium glutamate and succinate; recovered from coma; died later from post-operative pulmonary oedema
23	67	M	Portal cirrhosis; bleeding oesophageal varices; polycythaemia vera	2 Died	Two days before study patient started to bleed, rapidly passed into coma, and died	250-167	Not seen until in coma; given intravenous sodium glutamate on day of death
24	53	M	Alcoholic cirrhosis	31 Died	Drowsy during part of study	95-245-96	Died of pneumonia; peak blood-ammonia level coincided with onset of neurological symptoms
25	57	M	Portal cirrhosis; bleeding oesophageal varices	20 Recovery	For one day very drowsy after transoesophageal ligation of varices	214-25	..
26	55	M	Alcoholic cirrhosis	7 Recovery	Confused and disoriented	195-100	Improvement coincided with fall in blood-ammonia level
27	43	M	Alcoholic cirrhosis; bleeding oesophageal varices	2 Died	Admitted in deep coma, improved on therapy	169-108	Improvement followed treatment with intravenous sodium glutamate; blood-ammonia level not estimated before therapy started; patient died of uncorrected hypokalaemic alkalosis
28	34	M	Alcoholic cirrhosis; bleeding oesophageal varices	2 Died	In deep coma when first seen; died next day	158-132	Blood-ammonia level not determined until after patient had been in coma 24 hr.
29	40	M	Alcoholic cirrhosis	2 Died	In semicomma for a week before study; died in coma	103-129	Patient seen only 48 hr. before death blood-ammonia level not estimated at onset of coma.

120 g. of protein on Oct. 5; and the highest blood-ammonia level of 408 µg. per 100 ml. corresponded to an intake of 85 g. of protein on Oct. 7.

Case 9.—A woman, aged 24, received a blood-transfusion for post-partum haemorrhage four months before admission on Dec. 11, 1953. She was well until nine days before admission, with malaise, nausea, and vomiting; two days later she became jaundiced.

On admission she was deeply jaundiced, drowsy, and disoriented. Apart from these findings physical examination was negative. Over the next two days her condition became worse; she was very drowsy and slept unless stimulated, when, if roused, she was disoriented and excitable. Treatment was started with cortisone 400 mg. daily.

Subsequent Progress.—On Dec. 14 she was stuporous but, if stimulated, she had bouts of screaming. Her blood-ammonia level was 232 µg. of ammonia nitrogen per 100 ml. On Dec. 15 she was comatose, showing only a feeble response to painful stimuli. Her blood-ammonia level was 254 µg. of ammonia nitrogen per 100 ml. in the morning. In the afternoon her physical condition was unchanged, but her blood-ammonia level had fallen to 156 µg. of ammonia nitrogen per 100 ml., and it fell still further to 74 µg. per 100 ml. after the administration of intravenous sodium glutamate 25 g. In response to the glutamic-acid therapy there was a slight clinical improvement in that, although remaining in coma, the patient reacted by feeble movements to light touch. On Dec. 16 she was in deep coma until she died soon after midnight; two hours before death muscle twitching developed. The blood-ammonia level rose from 234 µg. of ammonia nitrogen per 100 ml. in the morning to 383 µg. per 100 ml. in the afternoon. Necropsy showed acute yellow atrophy of the liver.

Comment.—This patient showed the progression of hepatic coma from stupor to deep coma, and over this period her blood-ammonia level rose from 232 to 383 µg. of ammonia nitrogen per 100 ml. Glutamic-acid therapy was associated with a transient fall in the blood-ammonia level but did not produce any definite clinical improvement.

In this investigation electro-encephalography showed changes closely correlated with the clinical and biochemical findings, and revealed that some patients with

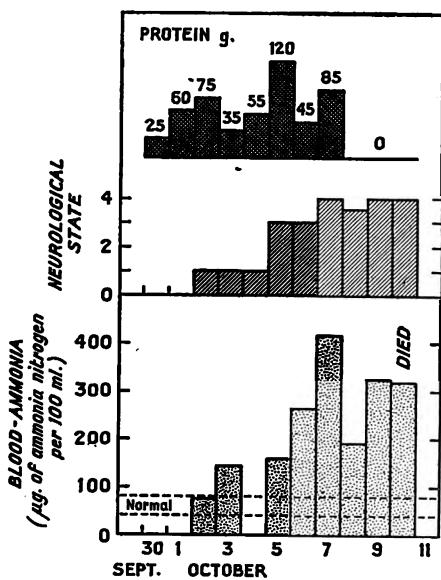


Fig. 2—Case 5: correlation between blood-ammonia level and neurological state in terminal hepatic failure. Electro-encephalography was not done.

disturbed consciousness do not show the abnormal rhythm attributed to hepatic coma. In these patients the blood-ammonia level was not much raised, and they have been excluded from the series because the cause of their neurological disturbance was considered to be due to other complications of hepatic disease—e.g., electrolyte disorders, septicæmia, severe pulmonary infection, and neurological disorders associated with chronic alcoholism.

Of the 29 patients 11 were treated with glutamic acid, with the following results:

Number of patients treated	11
Number of patients who improved on therapy	6
Number of patients who recovered from hepatic coma	3
Number of patients who left hospital	1*

* 2 patients died of intercurrent disease.

To 3 patients in deep coma only one infusion of sodium glutamate 25 g. was given; all of these died without showing any improvement. Of 8 patients treated with intravenous glutamic acid in repeated doses earlier in the disease 6 improved temporarily, and 3 recovered.

We tried to obtain objective evidence of the value of glutamic-acid therapy by observing its effect on peripheral blood-ammonia levels. In all 7 cases in which this was studied the blood-ammonia level fell after the administration of glutamic acid, and in 4 patients this was followed by clinical improvement. The results of one such experiment are given in fig. 3, which shows that the blood-ammonia level fell after the administration of intravenous sodium glutamate on two occasions (between the two infusions intravenous therapy was continued with glucose). Although a temporary clinical improvement took place in this patient, his condition deteriorated and he died in hepatic coma. In this case the sodium glutamate became decreasingly effective in lowering the blood-ammonia level as the patient's condition became worse.

Discussion

In any discussion of hepatic coma it is important, first of all, to stress the concept that there is not a single disorder attendant on acute or chronic deterioration in hepatic function. The susceptibility of patients with liver disease to infection, the electrolyte disturbances associated with advanced cirrhosis, and the development of hypoglycaemic attacks in patients with cirrhosis are only a few of the disorders which may cause a variety of symptoms, including neurological disturbances. In addition, chronic alcoholism, one of the major causes of cirrhosis, has associated neurological diseases—e.g., the Wernicke-Korsakoff syndrome and delirium tremens. We are concerned here only with a specific biochemical abnormality which our observations indicate to be a cause of consistent neurological symptoms and electro-encephalographic changes, both of which may be completely reversible. In our experience most cases of so-called hepatic coma are due to this specific abnormality—ammonia intoxication.

The results reported here show a correlation between the neurological symptoms and the ammonia levels in the peripheral blood in hepatic coma in 28 patients with cirrhosis of the liver and 1 with virus hepatitis. This observation alone does not establish that ammonia intoxication causes neurological conditions, but other experimental and clinical evidence supports this concept.

Ammonia is known to be very toxic to animals; to rabbits it is lethal at a concentration of about 1 part in 20,000 (Baldwin 1952). The Eck-fistula dog, when given ammonium salts, urea, or meat, develops a neurological syndrome characterised by ataxy, amaurosis, coma, and sometimes death, which is called "meat intoxication." The episodes of intoxication are preceded by high ammonia levels in the peripheral blood, and the symptoms may persist although the blood-ammonia level has fallen to nearly normal. This syndrome can be induced by repeated small injections of intravenous urease, when

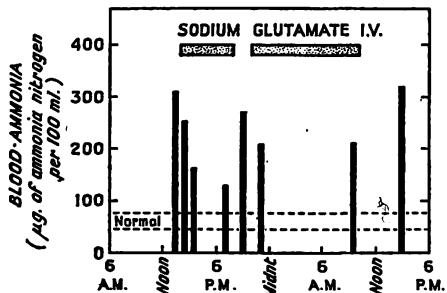


Fig. 3—Case 16: effect of intravenous sodium glutamate on blood-ammonia level. In each instance the intravenous infusion of sodium glutamate was followed by a fall in blood-ammonia level, which rose again when the infusion was discontinued.

both the symptoms of meat intoxication and the same pattern of blood-ammonia levels are observed (Riddell et al. 1954).

In cirrhosis of the liver symptoms identical with those of the onset of hepatic coma have been produced by the oral administration of ammonium salts and compounds which might liberate ammonia, such as urea (Phillips et al. 1952). Treatment of hepatic coma by a method which aims at enhancing the activity of one of the mechanisms of detoxication for ammonia—i.e., glutamic-acid therapy—is effective in some cases (Walshe 1953). Our results show that glutamic-acid therapy may cause clinical improvement and its use is followed by a fall in blood-ammonia level.

It is believed that the observed changes in peripheral blood-ammonia levels in hepatic coma do not give more than a general indication of the changes in ammonia metabolism which take place in the brain-cells, where ammonia is constantly being formed and then removed by the glutamic-acid/glutamine system (Weil-Malherbe 1950).

While in "meat intoxication" in the Eck-fistula dog and the episodic stupor which sometimes follows portacaval anastomosis in man the part played by ammonia intoxication appears clear, this is not always so in patients dying of liver failure. In such patients there are commonly present other disorders which may cause changes in consciousness—e.g., electrolyte disorders, hyponatraemia, hypokalaemia, septicæmia, and severe respiratory infections. Any of these may occur in association with ammonia intoxication.

Our experimental findings do not warrant a discussion of the treatment of hepatic coma, but certain observations may be made. First, we must emphasise again the observations of Davidson and his co-workers (Gabuzda et al. 1952, Phillips et al. 1952) on the potential dangers of a high-protein diet and of ammonium-containing compounds in decompensated liver disease; but the therapeutic value of protein in compensated liver disease must also be emphasised. Glutamic-acid therapy in hepatic coma has not yet been proved to be of value. In patients with terminal hepatic failure little can be expected except some temporary improvement, but in patients in whom the symptoms are due to relatively mild ammonia intoxication the chances of recovery may be enhanced by treatment with glutamic acid, whose greatest usefulness may be in patients showing evidence of impending coma after haemorrhage from oesophageal varices.

Summary and Conclusions

In hepatic coma the metabolism of ammonia is deranged.

The evidence for the existence of ammonia intoxication in hepatic coma is discussed, and it is believed that it is sufficient to base therapy on this concept of ammonia intoxication.

The place of glutamic-acid therapy in hepatic coma is discussed.

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THE TREATMENT OF ERYTHROBLASTOSIS FÆTALIS WITH RH HAPten

REVIEW OF A HUNDRED CASES

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THE suggestion that erythroblastosis foetalis, foetal oedema, icterus gravis neonatorum, and anaemia of the newborn were manifestations of a single disease was first put forward by Diamond, Blackfan, and Baty (1932). Darrow (1938) suggested that this disease was caused by destruction of foetal red cells by some immunity reaction. Levine and Stetson (1939) reported an agglutinin in the blood of a mother delivered of a dead foetus; this antibody had properties similar to those of agglutinins which had been produced in rabbits by the injection of red cells of *Macacus rhesus* (Landsteiner and Wiener 1940).

From this beginning has expanded our modern concept of erythroblastosis foetalis as a disease produced by maternal immunisation to a foetal-blood factor inherited from the father. This Rh factor has been obtained from the stroma of human red cells by Belkin and Wiener (1944) and Calvin et al. (1946). Carter (1947) reported a crude red-cell fraction which inhibits anti-D (anti-Rh_D) serum and described this in detail (1949) under the name of Rh hapten. This substance is produced from Rh-positive (pooled CDE positive) human red cells by protein precipitation with alcohol and further extraction of lipid constituents, originally with ether, at present with the non-inflammable compound dichloromethane, as suggested by Smolens (1952). 100 mg. of the substance so extracted, when mixed with 1 ml. of a potent anti-D serum and the mixture incubated at 37°C for 30 minutes, will absorb a high percentage of Rh antibodies from that serum, as determined by serum titrations and by quantitative nitrogen determinations of the washed serum-exposed fraction particles.

Present Investigation

The fraction has been injected intramuscularly into more than 500 sensitised Rh-negative pregnant women, and I report here the results obtained in the first 100 cases treated at the Western Pennsylvania Hospital in Pittsburgh. Although the clinical material is heterogeneous, consisting of cases presenting in sequence, and although many of these women received treatment which was inadequate by present standards—which have been achieved only by trial and error—the results were promising (table 1). All the serological procedures

TABLE I—RESULTS

Women treated	100
Women giving birth to Rh-negative babies	15
Test sample				85
(1) Number with no history of previous erythroblastotic child	29
(2) Number with history of one or more erythroblastotic children and/or transfusions	56
Result in subsample (1): Normal babies	27
Babies died after birth	2
Result in subsample (2): Normal babies *	20
Normal after simple transfusion	6
Normal, 1 exchange transfusion	2
Slightly retarded (1 not transfused, 1 with simple transfusion)	2
Died after birth	8
Stillborn	18

* All infants not receiving blood-transfusions yet developing normally.

N.B.—Those babies transfused were delivered at hospitals other than the Western Pennsylvania Hospital.

were done in the laboratory for research immunology at the Western Pennsylvania Hospital, and the presence of maternal Rh antibody was confirmed in each case by Dr. Bruce Chown of Winnipeg.

Inasmuch as it is common experience among investigators in the field to observe cases of normal Rh-positive children born to sensitised Rh-negative mothers who had not previously had babies with erythroblastosis, I am not emphasising the results in subsample 1. However, it seems unlikely that results such as these would occur in 29 consecutive cases without treatment. Subsample 2 has been studied in detail, and a complete chronicle can be obtained from me. The cases included in this study are those in the Pittsburgh area—treated sensitised women delivered in hospitals near enough for observation of the progress of the infants. These women came to the Western Pennsylvania Hospital for treatment. Of the 56 cases in subsample 2, 46 were referred by outside physicians because of previous difficulties due to Rh sensitisation. Since a few women came in for one or two injections and then abandoned the project, only those are included who received at least 800 mg. of red-cell fraction during a pregnancy. However, every case in the Pittsburgh area in which 800 mg. or more was injected is considered consecutively. Each live-born baby in the treated series was observed by me. Extensive study was made of hospital records to obtain all the facts available concerning each pregnancy in each case before the one in which the mother was treated.

The red-cell fraction is used primarily for the treatment of the Rh-negative sensitised women rather than for the infants after they are born. Each prospective mother is under the care of her own physician and has been referred by him for injections of the red-cell fraction at his request. The current regimen requires a patient who has lost one or more infants because of erythroblastosis to begin treatment not later than the third month of pregnancy, and preferably just after the first missed period. In some cases treatment is begun before pregnancy is established. The already pregnant patient is admitted to hospital and given 400 mg. of red-cell fraction four-hourly day and night until 18 injections have been given. She is then discharged with a supply of red-cell fraction, 200 mg. per ampoule, and her husband is instructed to inject the contents of one ampoule daily. This is continued until term, with the patient reporting every week or every two weeks for antibody titrations and a new supply of ampoules.

The contents of one ampoule (200 mg. in alcoholic solution) are suspended in 6 ml. of sterile physiological saline solution, and the whole is injected slowly into the gluteal muscles from a 10-ml. syringe and a 20-gauge 2-inch needle. No reactions have been observed except occasional local soreness. The regimen outlined above leads to the administration of a greater volume of the red-cell fraction than was given to most of the women in table I. There is a tendency with experience to use larger dosages of the red-cell fraction and to attempt to keep the patient saturated.

Discussion

The mode of action of red-cell fraction in the body is not clear. The obvious explanation is that the material is a hapten, and that it neutralises maternal antibodies to Rh. However, the substance seems to exert a directly protective effect on red cells of the infant. In this laboratory maternal antibody titres have shown a consistent falling off under treatment with the red-cell fraction. Goldsmith (1950) has reported similar observations. Some workers have not observed this, but perhaps the smaller volume of total injections explains why they have not done so. The importance of beginning injections of the red-cell fraction very early may be explained by the postulate that, if this substance is hapten, it is

TABLE II—RELATION OF OUTCOME TO MATERNAL HISTORY AND REFERRAL

Outcome	Not referred		Referred
	No previous affected infant	Previous affected infant	
No clinical disease ..	19	4	13
Recovered ..	8	1	12
Died, no kernicterus ..	2	1	7
Kernicterus ..	0	0	0
Stillborn ..	0	4	14
Totals	29	10	46

of value to use it at least as soon as there are formed elements in the foetal circulation. According to Patten (1946) the foetal heart-beat is established by the end of the third week after fertilisation.

It is difficult to elucidate the real significance of any method of treatment of erythroblastosis, because studies in the natural history of the disease are almost non-existent. Several papers have been published which have given results of pregnancies in Rh-negative sensitised women, but none of these constitute presentations of natural history, because in every case attempts were made to alleviate the disease. Allott and Holman (1949) reported a study of 117 infants with a total mortality of 56%—a mortality of 48% for infants from mothers sensitised only in the current pregnancy, and a mortality of 71% for infants from mothers who have had previous erythroblastotic babies. A comparable breakdown for the present series gives a total mortality of 33%—a mortality of 7% for babies whose mothers became sensitised to Rh with the current pregnancy, and a mortality of 47% for infants whose mothers had erythroblastotic babies previously.

Chown (1952) suggests that the results of treatment should be categorised by assessing whether a current treated pregnancy showed an improved outcome over a previous one or provided a less promising result. Such an analysis of the 56 cases in subsample 2 (table I), after the omission of 14 which, although presumptive, did not provide histories adequate to prove erythroblastosis unequivocally, gives the following picture: improved outcome, 18 cases; poorer outcome, 8 cases; change in results negligible, 16 cases.

The studies of Vaughan et al. (1950), at Harvard Medical School, have provided information as to the relation of outcome to maternal history. A comparison of their series with the present one is of value only if variables are taken into account. The period of their reported investigation includes many cases in which labour was induced before term, a practice which Vaughan et al. feel may conduce to the incidence of kernicterus. With rare exceptions the infants reported in our series were allowed to go to term. In the Harvard series, with exchange transfusion the method of treatment, there were 26% stillborn to 21% in our series, and 54% surviving babies to 67% in our series. The outstanding difference in the two series may be found in those infants with no clinical disease: 18% in the Harvard series and 42% in ours. This difference in the number of normal infants is the only one which can be concluded to have high statistical significance (t of 3.9 at the 0.01 level).

Table II is modelled on table IV of Vaughan et al. (1950). "Referred" means any woman who had her previous erythroblastotic baby in another hospital; "not referred" means one who had her previous erythroblastotic baby in the Western Pennsylvania Hospital.

The category "no clinical disease" in table II is not identical with "normal babies" in table I. "No clinical disease" means entirely free from clinical evidence of

erythroblastosis, whereas "normal babies" include all babies not transfused yet developing normally, of whom a few had very mild clinical disease, such as would be overlooked in the average practice.

Summary

The results of injecting red-cell fraction into Rh-negative sensitised women during their pregnancies are presented in detail as regards the 85 Rh-positive infants.

The method of administration and the possible action in the body of the red-cell fraction are discussed.

The results are analysed, and the conclusion is drawn that treatment of the mother with the red-cell fraction increases the number of normal babies.

I am indebted to Dr. Bruce Chown, of the Children's Hospital, Winnipeg, Canada, for his kindness in checking parent and infant phenotypes and maternal antibody titres and for suggestions and interest. I am grateful also to Mr. Daniel F. Jackson, now with the New York State University College of Forestry, for his statistical analyses of the data. Mr. Vincent Yakulis did much of the laboratory work and Mr. Daniel F. Jackson, Mrs. Elizabeth Lewis, and Mrs. Betty deWeeger assisted with "record-room" research.

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URINARY EXCRETION OF POLYVIDONE

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A SOLUTION of polyvidone (polyvinylpyrrolidone) was first used as a substitute for plasma by Hecht and Weese (1943). We used a 3.5% solution whose detailed composition has been described by Thrower and Campbell (1951); its viscosity, colloidal osmotic pressure, and tonicity are about the same as those of normal human blood.

In a clinical trial of this solution one of us (A. W. W.) infused 500-4000 ml. into each of 75 patients whose blood volume was judged on clinical grounds to be reduced (table I). 23 of the patients died of the effects of their disease or injuries. At necropsy of 20 of these no macroscopical or microscopical evidence was obtained of accumulation of polyvidone in liver, spleen, kidneys, lung, or lymph-glands, but in the absence of a specific stain for polyvidone this evidence is inconclusive. No evidence of toxicity was obtained.

Polyvidone is not metabolised in the body (Ravin et al. 1952), and it is important to know what happens to it after it has been infused. In these patients the direct measurement of changes in plasma volume was impracticable, and measurements of the plasma-polyvidone levels were unsatisfactory; hence the rate of loss of polyvidone from the circulation could not be ascertained. It was possible, however, to measure the quantity of polyvidone excreted in the urine, and from these observa-

TABLE I—MATERIAL INVESTIGATED

Condition	No. of patients	No. of deaths
<i>Shock due to severe accidental injury operation, or blood-loss:</i>		
Severe accidental injury	6	3
Severe blood-loss associated with surgical operation	11	4
Shock due to surgical operation	36	1
<i>Reduction in blood volume associated with peritonitis, intestinal obstruction, or paralytic ileus:</i>		
Peritonitis	14	11
Intestinal obstruction or paralytic ileus	8	2
Total	75	21

tions some conclusions have been drawn about the possible distribution of polyvidone in the body.

Methods

After operation in 20 cases the urinary content of polyvidone was measured by the method of Thrower and Campbell (1951) with a Spekker absorptiometer with Ilford blue-green spectrum filter; readings were taken a minute after the addition of the iodine reagent. The analyses were usually continued until only traces of polyvidone could be found. The duration of the collections varied from 45 to 260 hours after the start of the polyvidone infusion and exceeded 72 hours in 13 cases and 100 hours in 11 cases. These 20 cases have been considered first according to the total quantity of polyvidone excreted, and secondly according to the rate of excretion (table II).

TOTAL QUANTITY OF POLYVIDONE EXCRETED

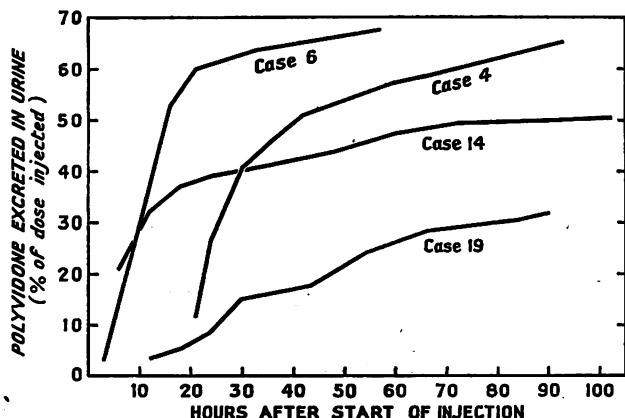
Polyvidone equivalent to more than 70% of the quantity injected was recovered in the urine of 5 patients; in 9 others the equivalent of 50-70%, and in 5 patients of 40-50%, of the dose was recovered; in 1 case less than 30% was recovered after each of two infusions. The largest quantity recovered was 78% of the dose within 72 hours after an emergency gastrectomy (Polya) for a perforated duodenal ulcer in a patient to whom 500 ml. of 'Plasmosan' (17.5 g. of polyvidone) had been administered. There did not appear to be any relationship between the quantity of polyvidone administered and quantity excreted in the urine; the smallest recovery (27%) followed the largest dose (1500 ml. of plasmosan containing 52.5 g. of polyvidone). Another patient (case 12), who received two separate infusions, excreted 51% of the total dose; after the first infusion only 33% of the dose was excreted, but after the second infusion the equivalent of 86% of the second dose was excreted; this suggests that some polyvidone from the first infusion was retained until after the second infusion had been administered.

RATE OF EXCRETION

When the urinary excretions of polyvidone were plotted against time, it was evident that the patients fell into four groups, typical examples of which are shown in the accompanying figure :

(1) In the first group (exemplified by case 6 in the figure) there were 5 patients who each excreted more than 50% of the dose (and 3 more than 60%) within 24 hours of the infusion; the rate of excretion then fell off, but 2 had excreted more than 70% in 72 hours, and 1 other more than 70% in 90 hours.

(2) The main group of 13 patients, most of whom excreted 30-50% in 24 hours, can be divided into two parts: (a) 3 patients in whom excretion began as rapidly as in the first group, 2 excreting more than 30% of the dose within 12 hours (exemplified by case 14 in the figure), but the rate of excretion fell off between 12 and 24 hours; and (b) the remaining 10 patients, whose excretion began slowly and then increased rapidly with the result that, despite the initial delay, in 5 of these patients more than 40% was excreted within 36 hours (exemplified by case 4 in the figure).



Patterns of urinary excretion of polyvidone in four patients representing four different types of excretion.

(3) The last group, of 2 patients who excreted less than 10% in 24 hours and only 30% in 80 hours (exemplified by case 19 in the figure).

The most rapid early excretion was of 7 g. of polyvidone, equivalent to 21% of the dose within 6 hours, but this patient excreted only 39% in 24 hours and 50% in 102 hours. Small quantities of polyvidone were recovered from the urine within 3 hours of the start of an infusion of plasmosan. When excretion was at its height, the urinary concentration of polyvidone was usually 1-2%, but higher concentrations up to 5% were also found.

There seems to be some relationship between the total quantity of polyvidone excreted in the first 24 hours and the rate of formation of urine. Of the 7 patients who excreted more than 60% of the dose of polyvidone 5 excreted more than 55% of the dose in the first 24 hours and during this period excreted more than 800 ml. of urine. Of the remaining 2 patients 1 excreted 27% of the dose in the smallest 24-hour volume of urine (405 ml.) and the other excreted 47% of the dose in the largest volume of urine (1375 ml.) of this group. In the remaining 13 patients the lower outputs of polyvidone during the first 24 hours were usually associated with smaller 24-hour volumes of urine. When the output of polyvidone had been small during the first 24 hours, diuresis in the second 24-hour period was often accompanied by the excretion of a large quantity of polyvidone.

Discussion

The rate of urinary excretion of polydisperse macromolecules, such as polyvidone and dextran, has been shown in uninjured animals to be inversely proportional to their molecular weight (Grotte et al. 1951, Steele et al. 1952). When the excretion of polyvidone was plotted against time, it was found in 18 out of our 20 cases that the shape of the curve was similar to that which Thrower and Campbell (1951) had suggested was typical for polyvidone. These curves closely resemble that for the excretion of inulin which Schwartz et al. (1949) stated was characteristic of the excretion of a non-metabolisable substance of large molecular weight. Ravin et al. (1952), who injected polyvidone labelled with I^{131} or C^{14} into dogs, rats, rabbits, and man, concluded that polyvidone was not metabolised, and that excretion by routes other than the urine was insignificant. Although the shape of the curves was typical, there was considerable variation in the total quantity of polyvidone excreted and in the time at which rapid excretion began. There was a delay in the onset of excretion of polyvidone of 12 to 24 hours or more in 9 of 20 people, the most likely cause of which seemed to be postoperative oliguria. Ravin et al. (1952) found that the total quantity of polyvidone excreted was independent of the rate of formation of urine when this exceeded 800-1000 ml. per 24 hours; this rate was achieved during the first 24-48 hours in only 8 of our 20 patients.

Detailed characterisation of the distribution of molecular weights in the polyvidone preparation used in these experiments was not available to us. It seems likely, however, that, if the equivalent of more than 60% of the polyvidone in a standard preparation was excreted within 24 hours of infusion by 3 people, this preparation contained a high proportion of material of low molecular weight. This conclusion is supported by the recovery of 70-80% in 4 cases. Ravin et al. (1952) concluded that, for polyvidone, molecules having a molecular weight of 40,000 were the largest that could be excreted in the urine. Since polyvidone is not metabolised in the body, this would imply that nearly 80% of the polyvidone in this preparation had a molecular weight of less than 40,000. Although osmotic effect is inversely proportional to size, increase in plasma volume depends on the retention of the active agent within the blood-vessels. Other capillaries as well as those of the renal glomeruli are permeable to polyvidone of a molecular weight of less than 40,000; hence within a short time after the infusion

TABLE II—URINARY EXCRETION OF POLYVIDONE

Case no.	Age (yr.)	Sex	Diagnosis and treatment	Volume of plasmosan injected (ml.)	Dose of polyvidone (g.)	Percentage of total dose of polyvidone excreted in urine			Duration of estimation of urinary polyvidone (hr.)
						In 24 hr.	In 48 hr.	Total	
1	37	M	Perforated duodenal ulcer; emergency partial gastrectomy	500	17.5	64.7	73.2	78.0	72
2	31	M	Perforated duodenal ulcer; emergency partial gastrectomy	500	17.5	56.1	64.7	77.2	135
3	54	M	Carcinoma at pelvic rectal junction; excision and primary anastomosis	1000	35.0	60.3	63.0	76.9	192
4	42	M	Carcinoma of stomach; partial gastrectomy	..	1000	35.0	26.7	53.3	72.08
5	49	M	Chronic duodenal ulcer; partial gastrectomy	..	1000	35.0	55.8	63.7	68.3
6	49	M	Gangrenous appendicitis; pelvic peritonitis	..	500	17.5	61.0	66.2	67.4
7	50	M	Chronic duodenal ulcer; partial gastrectomy	1000	35.0	47.1	57.1	64.0	108
8	26	M	Perforated duodenal ulcer; emergency partial gastrectomy	500	17.5	26.7	59.6	59.6	48
9	24	M	Perforated duodenal ulcer; emergency partial gastrectomy	1000	35.0	37.7	53.3	58.5	72
10	55	M	Inoperable carcinoma of stomach; laparotomy	1000	35.0	43.1	51.2	55.6	96
11		M	Carcinoma of pancreas; partial duodenopancreactectomy	1000	35.0	11.4	40.2	53.2	132
12	55	M	Carcinoma of stomach; total gastrectomy	..	(1) 1000 (2) 500	35.0 17.5	13.4 21.0	15.8 44.2	33.5 85.9
13	41	M	Volvulus of cæcum and ascending colon; reduction	500	17.5	50.4	157
14	52	M	Duodenal ulcer, haematemesis; emergency partial gastrectomy	1000	35.0	39.0	43.5	50.0	102
15	48	M	Carcinoma of stomach; partial gastrectomy	1000	35.0	..	48.0	49.4	72
16	66	F	Carcinoma of rectum; abdominoperineal excision	500	17.5	30.3	38.7	48.5	168
17	40	M	Chronic duodenal ulcer; partial gastrectomy	1000	35.0	34.3	44.5	46.3	96
18	51	M	Chronic duodenal ulcer; partial gastrectomy	..	500	17.5	3.27	41.95	45.4
19	37	M	Chronic duodenal ulcer; partial gastrectomy	..	500	17.5	8.84	20.0	42.4
20	62	F	Carcinoma of ascending colon; right hemicolectomy; ileus	(1) 1500 (2) 1500	52.5 52.5	14.1	26.8 28.2	27.4	26 58

a large proportion of these smaller molecules will be distributed in the interstitial fluid rather than in the plasma. As the level of small polyvidone molecules in the plasma is lowered by their excretion in the urine, other small polyvidone molecules probably pass back from the interstitial fluid into the plasma and are then in their turn available for excretion. Possibly variation in this type of equilibration may explain some of the differences observed in the urinary excretion of polyvidone. A preparation with such a high potential wastage in the urine is unlikely to produce consistently large and lasting increases in plasma volume.

Summary

The urinary excretion of polyvidone after the infusion of a 3.5% solution of polyvidone (plasmosan) was measured in 20 patients.

The total urinary excretion of polyvidone was equivalent to more than 70% of the dose in 5 patients, 50–70% in 9, 40–50% in 5, and less than 30% in 1 patient.

Within 24 hours of the infusion the equivalent of more than 55% of the dose was excreted by 5 patients, 30–50% by 13, and less than 10% by 2 patients.

Possible explanations of these variations are discussed.

Messrs. May & Baker Ltd. supplied the plasmosan.

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HYPERTENSION AND "VENOUS" LEG ULCERS

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In a series of patients with either post-thrombotic or varicose ulceration of the leg the arterial blood-pressure was determined (Anning 1949, 1952). The men formed a group too small for conclusions to be drawn from their blood-pressure readings, but after division into age-groups the blood-pressure records of the women were compared with the figures presented by Robinson and Brucer (1939) based on 3405 American women taken at random. The proportion of ulcer patients with hypertension was found to be significantly higher than in Robinson and Brucer's controls. The criteria of hypertension used by these workers have been criticised by Hamilton et al. (1954), who publish tables showing the mean casual arterial blood-pressure of a sample of the general population, thus making it possible to determine whether the average arterial blood-pressure of leg-ulcer patients is within the normal range or not. The results of such a comparison are presented here.

Investigation

In this investigation the casual arterial blood-pressure of 696 women and 316 men with either post-thrombotic or varicose leg ulcers was determined with a mercury Riva-Rocci sphygmomanometer. The precautions and methods of Hamilton et al. (1954) were used, though only about 85% of the observations were made by me, the remainder being made by several house-physicians. In about 0.5% the blood-pressure was determined when the patient was in bed in hospital. All the patients were weighed. The series includes the patients considered in previous papers (Anning 1949, 1952) together with others examined since.

Tables I and II show the results obtained compared with those of Hamilton et al. (1954). It will be noted that there is a significant difference—i.e., more than twice the standard error of the difference between the means—between the systolic and diastolic pressures of women aged 35–74 and the diastolic pressures of men aged 40–54. There is also a significant difference between the systolic pressures of men aged 40–44 and men aged 50–54. In these various groups it is shown that the ulcer patients have a higher arterial blood-pressure than the sample of the general population. Groups containing fewer than 20 patients have not been compared.

Discussion

The sample of the population investigated by Hamilton et al. (1954) included 421 women and 276 men with varicose veins out of a total of 1204 women and 827 men. These workers found that women with varicose veins showed a significantly more rapid rise of systolic pressure with age. This is of importance in relation to the ulcer patients, many of whom had varicose veins. In addition it would "weight" the control group, tending to lessen the difference between the groups.

In the higher age-groups the difference between the groups tends to become less or to be reversed. This is, no doubt, partly because of the small numbers compared; but there is a probability that hypertensive patients will die before reaching a great age, and this will tend to reduce or obviate the difference between the groups as the age-groups become older.

The cause of the relationship between hypertension and ulceration from defective venous circulation is obscure and has been discussed elsewhere (Anning 1952). Hypertension with varicose veins or the predisposition to venous thrombosis might possibly develop in the same families, but this seems unlikely. In the present series there is no evidence that body-weight is a factor. The opening up of arteriovenous shunts after deep venous

TABLE I—ARTERIAL PRESSURES OF 696 WOMEN WITH LEG ULCERS COMPARED WITH CONTROLS

Age (yr.)	No. of women	Arterial blood-pressure (mm. Hg)							
		Systolic				Diastolic			
		Mean	Standard deviation	Difference of means	Standard error of difference of means	Mean	Standard deviation	Difference of means	Standard error of difference of means
20–24	(a) 2 (b) 68	122.5 118.7	12.7 8.82	3.8	..	82.5 72.1	7.1 7.61	10.4	..
25–29	(a) 7 (b) 103	120.7 122.7	8.82 12.6	-2.0	..	74.3 76.1	9.1 9.1	-1.8	..
30–34	(a) 20 (b) 108	126.5 120.5	13.56 14.8	6.0	3.34	83.2 74.5	7.95 8.9	8.7*	1.97
35–39	(a) 42 (b) 119	136.8 127.5	18.28 16.9	9.3*	3.27	87.0 79.3	12.19 11.5	7.7*	2.15
40–44	(a) 58 (b) 122	141.9 133.9	23.27 19.7	8.0*	3.69	87.7 82.1	14.08 12.4	5.6*	2.16
45–49	(a) 77 (b) 114	153.3 133.8	27.64 22.9	19.5*	3.80	91.6 82.1	13.93 11.6	9.5*	1.93
50–54	(a) 114 (b) 131	163.0 146.6	28.65 27.5	16.4*	3.59	93.3 87.8	14.29 14.7	5.5*	1.85
55–59	(a) 100 (b) 108	167.2 153.5	31.54 28.7	13.7*	4.19	95.6 88.6	15.23 14.8	7.0*	1.97
60–64	(a) 102 (b) 87	176.9 159.1	32.81 27.4	17.8*	4.38	101.8 92.4	7.63 15.4	9.4*	1.81
65–69	(a) 72 (b) 74	182.9 172.9	32.68 26.7	10.0*	4.83	102.2 94.0	15.32 15.3	8.2*	2.52
70–74	(a) 64 (b) 60	193.6 175.3	37.69 27.6	18.3*	5.80	104.0 93.1	18.81 14.5	10.9*	3.00
75–79	(a) 25 (b) 26	176.4 177.1	21.51 32.6	-0.7	7.60	95.6 97.3	9.93 18.1	-1.7	4.06
80–84	(a) 12 (b) 11	185.4 198.0	32.14 31.1	-12.6	..	98.7 96.8	16.64 18.5	1.9	..
85–89	(a) 0 (b) 1	190.0	110.0

(a) Present series. (b) Controls of Hamilton et al. (1954).

* A significant difference of means.

thrombosis (Brewer 1950, 1951) and their importance in the aetiology of varicose veins (Piulachs and Vidal-Barraquer 1953) may prove to be of significance in relation to hypertension in these patients. The question whether such shunts lead to a rise in arterial pressure cannot be answered at present. In osteitis deformans arterial degeneration, sometimes with hypertension, is found in most patients aged more than 50 (Hunter 1946). This is a condition in which arteriovenous shunts tend to occur in affected bones, but there is no evidence that they are related to the rise in arterial pressure. Perhaps hypertension is a coincidental finding which, in patients with a defective venous return from the lower limbs, predisposes to ulceration.

TABLE II—ARTERIAL PRESSURES OF 316 MEN WITH LEG ULCERS COMPARED WITH CONTROLS

Age (yr.)	No. of men	Arterial blood-pressure (mm. Hg)							
		Systolic				Diastolic			
		Mean	Standard deviation	Difference of means	Standard error difference of means	Mean	Standard deviation	Difference of means	Standard error difference of means
20-24	(a) 6 (b) 60	128.3 123.0	11.43 12.52	5.3		80.8 73.8	6.10 9.83	7.0	
25-29	(a) 12 (b) 82	132.9 124.1	17.52 14.0	8.8		86.2 74.1	9.83 9.9	12.1	
30-34	(a) 17 (b) 90	131.2 122.8	10.63 13.9	8.4		85.0 73.9	8.57 9.7	11.1	
35-39	(a) 40 (b) 90	126.2 125.2	15.31 14.1	1.0	2.83	82.1 77.8	12.50 8.9	4.3	2.16
40-44	(a) 40 (b) 99	137.2 127.4	15.44 17.7	9.8*	3.02	86.2 77.0	14.17 12.9	9.2*	2.58
45-49	(a) 42 (b) 79	134.7 130.9	20.70 18.3	3.8	3.79	85.6 80.0	10.32 10.5	5.6*	1.97
50-54	(a) 35 (b) 87	149.0 134.5	23.15 19.8	4.44		90.1 82.2	19.04 11.6	7.9*	3.34
55-59	(a) 32 (b) 60	140.6 145.5	30.90 24.4	14.5*		88.1 87.2	14.34 13.7	0.9	3.09
60-64	(a) 36 (b) 52	161.1 154.2	28.32 33.1	4.9	5.45	92.6 87.9	17.14 18.7	4.7	3.85
65-69	(a) 20 (b) 46	159.0 152.1	33.75 25.9	6.9	6.57	89.7 85.2	12.61 15.1	4.5	3.59
70-74	(a) 14 (b) 27	152.1 161.4	35.87 34.3	6.9	8.45	85.3 86.9	15.25 18.0	-1.6	
75-79	(a) 17 (b) 4	168.2 150.0	21.81 37.7	-9.3		90.8 82.5	12.86 20.2	8.3	
80-84	(a) 5 (b) 5	172.0 174.5	19.64 22.8	-2.5		87.0 91.0	5.09 9.0	-4.0	

(a) Present series. (b) Controls of Hamilton et al. (1954).

* A significant difference of means.

Summary

The casual arterial blood-pressure of 696 women and 316 men with either post-thrombotic or varicose ulceration of the limbs was compared with that of a sample of the general population determined by Hamilton et al. (1954).

The systolic and diastolic pressures of women, aged 35-74, with ulcers are significantly higher than those of controls. Of the men with ulcers those in some age-groups also had higher pressures.

The possible causes for these findings are discussed.

I am grateful to Dr. John T. Ingram, Dr. F. F. Hellier, and other colleagues and practitioners who have referred patients to me, and to Prof. G. W. Pickering for allowing me to see the paper by himself and his collaborators before publication.

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IDIOPATHIC HYPERCALCÆMIA OF INFANTS

LOW-CALCIUM TREATMENT

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In idiopathic hypercalcæmia of infants (Lightwood 1952, Payne 1952) many of the symptoms (e.g., anorexia, constipation, and loss of muscle tone) may be the result of the hypercalcæmia itself. The cause of the hypercalcæmia is not yet established, but possible factors are impairment of renal excretion of calcium and excessive absorption of calcium from the gut. The latter might well occur in infants fed on cow's milk (which contains four times as much calcium as does human milk), patent cereals (many of which are fortified with calcium), and vitamin-D supplements. Whatever the cause, it seemed to us likely that a low-calcium diet would relieve the condition, and we therefore decided to try such a treatment.

Methods

It is not simple to make up an artificial low-calcium milk, because nearly all commercial casein contains calcium caseinate. Our first method, therefore, was to pass milk through a column of cation-exchange resin in such a way that most of the calcium was removed in exchange for potassium, sodium, and magnesium in about normal proportions. Black and Milne (1952) used the same principle to prepare a low-potassium diet. Our second method was to make up an artificial milk with a special low-calcium casein.

The apparatus used for the first method is shown in fig. 1. The main glass tube is about 24 in. long with an internal diameter of 1 in. It contains at least 100 g. of 'Amberlite' resin no. IR 120 H, making a column about 10 in. high. The outflow tube is flexible and usually raised so that the level of fluid cannot fall below the top of the column; this prevents air from getting into the column and lowering its efficiency. When desired, the tube can be lowered and the fluid in the resin column drained off.

The column of resin rests on a perforated porcelain filter disc covered with a thin layer of cotton-wool to prevent small particles of resin from getting through the perforations. This base is set in position with the tube already partly full of water so that no air will be trapped in or under it. The resin is next washed into the tube with plenty of water, the excess of which drains away through the outlet.

When the resin has sedimented, the top of the column is covered with another thin layer of cotton-wool to prevent the upper layers from being disturbed by inflowing solutions, and the fluid level is adjusted to the top of the column. Fluid is run into the tube from a separating funnel, whose neck is stoppered with a bung bored to take an air-inlet tube, which reaches to the bottom of the chamber. The air which is drawn in bubbles up through the contents of the funnel and helps to prevent the cream from separating from the milk.

The resin is conditioned by running through it 500 ml. of a solution containing potassium, sodium, and magnesium at about forty times the concentrations found in cow's milk.

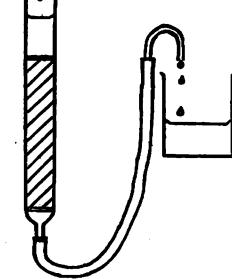


Fig. 1.—The apparatus.

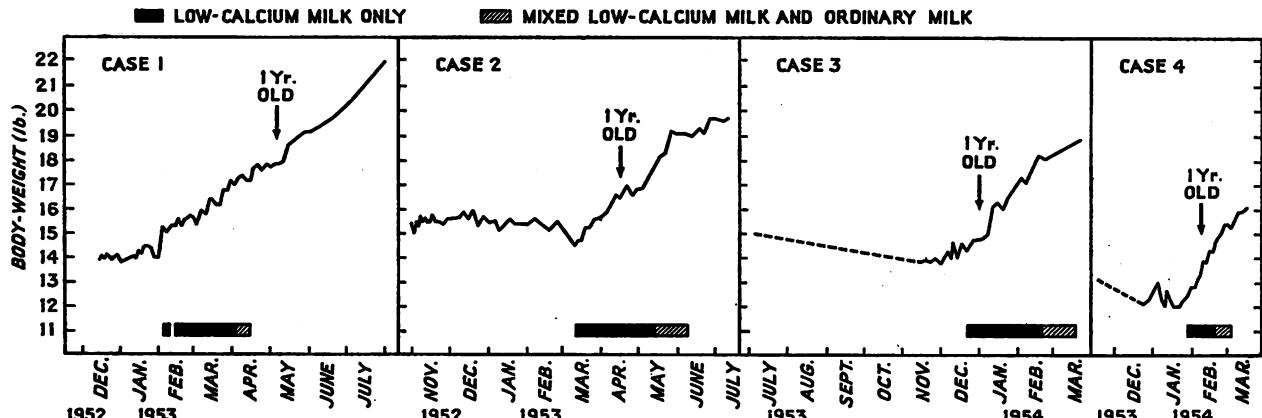


Fig. 2.—Weight charts of 4 infants with hypercalcæmia, showing gain in weight on low-calcium milk. Interrupted lines denote weights before admission to hospital.

(0.8 M sodium chloride, 1.6 M potassium chloride, and 2.4 M magnesium sulphate) at a rate of about 150 drops a minute. The fluid level is adjusted to the top of the column. The column is next washed through with 500 ml. of a 1/40 dilution of the above-mentioned solution—i.e., equal to normal milk concentrations—at the same rate, and the fluid level is again adjusted to the top of the column. The resin is now charged with potassium, sodium, and magnesium in the correct proportions and is free from calcium.

When required, a pint of fresh milk can be run through the column at 150 drops a minute. The effluent is clear at first but gradually becomes milky. A volume equal to that initially present in the apparatus (about 80 ml.) is rejected, and all the subsequent effluent is collected. When the outflow has nearly ceased, the outlet tube is lowered, and the milk remaining in the apparatus is run off as completely as possible. The milk is immediately bottled as separate feeds and may be sterilised in the usual way.

After use the apparatus is emptied and the resin repeatedly washed in water, the resin being allowed to sediment, and the supernatant fluid being decanted until it is perfectly clear. The apparatus is thoroughly cleaned with soap and hot water and well rinsed. It is then reassembled and the column prepared as described.

Analysis of samples of milk treated in this way gave the following approximate cation concentrations compared with untreated cow's milk :

	Untreated	Treated
Calcium (m.eq. per litre) ..	60	1-5
Potassium ..	35	70
Sodium ..	20	40
Magnesium ..	10	15

Another form of low-calcium milk has been made up from Allen & Hanburys' "low-ash casein," which contains only traces of calcium. This protein is highly acid, and is first treated with alkali (about 60 ml. of N NaOH per 100 g.) to adjust the pH to the iso-electric point of casein (4.7). At this pH the protein is almost insoluble and is washed once with water and twice with acetone, allowing it to sediment, and drawing off the supernatant between washings. It is subsequently dried first in a stream of warm air and finally in a vacuum desiccator over P_2O_5 . More recently we have found that even casein which contains large amounts of calcium can be rendered almost calcium-free by dissolving, precipitating at pH 4.7, washing, and drying.

This casein is used to make up an artificial milk approximating to human milk, except that the calcium content is low. To obtain 1 litre of milk, 20 g. of prepared casein is treated with 368 ml. of distilled water + 2.0 ml. of 4 N potassium hydroxide + 2.0 ml. of 2.5 N sodium hydroxide, mixed well, and stood for 1/2–1 hour at room-temperature with repeated gentle mixing to dissolve. Next the following solutions are added and mixed well : 2.0 ml. of 2.25 M dipotassium hydrogen phosphate, 2.0 ml. of 0.5 M potassium dihydrogen phosphate, 2.0 ml. of 0.5 M sodium sulphate, 2.0 ml. of 1.5 M magnesium chloride. This solution will keep for a few days in the refrigerator. On the day of use 500 ml. of water + 70 g. of lactose are added and the mixture is warmed to dissolve, autoclaved at 5 lb. for 10 minutes, and cooled. 60 ml. of this is added slowly, stirring with a sterile glass rod, to

60 ml. of pasteurised cream containing 50% fat. Next the diluted cream is added to the rest of the mixture, which is bottled as individual feeds in sterile containers and put in the refrigerator until wanted. The final composition of such a milk is as follows :

Fat ..	3 % (by calculation)
Lactose ..	7 % "
Casein ..	2 % "
Calcium ..	2 m.eq. per litre (by analysis)
Potassium ..	18 "
Sodium ..	9 "
Magnesium ..	6 "
Chloride ..	7 "
Phosphate ..	15 mg. per 100 ml. as phosphorus (by analysis)
pH ..	7.0 (by analysis)

These values are close to those given for human milk—e.g., Hawk et al. (1947)—except for the calcium, which is normally 15 m.eq. per litre.

Results

Both milks were palatable and taken satisfactorily ; one child took the artificial human milk more readily when it was flavoured with 'Marmite.' Both milks showed rapid separation of the cream, especially when heated. After autoclaving at 5 lb. for 15 minutes the cream of the resin-treated milk could be resuspended by shaking : this was, however, impossible with the artificial human milk, which was therefore not heated after addition of the cream.

On our régime the child is given a low-calcium diet based on low-calcium milk. For supplementary carbohydrate 'Farola' is used, because this is a plain semolina to which no calcium has been added. Supplementary iron is also given. No extra vitamin D is allowed, but orange juice or ascorbic acid is given as usual, and marmite as a source of the vitamin-B group. When the serum-calcium level has fallen below 6 m.eq. per litre (12 mg. per 100 ml.), the low-calcium milk is progressively replaced by ordinary cow's milk. Sooner or later spontaneous recovery may be expected, and the infant can return to a normal diet. Since our artificial human milk lacks many ingredients of the natural secretion, it may be unwise to use it as the principal item of diet for more than a month ; by this time it should be possible to substitute for it, in part at least, cow's milk.

4 infants with idiopathic hypercalcæmia have now been treated. The 1st received resin-treated cow's milk, the 2nd resin-treated human milk, the 3rd artificial human milk followed by resin-treated cow's milk, and the 4th artificial human milk. In every case there were (1) an improvement in the general well-being of the child within a few days, with increased appetite and cessation of vomiting ; (2) a rapid gain in weight, whereas previously weight gain had been very slow or had ceased ; and (3) a fall in serum-calcium level, reaching normal

levels in 2-6 weeks. Weight charts are given for each child (fig. 2).

These results must be interpreted with caution because spontaneous recovery is usual. Nevertheless they are encouraging enough to justify the further use of a low-calcium diet in the treatment of this condition.

We thank Dr. J. Apley, Dr. B. D. Corner, and Prof. A. V. Neale for permission to publish the results of treatment in case 1, cases 2 and 3, and case 4 respectively; and Mr. H. Donaldson and Mr. L. Haugh, A.I.M.L.T., for their help in making the special milks.

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STERILISATION OF SYRINGES AND NEEDLES

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THE sterilisation of syringes and needles for use in hospital wards, theatres, and special departments has become accepted as an essential service and one that is usually organised and controlled by the pathological laboratory. Various techniques have been described, but all leave something to be desired.

At the Kingston Group Laboratory sterilisation in aluminium containers has made the supply of sterile equipment easy and convenient to small hospitals in the group, to general practitioners, and for the use of laboratory staff on domiciliary visits.

Syringes

The traditional ward method of sterilisation by boiling in water covered every type and size of syringe. For hypodermic injections it still appears an adequate and cheap method and will remain so, unless ready-made plastic injectors or cartridge syringes are developed at a very cheap price. There is very little evidence of accidental infections with boiled-up hypodermic syringes and needles; and, if the laboratory-controlled syringe service is not to become unwieldy and expensive, it is probably best to leave the ordinary ward steriliser to deal with many of the hypodermic syringes. We do provide 2-ml. syringes which are used for hypodermic purposes on many occasions, but the Medical Staff Committee decided that the laboratory should not be asked to provide smaller syringes.

The laboratory undertakes this service for two reasons: (1) the laboratory staff can be expected to understand and guarantee the sterility of the syringes; and (2) the laboratory is interested in obtaining good specimens for test purposes, and it is for taking specimens that most syringes are used. Since water, even in minute quantities, may ruin specimens for many tests, the method of sterilisation must be dry, and the use of ovens and the control of their temperatures falls into line with other laboratory procedures.

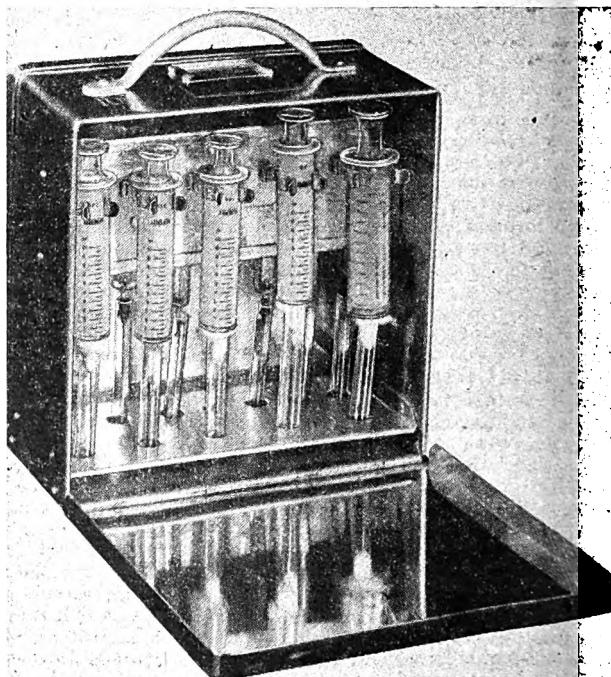
In most laboratory syringe services the syringe, usually with needle attached, is placed in a glass tube with a cotton-wool plug at the bottom, the whole being wrapped in either 'Cellophane' or kraft paper. This involves having a stock of different sizes of glass tubes, adding one more easily broken object, at about two shillings a time, to the all too easily broken syringe. It involves the cutting of cellophane into appropriate sizes and the wrapping of each syringe separately. In the ward or in the theatre it calls for the laying out of several

syringes which, once removed from their wrapping, are no longer sterile.

An aluminium container (see figure) was therefore devised in which syringes can be stacked in the numbers most likely to be needed, and the needle can be inspected and a syringe selected without interfering with sterility, and which can be safely carried on a ward trolley or in a doctor's car. It takes a moment to fill, stacks easily in the steriliser, and in practice has enormously reduced breakages both of syringes and of other glassware. The present container measures $8\frac{1}{2} \times 8\frac{1}{2} \times 4\frac{1}{2}$ in. and has a handle on top and doors which flap down on either side, lying flat on the table. The syringe-holding clips accommodate on one side 5 \times 2 ml. and 2 \times 5 ml. syringes, and on the other 4 \times 10 ml. and 1 \times 20 ml. In my daily outpatient clinic one container is usually enough. Wards are given a stock according to experience. There appears to be no point in making the containers larger, because it is better for a busy ward to have more than one, and that all should be returned at short intervals for servicing.

The syringes clip on in an upright position but are not disturbed by shaking or if the container is laid on its side. The needle is protected by a glass tube measuring $3 \times \frac{1}{2}$ in. Round the neck of the needle and occluding the glass tube is a small plug of cotton-wool. So long as the wool is there, the needle is sterile; when a syringe is used, the wool is thrown away. After use the syringe is rinsed in cold water and returned to its place, the absence of the cotton-wool indicating that it has been used. The syringes are oiled or coated with silicone. The container is, of course, opened only for as long as is necessary to take out the syringe and closed immediately, and repeated cultures show that no detectable contamination of the interior takes place in ordinary use.

The containers pack very well in the ordinary dry oven and are sterilised by exposure to 160°C for 1 hour. The syringes may be (1) all glass, (2) glass with annealed metal nozzles, of which we use mainly Chance's 'Interchangeable,' or (3) glass with metal ends—e.g., 'Balco'—of which the cement stands up to dry heat. In practice the last-named proves best for ward use, and breakages since the introduction of such syringes in metal containers



The aluminium container with syringes.

have been greatly reduced. All these syringes are Luer fitting. Part of the servicing of the syringe is to test for air leakages, because although modern cements do not run at 160°C they become granular after a time and might not be airtight. They can, of course, be re-cemented. Aluminium containers have not entirely abolished cellophane-wrapped syringes, which may still have a place for certain functions and where only an occasional stand-by syringe is wanted.

In supplying small hospitals and clinics at some distance from a group laboratory these syringe containers appear to be ideal. No attempt has yet been made to calculate whether monetary savings could be made in a group by cutting down on sterilisers or on time spent on sterilising techniques in wards. If made they would be small in relation to the total budget. But in comparison with other syringe-service techniques there is a considerable saving of time, with the result that the output of syringes is greatly increased and the servicing charge per syringe greatly decreased.

Lumbar-puncture Sets

Lumbar puncture is not without its bacteriological hazards, and it is important that the equipment used should be completely sterile. Here again the old technique of boiling the needles and then bringing them to the patient's bed in a container either of water or of spirit was far from perfect. In addition to the lumbar-puncture needle there may also be needed a syringe for injection of a local anaesthetic, a syringe for withdrawal of cerebro-spinal fluid, and a manometer. In children's wards the manometer is seldom used, and the needle is usually shorter and finer than for adults.

Accordingly two sets of lumbar-puncture equipment are provided. For the children's ward an aluminium container measuring 8 x 2 x 1½ in. is lined with lint and packed with a needle protected by a glass tube, a 2-ml. syringe, and a 10-ml. syringe, the latter with 'Record'-size fitting because no lumbar-puncture needle appears to be made with Luer fitting. After sterilisation the aluminium container is sealed with tape. For adults a container measuring 15 x 2 x 1½ in. is packed with manometer, needle, and a 2-ml. syringe and sealed with tape. Wards carry a stock of these containers according to their experienced need, and the doctor doing a lumbar puncture can be sure that he has a complete set of sterile equipment ready to hand. Many manometers are sealed with a cement which does not stand dry heat, and in such a case the container is autoclaved.

Petri-dish Holders

Having had much difficulty with the copper containers for 4-in. glass culture plates which are traditional in every bacteriology department, we decided to try aluminium. To our surprise no supplier whom we asked knew of any firm making such containers, although spun aluminium for cylindrical containers is familiar to every housewife. Later it appeared that others had already tried this idea, and we are now using such a container. In practice it is superior in every way to the familiar copper box. It is seamless, will wear for years as domestic aluminium ware proves, and is cheaper.

Summary

Aluminium containers for syringes are described which make the provision of a sterile syringe service cheaper and simpler. Other aluminium boxes for lumbar-puncture needles and petri dishes are also described.

The prototypes of these boxes were paid for by a grant from the research fund of the South West Metropolitan Regional Hospital Board. Most of the details were worked out by Mr. G. Phillips, chief technician, in conjunction with Mr. W. M. England, of Messrs. R. B. Turner & Co. Ltd., to whom we are indebted for the illustration.

Reviews of Books

Tuberculosis in Childhood and Adolescence

F. J. BENTLEY, M.D., F.R.C.P., D.P.H., senior physician; S. GRZYBOWSKI, M.D., M.R.C.P., senior registrar, High Wood Hospital for Children, Brentwood, Essex; B. BENJAMIN, B.Sc., F.I.A., formerly statistician, London County Council. London: N.A.P.T. 1954. Pp. 259. 30s.

In their detailed account of the course of pulmonary tuberculosis in 1049 children between the ages of 3 and 15 years admitted to the High Wood sanatorium, Essex, during 1942-46, Dr. Bentley and his colleagues have clarified some aspects of the natural history of primary tuberculosis and have considered its epidemiology and incidence. They always have facts to support their views, and their opinions will interest everyone sharing in the care of children with primary pulmonary tuberculosis.

The opening chapter deals with terminology. Then follow chapters on simple primary pulmonary tuberculosis, on segmental lesions, on the influence of age on prognosis, on calcification and secondary infection, and on the management of primary infection. Finally, there are three chapters on chronic (bronchogenic) pulmonary tuberculosis in adolescents and its relation to primary infection. This is in some ways the most important section in the book, because it brings to our attention again one of the most pressing questions in tuberculosis today—that of adolescent phthisis. How often does the chronic disease follow primary infection acquired a short time earlier and incompletely healed, and how much is it due to exogenous reinfection? The importance of this question cannot be exaggerated, for half the children leaving school at 15 years fail to react to tuberculin and most of them are infected within the next few years. The related question—how does bronchogenic tuberculosis arise?—also receives fair treatment.

Tuberculosis is difficult to understand. Few people have the opportunity of seeing the whole picture in a population; the cycle of infection and the possibility of clinical illness spans many years and generations rather than individuals. The authors have tried to overcome the difficulty of dealing with selected material by their "death investigation." But retrospective examination of clinical notes is usually unsatisfactory, and this chapter does not carry the weight of those based on the authors' own data. Even so, it shows that contact clinic work alone, though desirable for other purposes, will not in itself prevent infection or the onset of the serious haemogenous or neurological complications.

This authoritative statement of the problem of the primary infection will help to focus attention on the fundamental importance of the primary infection in the natural history of tuberculosis. Production and print are excellent, and the reproduction of the radiographs is far above the usual standard. A book to have and use.

Abilities of Babies

A Study in Mental Measurement. RUTH GRIFFITHS, M.A., PH.D., DIP.ED., F.B.P.S. London: University of London Press. 1954. Pp. 229. 20s.

Dr. Griffiths points out that there are three main directions in which man's development differs from that of the higher animals: he achieves the erect posture; this frees the hands, which he uses in manipulative skills; and he learns to speak and to understand speech. "The arresting fact is that all these three aspects of development . . . are achieved by the average baby within the short span of the first fifteen months of his life. This is an enormous achievement . . . which lays the foundations of all that comes afterwards." Dr. Griffiths set out to observe the development of ability in many children under two years old, and finally to test 571 (mostly in infant-welfare centres) in order to establish a scale of development. This sort of thing has been done before, notably by Gesell; but it is all to the good to have a fresh investigation of a difficult subject, with standards based on Kensington instead of Connecticut. By careful investigations, Dr. Griffiths attempts to provide balanced scales of development in five directions—locomotor, personal-social, hearing and speech, hand-and-eye development, and performance (the ability to reason in practical situations or manipulate materials intelligently).

Without using her methods and comparing them with others it is difficult to know how far she has succeeded; but her care, and her own ability to see a situation whole, make an encouraging impression.

How much will this help a doctor trying to decide whether a baby is mentally defective, deaf, or emotionally deprived? Very little, directly, for most doctors (rightly) leave specific testing to the practised expert—though there is nothing in her tests that a physician whose work lay in this field could not master with ease if he took the trouble. On the other hand, the reports of the tests, which in this book are expressed as histograms of the quotients obtained in the five separate groups, should be very interesting. Thus one can see at a glance that although a deaf child has a G.Q. (general quotient) of 82, speech development is only 48, personal-social 75, and locomotor, hand-and-eye, and performance nearly 100. Graphical representation is as telling here as in reports of sugar-tolerance tests or audiograms. Dr. Griffiths does not, however, "claim any great predictive value for the new procedure," which has been in use for too short a time for the babies' test results to be compared with their performance in later childhood.

Mammalian Germ Cells

A Ciba Foundation Symposium. Editor: G. E. W. WOLSTENHOLME, O.B.E., M.B., assisted by MARGARET P. CAMERON, M.A., and JESSIE S. FREEMAN, M.B. London: J. & A. Churchill. 1953. Pp. 302. 30s.

THE twenty-four articles in this symposium provide lucid descriptions, further enhanced by discussions, of pioneer biochemical and endocrinological investigations in the assessment of the fertility of ova and spermatozoa.

The articles are almost equally divided between the two germ-cells and there is a slight preponderance of contributions from this side of the Atlantic. Most of the work is concerned with farm and laboratory animals; only three of the articles deal with human fertility. The fundamental problem is the search for ways of reducing Nature's waste of genetically valuable germ-cells, and the emphasis is on artificial insemination and superovulation. Of particular interest is the possibility of preserving the living germ-cells for long periods at low temperatures.

But all advances have possible drawbacks, and in his foreword Mr. S. J. Folley, D.Sc., F.R.S., gives a clear warning: "The technical advances foreshadowed by the researches reported in this volume are primarily envisaged as applicable to stockbreeding. The fact must be faced that they can also be applied to man, and society will have to consider seriously how best to handle these new possibilities which may be fraught with as much significance and danger of misapplication as the discovery of how to release the energy of the atomic nucleus."

Origins of Psycho-Analysis

Letters to Wilhelm Fliess, Drafts and Notes, 1887-1902. SIGMUND FREUD. Editors: MARIE BONAPARTE; ANNA FREUD; ERNST KRIS. Authorised translation by ERIC MOSBACHER and JAMES STRACHEY. London: Imago Publishing Co. 1954. Pp. 486. 30s.

In chapter XIII of his *Life of Freud* Ernest Jones has provided so illuminating an account of Freud's relationship with Wilhelm Fliess that most of the novelty of this remarkable correspondence has been anticipated. There is, however, much that rewards the reader interested in the birth-pangs of a revolutionary theory, and the intellectual and emotional crises of a man of genius. The book contains, moreover, drafts of various essays and notes which are significant for the early history of psycho-analysis, as well as Freud's lengthy and sustained, but unfinished, effort to provide a neurophysiological basis for psychology and to furnish us, as its opening sentence put it, "with a psychology which shall be a natural science; its aim, that is, is to represent psychical processes as quantitatively determined states of specifiable material particles"—namely, the neurones. Though it was doomed to failure at that stage of physiological and psychological knowledge, it was almost inevitable that the project should be attempted by a man of Freud's training and that it should contain, hidden behind anatomical and physiological terms, concepts that he

used freely in his subsequent purely psychological writings. The book is supplied with many helpful footnotes, and a concise introduction by Ernst Kris.

Microbiology and Human Progress

MADELEINE PARKER GRANT, PH.D., professor of biology and bacteriology, Sarah Lawrence College, New York: Rinehart. London: Allen & Unwin. 1953. Pp. 718. 48s.

"THIS college text was written for introductory courses in bacteriology . . . for students whose major interests may lie outside the field of science." Such eclectic opportunities in education are rare in our universities, and for this reason the idea deserves sympathetic attention. Professor Grant has read widely and her attempt to present the phenomena of microbiology as illustrations of general biological principles is imaginative and interesting. Almost half the book is devoted to the "microbic foes of man" and this is far less satisfactory. The shorter section on "microbic friends" is also disappointing, for such a book as this would have been a proper place to correct the popular view that bacteriology is the province of the doctor alone.

Surgery for Dental Students

MICHAEL F. A. WOODRUFF, M.D., M.S. Melb., F.R.C.S., professor of surgery, University of Otago. Oxford: Blackwell Scientific Publications. 1954. Pp. 307. 30s.

THIS useful book, based on a series of lectures given by Professor Woodruff when he was a lecturer in dental surgery at the University of Sheffield, is designed for dental students qualifying in this country, and its contents cover the set syllabus. Each subject is dealt with concisely, clearly, and economically, and the text is well illustrated by photographs. These will be very welcome to dental students, who encounter general surgical conditions all too rarely during their training.

The University of Leeds

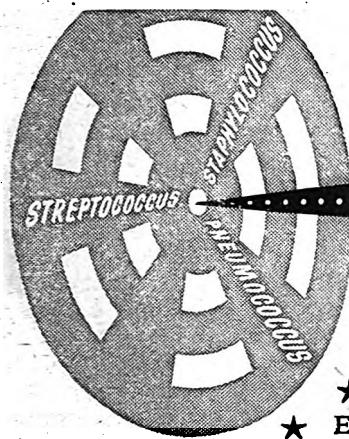
The First Half-Century. A. N. SHIMMIN, C.B.E., M.A., professor of social science, University of Leeds. Cambridge: University Press. (For the University of Leeds.) 1954. Pp. 230. 21s.

IN this handsome volume Professor Shimmin tells the story of how the university has honoured its motto "And Knowledge shall Increase." In the first part he traces the historical and geographical background to the university's growth and describes its rapid advance during the first fifty years.

The first step was taken in 1831, when the School of Medicine was opened. More than forty years later the Yorkshire College of Science was founded, and in 1887 the two bodies became part of the federal Victoria University, which split into the separate Universities of Manchester, Liverpool, and Leeds in 1903-04. The students are four times as many as in 1904, and it has been hard to keep a balance between science and arts. Professor Shimmin also discusses the problems of student welfare and the relationship of the city with the university, and in the second part of the book he describes the trend of present-day teaching and research in each faculty. Maurice de Saussure, the head of the department of fine art, has contributed graceful pen and wash drawings.

Arthur Rendle Short: *Surgeon and Christian* (London: Intervarsity Fellowship. 1954. Pp. 208. 8s. 6d.).—It is but eight months since Rendle Short died, and this interval does not allow of the effective critical appraisal he deserved. In this biography Mr. W. Melville Capper and Mr. Douglas Johnson, seeking to perpetuate the main message of his life and to throw into relief the principles which inspired it, give a good deal of space to his work for the Christian Brethren of Bristol and the West Country, but there are also interesting sections on his experiences as an undergraduate student, a young doctor, and a surgeon on the staff of a teaching hospital. Here much of the material is autobiographical, including his characteristic description of the day he thought that he had bungled hopelessly his final F.R.C.S. examination. "Filled with gloom and despair I took myself to a scientific library and got down a copy of the *Quarterly Journal of the Geological Society* containing Vaughan's paper on the Carboniferous. It was immensely comforting."

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See "LANCET" July 22nd 1899 p. 219



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THE LANCET

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Beyond Spens

THE Government's decision to find another £3 $\frac{1}{4}$ million a year for hospital doctors was surprising. At a time when taxation is too heavy, when wage claims are strongly discouraged, and when hospitals are being asked to cut their expenditure, it cannot have been convenient to add so large a sum to the incomes of a small number of people who, in the eyes of the public, are already well off. The decision was made for two reasons: first, because the Danckwerts award tipped the balance so far in favour of general practice that recruitment of able young doctors to the specialties was endangered; and, secondly, because some members of the Cabinet felt that consultants had not had a fair deal. The unfairness, of course, lies in the fact that, though the Government of the day accepted the reports of both the medical Spens Committees—on the remuneration of general practitioners and on the remuneration of hospital doctors—quite different "betterment factors" have been applied to practitioners and to consultants in translating the Spens 1939 figures into post-war money. Under the Danckwerts award practitioners gained 100% betterment; and though this was not distributed equally among them, and was conditional on a reduction in the size of the larger lists, their allowance for changes in the cost of living became far higher than the betterment factor of about 20% which was given to hospital staffs. Thus nobody could pretend that the financial recommendations of the second Spens Committee had really been fulfilled, and in making amends to the tune of £3 $\frac{1}{4}$ million the Government still fall short of fulfilling them. On the other hand, from the time that consultants accepted their contracts in 1949 there has been no legal obligation on the Government to revise the terms of these contracts; and if, as some suggest, hospital consultants are now to say "thank you for nothing" and press implacably for "every penny of Spens," they should remember that moral obligations are seldom as precisely assessable as legal ones. A moral claim—that is to say, a claim to what fair-minded people will think proper—differs from a legal claim in that the field of inquiry is larger.

The first Spens Committee was asked to consider "what ought to be the range of total professional income of a registered medical practitioner in any publicly organised service of general medical practice," and it concluded that before the war too many general practitioners had too low an income. Accordingly it recommended a range of remuneration which it hoped would increase the financial attractions of general medical practice both as against other professions and as against other branches of medicine; and, thanks to the Danckwerts award, this hope has

now been fulfilled. The second Spens Committee was asked to consider "what ought to be the range of total professional remuneration of registered medical practitioners engaged in the different branches of consultant and specialist practice in any publicly organised hospital or specialist service." Though it wanted to raise the financial status of men and women in training, it was concerned to maintain, rather than improve, the situation of the specialist or consultant, and its proposals were designed to give him, in relation to other people, a position such as he held before the war. On a general view, it is arguable that this object, too, has been attained¹—at least for the part-time consultant, whose opportunities for private practice remain greater than was expected. The relatively unsatisfactory position of the whole-time consultant might best be dealt with, not by any general raising of consultant remuneration but by applying the Spens recommendation about expenses to the whole-timer and by allowing him to take fees for domiciliary consultations—a change which is demonstrably desirable for the proper working of the service.²

The post-war redistribution of national income in favour of the wage-earner, and the taxation by which it is maintained, have combined with rising prices to hit the salaried middle classes; and few among them can afford the amenities of 1939, at any rate if they are paying for the private education of children. Hence the adequacy of doctors' remuneration cannot be judged simply by whether they feel that they are comfortably off. The ultimate test is whether the main purpose of the Spens proposals has been achieved: do enough recruits of the right type still apply to take up medicine, and do enough doctors of the right type think it worth their while to train for a specialty? Certainly the public will be ill served if doctors cannot maintain a decent standard of life or if they are preoccupied with getting money or making ends meet. They will be even worse served if too many intelligent boys and girls decide that medicine is too unremunerative for them to take up, or if too many intelligent doctors decide that they cannot afford to be anything but general practitioners. In so far as it has reason to believe that any of these things are happening or likely to happen the profession can reasonably urge that scales of payment should be altered. But whatever claims it makes for revision of remuneration in the National Health Service should arise from the requirements of that service at the time of the claim. The public interest is a sounder basis for negotiation than the litigious reiteration of former rights whose present validity is in doubt.

The two medical Spens reports were brilliant and influential documents, and the one on consultants and specialists showed exceptional insight and foresight. It abolished the state of affairs by which many doctors could not afford to train as specialists unless they had private means. It gave the same basic pay to consultants in London teaching hospitals and in the district hospitals of the remotest region, and to those in the oldest and in the newest specialties. It introduced a novel system by which, while age and service had their due, allowance was made for out-

1. Central Consultants and Specialists Committee, Bulletin no. 3; pp. 4 and 7.
 2. See *Lancet*, Jan. 23, 1954, p. 210.; Feb. 13, p. 366; Feb. 20, p. 412.

standing merit. At a time of egalitarian revolution, it insisted that the range of remuneration should remain wide. And finally it introduced the principle that experts working in a public service should have the kind of livelihood they could earn outside it—a principle repugnant to many administrators but profoundly important if public services are to be more than second-rate. Nevertheless, though in all this "consultant Spens" justifies its description as a charter, it scarcely qualifies as an infallible work of revelation. In the first place (assuming equal betterment over 1939 money values) it made the remuneration of specialists so superior to that of practitioners that it defeated the intention of the previous Spens Committee, which wanted to make general practice "sufficiently attractive to prevent all the abler men endeavouring to enter specialist practice." Equally serious, however, was its failure to make any distinction between consultants and specialists, and its consequent assumption that all the doctors in a hospital were either consultants or were training to become consultants. As soon as the Ministry of Health began to consider the offer of contracts, it could not but observe that in many departments of medicine—notably in psychiatry, pathology, venereal diseases, and tuberculosis—there are not a few doctors whose continued services are very necessary to the hospital but to whom their colleagues turn as specialists rather than as consultants. To meet this difficulty the Ministry, with the reluctant acquiescence of the profession, made a major departure from the Spens charter and invented the grades of senior hospital medical officer (S.H.M.O.) and junior hospital medical officer, tenable only in certain specialties. Up to now the representatives of the profession have been unwilling to agree to appointments to this grade in the main departments of medicine; for, with good reason, they fear the possibility that administrators, intent on saving money, may see in such lesser appointments a means of economising on consultants. But here again, when it comes to running the hospitals, we come up against hard facts. If, in order to prevent future disappointment, the number of young men allowed to train for consultant posts is henceforward to be strictly related to the number of consultant posts expected to fall vacant, there will no longer be enough trainees in the hospitals to ensure that the necessary medical and surgical work gets done. Much essential work is undertaken by those senior registrars who, because they have not yet secured posts as consultants or S.H.M.O.s, are now described as redundant. The truth is that few if any of these are really redundant; and, if our existing system has no place for them, we shall evidently have to make such alterations in the system as will enable them to go on using their skill to advantage. This is as necessary for the sake of the hospitals as it is for the sake of the registrars themselves, who were encouraged by the Ministry and the profession to train themselves for consultant posts which have not materialised. Their plight has become a standing reproach to us all.

What seems to be needed to restore health to the hospital medical service is that all parties shall agree to go back to the point where the Spens Committee (as we can now see) failed in prescience—the point at which it lumped consultants and specialists

together. In our opinion the proper title for a person who has completed his training in a specialty, or has spent some years in specialised activities, is that of specialist, and we see no reason why appointment as a specialist (working under some degree of supervision by a consultant) should not be the route by which consultant rank is normally approached. The transference of S.H.M.O.s to the new grade would not only give them a more suitable title but also rescue them from a backwater where no current flows—a backwater from which very few have been able to regain the main stream. To the registrars who have been miscalled redundant, appointment as specialists would give time to prove their capacity to become consultants, or at the worst it would enable them to continue (as members of a team though not at its head) the kind of work they have chosen. To achieve these ends without jeopardising the position it has to defend, the Joint Consultants Committee will doubtless have to make conditions: it will need power, for example, to control, with the Ministry, the numerical relationship of specialist and consultant posts. But we feel sure that better and more rational arrangements can be made for hospital medical staff—provided consultants are ready to think beyond the Spens report and to follow the spirit rather than the letter of that famous text.

Renin

ALMOST sixty years ago TIGERSTEDT and BERGMAN¹ showed that the injection of a saline extract of fresh rabbit kidney into normal rabbits caused a rise of arterial blood-pressure. They recognised that with repeated injections the pressor effect diminished and eventually ceased—a feature termed tachyphylaxis. Despite a vast amount of investigation the significance of the renal pressor agent, known as renin, in human hypertensive disease is still far from certain. Renin is a protein enzyme obtained from renal cortex which reacts with its substrate, hypertensinogen (a plasma alpha-globulin), to form a substance of smaller molecular weight known as hypertensin. This is probably a polypeptide and is the active pressor agent, renin being inactive in the absence of its substrate. Hypertensin is labile and is rapidly destroyed and inactivated by a plasma enzyme known as hypertensinase. SKEGGS et al.² have recently shown that the chemical reactions involved are complex. By a counter-current distribution process they have separated hypertensin into two polypeptide fractions, which they term hypertensin I and II. The former is rapidly converted into the latter by another plasma enzyme. Both are active pressor agents and caused very considerable increases of both systolic and diastolic blood-pressure when injected intravenously in volunteers.

PICKERING and PRINZMETAL³ showed that the blood-pressure of rabbits starts to increase about thirty seconds after an injection of renin, the highest pressure being reached about two minutes after the injection; the pressor effect usually lasts thirty minutes or longer. Despite the property of tachy-

1. Tigerstedt, R., Bergman, P. G. *Skand. Arch. Physiol.* 1898, 8, 223.

2. Skeggs, L. T., Marsh, W. H., Kahn, J. R., Shumway, N. P. *J. exp. Med.* 1954, 99, 275.

3. Pickering, G. W., Prinzmetal, M. *Clin. Sci.* 1938, 8, 211.

phylaxis, BLACKET et al.⁴ have maintained hypertension in rabbits for as long as two weeks by infusing renin. The cardiac output is somewhat reduced after injections of hypertensin in man,^{5,6} the pressor effect being entirely due to peripheral vasoconstriction. The glomerular filtration-rate tends to rise and renal blood-flow falls considerably⁷; these differential effects are usually held to indicate constriction of the efferent glomerular arteriole. Such circulatory and renal haemodynamic findings are similar to those in essential hypertension,⁸ but unlike those in acute glomerulonephritis⁹ where afferent arteriolar constriction is thought to occur. DANIEL et al.¹⁰ have further investigated the effects of renin on the renal circulation of the rabbit by an angiographic technique. Angiograms taken shortly after the peak of the pressor response showed constriction of the smaller intrarenal arteries and increased renal circulation-time. In half the animals the ischaemia involved chiefly the peripheral cortex; in the rest it was more generalised. Some renal vasoconstriction was still present shortly after the blood-pressure had returned to normal. It seems very unlikely that renin is directly concerned in the aetiology of essential hypertension in man. HAMILTON et al.¹¹ have found that the condition we speak of as essential hypertension cannot be strictly defined, there being a continuous variation of blood-pressure levels in any group of selected age and sex, with no evidence of any natural division between hypertensive and normotensive people. HAYNES et al.¹² found no significant difference in the content of renin in blood obtained by catheterisation of the renal vein in patients with hypertension of varied origin and in control normotensive patients. A humoral mechanism is perhaps most likely in hypertension secondary to unilateral renal disease—usually chronic pyelonephritis^{13,14}—but the part played by renin has not been exactly defined either in this clinical disorder or in experimental hypertension secondary to renal ischaemia. In particular we are completely ignorant of the reason why some cases of chronic pyelonephritis are associated with hypertension while some are not.¹⁵

Renin has been shown to have a distinct diuretic effect in the rabbit and the rat—an effect that has not been demonstrated unequivocally in other species. PICKERING and PRINZMETAL¹⁶ showed that in rabbits injection of renin produced extreme diuresis, with increased loss of sodium and chloride, associated with proteinuria amounting to 100 mg. per 100 ml. ADDIS et al.¹⁷ described similar findings in the rat, but the proteinuria was more severe. Inactivation of renin

with respect to the pressor response led to loss of capacity to produce proteinuria. In the adrenalectomised animal the production of proteinuria was almost abolished. HUGHES JONES et al.¹⁸ showed that hypertensin was similarly active in causing polyuria in rabbits. The diuresis was shown to be due to inhibition of tubular capacity selectively to reabsorb sodium, chloride, and water. The sodium-chloride content of the urine approximated to that of plasma—which is typical of osmotic diuresis. It seemed most improbable that the diuretic effect was directly due to the pressor response. The polyuria was in some cases greatest when the blood-pressure had fallen to normal levels, and when the changes of the condition of glomerular filtration (shown by a raised filtration fraction) had disappeared. CROXATTO et al.¹⁹ have further investigated this diuretic effect in rats. Adrenalectomy or hypophysectomy inhibited the response, but selective extirpation of the adrenal medulla was without effect. The administration of either cortisone or deoxycortone restored the response to normal. The greatest polyuria observed was in an animal which excreted in one day urine amounting to 42% of its body-weight. It seemed in general that sodium depletion tended to inhibit, and sodium excess to increase, the diuretic response. Since the dose of renin necessary to produce diuresis is greater than the effective pressor dose, it might be unsafe to extend similar observations to man. The fact that deoxycortone restored the diuretic response in adrenalectomised animals is of especial interest. It is now well known that cortisone restores the impaired diuretic response to ingested water in Addison's disease, whereas deoxycortone is inactive in this respect. A recent report²⁰ on the administration of the natural salt-retaining hormone of the adrenal cortex (aldosterone or electrocortin) in the treatment of Addison's disease suggests that this steroid is also inactive in restoring the diuretic response.

Encephalitis Viruses

In the past thirty years we have learnt a good deal about the relationship between the many different viruses of epidemic encephalitis. Between 1915 and 1926 world-wide outbreaks of von Economo's disease appeared suddenly and then faded, leaving behind a residue of postencephalitic parkinsonism. The aetiological agent of von Economo's disease was never discovered, but its winter epidemic incidence differentiates it from newer forms of epidemic encephalitis which have appeared or been recognised since. The newer forms are usually localised to a particular geographic area which may appear to enlarge as investigations uncover more infected areas. The encephalitides include Australian X disease, recently identified with Murray Valley encephalitis²¹; the closely related Japanese B encephalitis, the virus of which has been responsible for outbreaks in Japan, China, Korea, and Malaya; the encephalitides of the

4. Blacket, R. B., Depoorter, A., Pickering, G. W., Sellers, A., Wilson, G. M. *Ibid.* 1950, 9, 223.
5. Bradley, S. E., Parker, B. *J. clin. Invest.* 1941, 20, 715.
6. Wilkins, R. W., Duncan, C. N. *Ibid.* p. 721.
7. Corcoran, A. C., Page, I. H. *Amer. J. Physiol.* 1940, 130, 335.
8. Goldring, W., Chasis, H., Ranges, H. A., Smith, H. W. *J. clin. Invest.* 1941, 20, 637.
9. Black, D. A. K., Platt, R., Rowlands, E. N., Varley, H. *Clin. Sci.* 1948, 6, 295.
10. Daniel, P. M., Prichard, M. M. L., Ward-McQuaid, J. N. *J. Physiol.* 1954, 124, 106.
11. Hamilton, M., Pickering, G. W., Fraser Roberts, J. A., Sowry, G. S. C. *Clin. Sci.* 1954, 13, 11. See *Lancet*, June 12, 1954, p. 1224.
12. Haynes, F. W., Dexter, L., Selbel, R. E. *Amer. J. Physiol.* 1947, 150, 198.
13. Langley, G. J., Platt, R. *Quart. J. Med.* 1947, 16, 143.
14. Pickering, G. W., Heptinstall, R. H. *Ibid.* 1953, 22, 1.
15. Longcope, W. T. *Ann. intern. Med.* 1937, 11, 149.
16. Pickering, G. W., Prinzmetal, M. *J. Physiol.* 1940, 98, 314.
17. Addis, T., Barrett, E., Boyd, R. I., Ure, H. J. *J. exp. Med.* 1949, 89, 181.

18. Hughes Jones, N. C., Pickering, G. W., Sanderson, P. H., Scarborough, H., Vandenbroucke, J. *J. Physiol.* 1949, 109, 288.
19. Croxatto, H., Barnafi, L., Camazon, L., Parra, V. *Endocrinology*, 1954, 54, 239.
20. Mach, R. S., Fabre, J., Duckert, A., Borth, R., Ducommun, P. *Schweiz. med. Wschr.* 1954, 84, 407. See *Lancet*, June 12, 1954, p. 1226.
21. Burnet, F. M. *Amer. J. publ. Hlth.* 1952, 42, 1519.

American continents (St. Louis, Eastern, Western, and Venezuelan equine); Russian Far Eastern encephalitis, reported from Russia and Siberia and recently from Czechoslovakia and Jugoslavia; and the closely related louping-ill, an encephalitis of sheep, rarely of man, in Scotland and the north of England, and our only representative of this group. The infectious agents of these diseases have some properties in common. They all characteristically produce summer outbreaks; all are small viruses with an extraordinarily wide natural and experimental host-range; and all are transmitted by biting arthropods. The localised geographic distribution of these infections, in contrast to the world-wide distribution of measles, influenza, and poliomyelitis, shows that man does not form the staple diet of the encephalitis viruses. Man is, in fact, a wholly dispensable link in a chain of infection which is made up in different cases of such widely different creatures as monkeys, horses, cattle, birds, mosquitoes, and ticks.

The relationship of the encephalitis viruses to one another and to certain tropical viruses, such as West Nile, Semliki Forest, and Bunyamwera viruses, has lately been investigated. OLITSKY²² has suggested that many of these viruses may have had a common ancestor whose behaviour in different areas was conditioned by local insect vectors or animal and bird reservoirs of infection, and he cites the typhus group of diseases as a useful analogy. The demonstration of viral haemagglutinins in tissues infected with some neurotropic viruses²³ and subsequently with various arthropod-borne viruses^{24 25} suggested a new weapon for research into these diseases. CASALS and BROWN²⁶ have taken full advantage of this method, and by modifying the technique for extracting viral haemagglutinins they have been able to study haemagglutination by many different arthropod-borne viruses. They find that these viruses can be divided into two groups, on the basis of the temperature and pH required for the agglutination reaction. Group A, which require 37°C and pH 6.4, comprise Eastern, Western, and Venezuelan encephalitis and Sindbis, a virus recently isolated in Egypt. Group B, which agglutinate at 4°C or 22°C and pH 7.0, comprise dengue types 1 and 2, Ilhéus, Japanese B, Ntaya, St. Louis, Uganda S, West Nile, and yellow-fever viruses. Serological tests by the agglutination-inhibition reaction have confirmed the groupings; there were considerable cross-reactions among viruses within the A and B groups but none between sera of one group and viruses of the other. Indirect evidence also suggests that Semliki Forest virus belongs to group A and Russian Far Eastern and louping-ill viruses to group B. Earlier serological studies by neutralisation and complement-fixation tests had shown some cross-reactions among these viruses; and SMITHBURN²⁷ has now completed an intensive study of this subject. He has carried out cross-neutralisation tests in mice with most of the arthropod-borne viruses investigated by his colleagues,²⁸ and has found some new relationships not hitherto revealed by neutralisation tests. His findings

22. Olitsky, P. K. *Amer. Nat.* 1946, 80, 401.

23. Hallauer, C. *Schweiz. Z. Path.* 1946, 9, 553.

24. Sabin, A. B., Buescher, E. L. *Proc. Soc. exp. Biol., N.Y.* 1950, 74, 222.

25. Chanock, R. M., Sabin, A. B. *J. Immunol.* 1953, 70, 271.

26. Casals, J., Brown, L. V. *J. exp. Med.* 1954, 99, 429.

27. Smithburn, K. C. *J. Immunol.* 1954, 72, 376.

agree in general with those of CASALS and BROWN, although the groupings shown by agglutination-inhibition tests are much clearer than those with neutralisation tests.

These most important studies may open the way to an understanding of how the different viruses have evolved from common ancestors, and of the factors underlying host differences and variations in virus pathogenicity in different areas. Perhaps, too, once these viruses have been neatly classified they may become more amenable to the efforts of those who are trying to domesticate them.

Annotations

BIRTHDAY HONOURS

ALL who have heard Sir Russell Brain's speeches and addresses in the past few years will have enjoyed their individual mixture of freshness and wisdom, and the remarkable range of his understanding. They will join with the fellows of his college in welcoming the new honour bestowed on a president who has the rare gift of bringing philosophy into affairs. Of the new knighthoods only one is conferred on a member of our profession in this country; but the choice is a most happy one, for Mr. R. C. Brock is one of those men who make medical history as well as writing about it. With his cardiologist colleagues at Guy's he has helped to turn the possible into the practicable and the practicable into the useful, and in so doing has shown himself one of the most able exponents of one of the most progressive parts of surgery. It is a pleasure also to record the knighthoods conferred on two Australian colleagues, Dr. A. P. Murphy, P.R.A.C.P., and Mr. H. H. Schlink, and the various appointments to Orders which are set out on p. 1287.

RECOVERY HOMES

NOWADAYS patients well enough to leave hospital are not necessarily well enough—as the almoners have lately pointed out¹—to go to convalescent homes; for such homes are not staffed or equipped to look after people who need any nursing or other special care. The convalescent homes committee of the King's Fund, with Sir Henry Tidy as chairman, have been looking into the "recovery homes" which some hospitals maintain, in order to decide what value they might have for the hospital service as a whole.² The committee thought at the outset that some existing convalescent homes might be adapted to take patients in the earlier stages of recovery, but experience has convinced them that it would not do. Most homes of the kind are not structurally suitable, nursing staff would be hard to get, and maintenance costs would go up. Recovery homes are set up and maintained by hospitals, which can of course supply the nurses. Only a few of the Metropolitan hospitals—and none of the London teaching schools—have recovery homes; but several large general hospitals elsewhere have established them, to relieve pressure on their beds. The Astley Ainslie Institution, attached to the Royal Infirmary at Edinburgh, the pattern recovery home of the country, defines itself as providing accommodation

"for patients in whom the disease has definitely begun to abate, or the risk of complications after operation is only slight, so that with proper care and nursing the patient is likely to progress to recovery."

The committee have adopted this definition. They visited ten hospitals and their country recovery homes,

1. Report on Convalescent Homes, to the Ministry of Health. Institute of Almoners, Tavistock House North, Tavistock Square, London, W.C.1; and see *Lancet*, June 5, 1954, p. 1176.

2. Recovery Homes. King Edward's Hospital Fund for London, 10, Old Jewry, London, E.C.2. Pp. 23. 1s.

and found the hospital authorities enthusiastic about the value of the plan. With one exception (a London hospital, far from country places) the homes were within a dozen miles of their parent hospitals.

All the authorities agreed that the home should be an integral part of the hospital, which supplies stores, food, drugs, and general services. The patients are visited at regular convenient intervals by senior residents and members of the consulting staff. At the homes which are over twelve miles from the parent hospital, the hospital arranges for a general practitioner to be on call in an emergency. About half the nursing staff are State-registered, and more or less permanent; student nurses take a turn of duty there, and find it stimulating, partly because of the rapid turnover of patients and partly because the trained staff have time to teach. The patients need the same skilled nursing care, and the same medical attention, as they would be getting in hospital, and the home provides it. Pre-students are sometimes allowed to do minor offices in the home; and this seems to be the one place where such young people may safely be allowed to come into contact with patients. (Such homes may therefore prove good training places for nursing cadets.) No operating-theatre or X-ray or other expensive equipment is needed, for these are all provided at the parent hospital.

The patients most suitable for admission are those with moderately severe medical, surgical, or gynaecological conditions who need 12-15 days in hospital and about the same time in the home. Long-term orthopaedic, geriatric, or chronic cases should be sent elsewhere, for they quickly block beds and change the whole spirit and purpose of the home. The hopeful name, the change of scene, and the rapid turnover in population all have a part to play in helping patients to recover quickly, and go back home: at the end of their stay they should not need convalescent care as well. If patients are properly selected, only about 30% of the medical, surgical, and gynaecological beds will be found to be discharging their occupants to the home. A common fear among hospital authorities who have not set up such homes is that the increased turnover in the wards may throw too much extra work on the nursing staff. In fact there have been no complaints of overwork from ward staff; and even where the rate of turnover is at its highest the addition of one extra nurse to the ward has been enough to cope with it.

Hospitals usually buy country houses to convert into recovery homes. These commonly have good grounds in which patients can refresh themselves, and which will also provide a large part of the vegetables and fruit needed. One such house was converted at a cost of £800 per bed, and another at a cost of only £470 per bed. The cost of maintaining a patient in a recovery home is less than half the cost of maintaining him in hospital, so the total cost per patient falls. Though hospital waiting-lists are reduced, and turnover increased, the committee could not find any evidence of a recognisable increase in the maintenance costs of a parent hospital as a result of having a recovery home. These findings should reassure hospital authorities longing for a recovery home but fearing to take the plunge; it should also wake a spirit of adventure in those who have not so far contemplated the possibility.

NEEDLE BIOPSY OF LUNG

THE investigation of a case in which radiography has shown a pulmonary lesion often reaches an impasse, with no clue to the diagnosis from bronchoscopy and bronchography and examination of sputum or bronchial secretions for malignant cells, fungi, and tubercle bacilli. In these circumstances needle biopsy under fluoroscopic control is tempting; but, because of the dangers of air-embolism, haemorrhage, and the dissemination of

infected material or neoplastic tissue, most physicians prefer to transfer the case to the surgeon for exploratory thoracotomy. Dutra and Geraci¹ recommend needle biopsy of the lung for a limited class of cases: the clinical evidence should point to an incurable malignant condition, the lesion should be peripheral, and attempts by other methods to clinch the diagnosis should have failed. The area of skin nearest the mass is found by fluoroscopy and marked, and the biopsy is done with a Vim-Silverman needle. They consider that needle biopsy should not be done if surgical treatment seems feasible—a point that is emphasised by one of their cases in which an implant of neoplastic cells in the needle track led to a subcutaneous tumour.

ADRENAL HYPERPLASIA AND NEOPLASIA

In the adrenal glands either a tumour (usually unilateral) or hyperplasia (which is bilateral) can produce virilism.² The abnormality is associated with a large excretion of 17-ketosteroids in the urine. When congenital it produces macrogenitosomia praecox in the male and pseudo-hermaphroditism in the female; there is often also a defect in the regulation of salt metabolism.^{3 4} If the abnormality arises after the external genitalia have developed in the fourth month of foetal life, then in the female the result is simply virilism, with hirsutism and enlargement of the clitoris. The male still shows macrogenitosomia if the lesion is prepubertal; since the adrenals are responsible for the abnormal output of hormone, the testes remain infantile, and in this way the disorder can be distinguished from other types of precocious puberty in the male. It is obviously difficult to recognise the abnormality in the male after puberty.

In congenital cases hyperplasia is the usual lesion; but otherwise a tumour—not necessarily malignant—is more common than hyperplasia, particularly before puberty. In either case the pattern of steroids secreted by the adrenal is abnormal.^{5 6} Jailer et al.⁷ have ably reviewed the effect of large doses of cortisone on the high output of 17-ketosteroids. From their own wide experience, and from the results reported by others, they show that cases of hyperplasia respond with a fall in 17-ketosteroids whereas cases of tumour do not. Cortisone usually produces a remission in virilism associated with adrenal hyperplasia, presumably by inhibiting the pituitary; but tumours of the adrenal seem to be independent of pituitary control and operation is the only treatment.

In Cushing's syndrome the secretion of the normal adrenal hormone is excessive; but there may be an abnormal pattern, and virilism and Cushing's syndrome can occur together. Although the results were less clear-cut than in virilism—the excretion of 17-ketosteroids in Cushing's syndrome is not necessarily very high—Jailer et al. found that the "cortisone test" may also be useful in differentiating tumour and hyperplasia of the adrenal in Cushing's syndrome. A tumour requires a unilateral operation. For hyperplasia producing Cushing's syndrome bilateral subtotal adrenalectomy may be required if the condition is progressive and disabling; destruction of the pituitary has also been tried successfully.

These are uncommon diseases. Virilism must be distinguished from simple hirsuties, and adrenal virilism

1. Dutra, F. R., Geraci, C. L. *J. Amer. med. Ass.* 1954, **155**, 21.
2. Jailer, J. W. *Bull. N.Y. Acad. Med.* 1953, **29**, 377.
3. Wilkins, L., Fleischmann, W., Howard, J. E. *Endocrinology*, 1940, **26**, 385.
4. Harris, C. F., Scowen, E. F. *Arch. Dis. Childh.* 1951, **26**, 423.
5. Pond, M. H. *J. Endocrin.* 1954, **10**, 202.
6. Bongiovanni, A. M., Eberlein, W. R., Cara, J. *J. clin. Endocrin.* 1954, **14**, 409.
7. Jailer, J. W., Gold, J. J., Wallace, E. Z. *Amer. J. Med.* 1954, **16**, 340.

from that produced by hypothalamic,⁸ pituitary, and gonadal disorders.² The diagnosis of Cushing's syndrome requires evidence of adrenal over-activity; and many women with obesity, hirsuties, hypertension, and diabetes have not got this syndrome. But the few unfortunate patients who have adrenal disorders can often be helped.

TOWARDS CLEAN AIR

FOR centuries private citizens and public committees have talked of smoke abatement. The outlook, however, has so steadily darkened that the "six counties overhung with smoke" which William Morris found such difficulty in forgetting, are now indistinguishable from most of their neighbours. The National Smoke Abatement Society (N.S.A.S.) in a memorandum¹⁰ addressed to the Committee on Air Pollution (the Beaver Committee), say that the reason effective action has never been taken is because there has never been an informed determined public demand for it. The London fog disaster of 1952, however, sharply increased interest in air pollution; and people are readier than they have ever been to attend to its causes and press for remedies.

The society believe the subject to be of such importance that smoke prevention should be among the first factors considered when the use of fuels is under discussion; and that all fuel policies, developments, and propaganda which are not in the interests of smoke prevention (such as propaganda for the overnight use of bituminous slacks on domestic fires) should not be countenanced. No change in legislation would be needed to achieve this—only a change in outlook among those responsible for fuel policies. Many other preventive measures could be applied under the existing laws: coal could be better cleaned, so that it emitted less sulphur dioxide and grit when it was burned; different types of plant could use appropriate grades of coal for smoke prevention, and the quality supplied could be consistent; stokers could be better trained; fuel-burning plant could be better maintained and managed, and the rate of modernising plant could be hastened; both in industry and in the home the use of gas and electricity could be extended; and the replacement of raw coal with solid smokeless fuel might proceed much faster than it does. Some 37 million tons of smokeless fuel is produced annually in Great Britain, of which only 5 million tons is available for domestic purposes. It has been estimated that—partly by increased production and partly by withdrawals from other markets—10 million tons could be made available for domestic use by 1957, and 15 million tons by 1962. Meanwhile the society urge that available supplies of smokeless fuels should be sent to areas which will benefit most from their use—such as smokeless zones.

Naturally research is needed, not only to develop new processes for the production of smokeless fuel, but on such pollution problems as the removal of sulphur dioxide, grit, and dust from flue gases; and on the pollution caused by steel and clay industries, coke ovens, cement manufacture, lime-burning, chemical processes, and road-vehicle exhausts. The last is an up-and-coming nuisance which we should do well to scotch in time. Diesel fumes thicken on our roads; and the plan to exchange London's 1800 clean and silent trolleybuses for diesel-engine motor-buses has already caused many protests.¹¹

Again, the N.S.A.S. think that local authorities proposing schemes for reducing air pollution get too

little encouragement. Initiative of this kind, they say, should be not only approved but stimulated by the Government; for too many local authorities are still inactive.

The law about smoke has remained substantially the same for three-quarters of a century, and is almost entirely of the too-late variety (in the sense that action can only be taken after a nuisance has been caused). The society suggest that new legislation should not only give local authorities better powers for setting up smokeless zones but should enable them to proceed against manufacturers whose chimney emissions exceed prescribed standards. It should also oblige manufacturers who are putting in new fuel-burning plant to have their plans approved beforehand by the local authority. Moreover, all boiler-men and furnace-men should be required to hold a certificate of proficiency; and local authorities should be obliged to employ only fully qualified smoke inspectors. Finally, the society suggest, the installation in houses or hotels of grates which cannot burn smokeless fuel should be prohibited.

The society, in their steady education of the public in this matter, have done good work and done it on a very small budget. They are fully justified in suggesting that they deserve a Government grant towards it, for no agency is better placed for creating the informed public opinion which alone can lift the cloud from us.

RECURRENT PANCREATITIS

PANCREATITIS is apparently commoner in North America than here. Several accounts of this disease have appeared in the U.S.A. during the last few years¹⁻³; and at the recent meeting in London of the American College of Surgeons Prof. Walter C. MacKenzie described his extensive experience of it in Canada.⁴ According to Phillips,⁵ it is usually a chronic relapsing disorder in middle-aged alcoholic men. There is a fairly characteristic pattern of attacks of upper abdominal pain, recurring on average three or four times a year, which are often precipitated by alcoholic or dietary indiscretion or by worry or fatigue.² The attack may be mild, lasting only a few hours, or of the severe "acute haemorrhagic" type that continues for several days. Vomiting is usual and there may be mild diarrhoea; pyrexia is seldom pronounced; loss of weight during the attack may be severe. In uncomplicated cases the patients are free of symptoms between attacks. Eventually fibrosis may lead to cyst formation or to calcification, which may be localised or diffuse. Occasionally severe fibrosis may produce bile-duct obstruction, but this is probably rare.

Confirmation of the diagnosis by clinical tests is often difficult. Radiographic evidence of pancreatic calcification, the presence of steatorrhoea, creatorrhoea, or glycosuria, or a raised serum amylase or lipase level are highly significant. But such evidence is to be expected only in severe attacks or when repeated episodes have considerably damaged the gland. In mild attacks and between bouts, investigations often yield negative results. Examination of the duodenal contents after administration of secretin has been recommended, but this test is tedious and difficult and the results are inconstant. With pancreatitis, as with so many diseases, the case-history is often a better guide than a group of tests. The acute episode is best treated conservatively with analgesics (but not morphine) and antibiotics. Atropine or, better, 'Probanthine' is given to decrease gastric and pancreatic secretion, and to relax the

8. Morley, T. P. *J. clin. Endocrin.* 1954, 14, 1.

9. Bauer, H. G. *Ibid.* p. 13.

10. To be had from the National Smoke Abatement Society, 30, Grosvenor Place, London, S.W.1. 1954. Pp. 15. 1s.

11. *Times*, May 6, et seq.

1. Malmon, S. N., Kirsner, J. B., Palmer, W. L. *Arch. intern. Med.* 1948, 81, 56.

2. Hersperger, W. G. *Sth. Med. J.* 1949, 42, 289.

3. Phillips, A. M. *Arch. intern. Med.* 1954, 93, 337.

4. See *Lancet*, May 29, 1954, p. 1126.

sphincter of Oddi; in an acute attack withdrawal of secretion through a Ryle's tube is valuable. Operation between attacks may be necessary if cysts are present, or to deal with associated biliary-tract infection. In addition, thoracolumbar sympathectomy, vagotomy, sphincterotomy, and pancreatectomy—alone or in various combinations—have all been tried, and "beneficial results are reported after each procedure."⁵

The cause of pancreatitis is still undetermined. Opie⁶ suggested that it is due to reflux of infected bile along the pancreatic duct, and this view has been widely held. There are, however, several objections to it, the chief of which is that pancreatitis without associated biliary-tract disease is not rare. Some observers^{7, 8} have, in fact, claimed that biliary disease, when present, is the result of the pancreatitis. Virus infections, such as mumps and virus pneumonia, may produce isolated acute attacks, but seem unlikely to be responsible for recurrent episodes. Probably one clue to aetiology lies in the high incidence of chronic alcoholism among patients with recurrent pancreatitis. Possibly chronic alcoholic gastroduodenitis produces oedema round the duodenal papilla, with consequent obstruction to the flow of pancreatic juice, followed by stasis and infection within the ducts.⁹ Klatskin and Gordon,⁷ in a study of familial essential hyperlipæmia with associated pancreatitis, found evidence suggesting that the former condition preceded and might cause the latter. But the majority of patients with recurrent pancreatitis show no sign of hyperlipæmia; and Professor MacKenzie believes that the essential factor is the development of a vascular lesion while the gland is under a pronounced secretory stimulus.

PROPHYLAXIS OF MEASLES COMPLICATIONS

In the U.S.A. gamma-globulin for the prophylaxis of measles in contacts has been obtainable until recently at the corner drug-store; but in the last year it has been temporarily withdrawn from the market owing to its wide use in the prophylaxis of poliomyelitis. This has had the effect of focusing attention on prevention of the bacterial complications of the disease by chemotherapy.

For some years the usual practice has been to give sulphonamides, or sometimes penicillin, to young children with measles for five or six days after the appearance of the rash, as a protective "umbrella" against pneumonia, otitis media, and other bacterial complications; and this has proved strikingly successful.¹⁰⁻¹¹ Karelitz and his associates¹² at the Willard Parker Hospital, New York, have now tried the effect of a single injection of the repository form of benzathine penicillin in 61 children with measles, and only 2 developed bacterial complications. The controls were 67 patients who received on admission four daily injections of aqueous procaine penicillin 300,000 units, 47 who received aqueous penicillin 600,000 units on alternate days for three doses, and an untreated series of 41 children. These groups were formed by alternate allocation of patients on admission, except that those with complications already present were alternated in the penicillin groups, which were thus fairly severely weighted. No bacterial complications occurred after admission to hospital in the procaine penicillin groups, but of the

5. Opie, E. L. *Bull. Johns Hopkins Hosp.* 1901, 12, 182.
6. Gambill, E. E., Comfort, M. W., Baggeneiss, A. H. *Gastroenterology*, 1948, 11, 1.
7. Klatskin, G., Gordon, M. *Amer. J. Med.* 1952, 12, 3.
8. Banks, H. S. *The Common Infectious Diseases*. London, 1949; p. 114.
9. Holbrook, W. P. *J. Amer. med. Ass.* 1944, 126, 84.
10. Coburn, A. F. *Ibid.* p. 88.
11. Karelitz, S., King, H., Curtis, B., Wechsel, M. *Pediatrics*, 1951, 7, 193.
12. Karelitz, S., Chang, C. C., Matthews, Z. E. *J. Pediat.* 1954, 44, 357.

untreated controls 28% had complications—mainly pneumonia. Karelitz et al. suggest that it is now clear that most bacterial complications of measles can be avoided by timely antibiotic therapy; and aqueous procaine penicillin, being relatively painless, has advantages over other depot penicillins. In this country quite satisfactory prevention of bacterial complications can still be obtained by the simpler and cheaper method of sulphonamide prophylaxis. This is one of the few forms—if not the only form—of routine sulphonamide prophylaxis that can be generally recommended.

"ARTIFICIAL HIBERNATION" IN THE WOUNDED

Not uncommonly severe injury is followed by a vasovagal reaction, which may possibly aid survival. Such a reaction can be prolonged by means of "artificial hibernation," which Huguenard¹ has defined as controlled inhibition of the autonomic nervous system with lowered metabolism, muscular relaxation, and twilight-sleep. Laborit and other French workers have brought about this "physiological alienation," in order to prevent or treat shock,² by means of various drugs, including a "lytic" mixture of chlorpromazine hydrochloride ('Largactil'), promethazine hydrochloride ('Phenergan'), pethidine, and diethazine hydrochloride ('Diparcol').

Last year, after visiting the front in Indo-China, Laborit and Huguenard³ suggested that such a mixture might usefully be administered to the wounded at any stage of evacuation behind the regimental aid-post. In the past year this method has been applied to nearly 250 casualties; and Chippaux et al.⁴ compare the results with those in a group of similar casualties treated by orthodox methods. They conclude that in 10 of 51 severely injured patients who died after orthodox treatment, the outcome might have been different if the lytic mixture had been given. This technique, they say, should be practised only at the place where full resuscitation and surgical treatment are to be carried out, after diagnosis and a decision about operation. The method does not reduce the amount of blood required for replacement, and its use should be preceded by full resuscitation. In Indo-China the conditions most likely to be benefited seemed to be severe burns, shock resistant to transfusion, blast injuries, and hyperpyrexia. The advantages are said to include easier anaesthesia with smaller doses, prevention of operation shock, and greater comfort in the early postoperative period. Against these must be set the difficulties of applying the method in the forward area, where the treatment of the most severe battle injuries is best undertaken; the need to observe the comatose patient closely for thirty-six to forty-eight hours; and, in the tropics, the necessity for air-conditioned accommodation.

These observations do not finally decide the value of "artificial hibernation" in the field; but at present this seems very limited.

1. Huguenard, P. *Anesth. Analg.* 1953, 10, 16.

2. See *Lancet*, 1953, ii, 1039.

3. Laborit, H., Huguenard, P. *Pr. méd.* 1953, 61, 1029.

4. Chippaux, C., Carayon, A., Roufflange, F., Fabre, A., Borieix, L., Lapalle, J. *Ibid.* 1954, 62, 504.

MESSRS. CHRISTIE

UNDER the heading of "In England Now" last week, a correspondent told the story of some people living in a caravan who owned a picture by Turner and were supposed to have had an offer of £6000 for it from a representative of Christie's. To anyone with knowledge of such affairs, this statement showed that the story could not be wholly veracious; for, though Messrs. Christie, as auctioneers, have been selling works of art for two centuries, they have never bought them or made offers of the kind described. We are sorry to have caused Messrs. Christie annoyance by this misleading mention of their name.

Special Articles

FEEDING CONVALESCENT PATIENTS NUTRITIONAL NEEDS AND PRESENT COST *

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LECTURER IN NUTRITION, DEPARTMENT OF MEDICINE, UNIVERSITY OF EDINBURGH; CONVENOR, CATERING COMMITTEE, ASTLEY AINSLIE, EDENHALL, AND ASSOCIATED HOSPITALS BOARD OF MANAGEMENT

THE National Health Service Act for Scotland, 1947, enjoins hospital boards to provide "general services" for the hospitals in their charge. As yet there has been no precise definition of what these services should be. So far as I know, the first attempt at any such definition was made in a recent editorial in *THE LANCET* (March 20, 1954) which said: "the responsibility of hospital managements is to provide an efficient hospital, to keep it warm, clean, and wholesome, to furnish it for the adequate reception of patients, to supply it with the necessary food and medicine, and to employ a competent staff." This seems a good definition which might well provide the basis for future legal interpretations of the Act. In that event we would have to consider carefully what is meant by "necessary food." In fact we might have to consider it very carefully indeed. Now that any dissatisfied patient can ask for free legal aid, it is quite possible that before very long a hospital board might find itself sued for failing to provide "necessary food." The expert evidence in such a case would be interesting and probably so contradictory and confusing as to embarrass even the lawyers.

I want to attempt some definition of what should be meant by "necessary food" for convalescent patients, not out of any special desire to help the lawyers in their task—still less to provide material for office-desk directives—but because I believe that all of us concerned with the care of convalescent patients want to see them properly fed and are now anxious about how this can be done on our present budgets.

"NECESSARY FOOD" FOR CONVALESCENCE

It is surprising that no recent textbook of medicine, surgery, or therapeutics seems to pay any special attention to the general nutritional needs of convalescent patients, though they sometimes give advice about feeding during recovery from certain specific diseases. Some of this advice dates from an age when medicine was more elegant, though perhaps less efficient than it is today—e.g., the importance of avoiding overcooked meats, or game that has been allowed to get "high." A new British textbook of medicine edited by Garland and Phillips (1953) provides an admirable essay by Dr. T. F. Main on the special problems of convalescence and rehabilitation, particularly the psychological problems; it is an essay well worth study. And yet, surprisingly, the book makes no mention of nutritional needs in convalescence.

The provision of food for convalescent patients presents quite a different problem from feeding patients in the wards of a general hospital. In a general hospital there are always some patients who are too sick to take more than a light diet. The other patients benefit accordingly; for the catering officer, with a fixed allocation per bed of foods such as meat and butter, has usually a comfortable surplus to distribute. Convalescent patients, on the other hand, whether at home or in homes or hospitals, should be eating at least a full well-balanced normal diet. I say "at least" on purpose, because

there are several categories of convalescent patients who actually need *more* food than a normal healthy person.

SPECIAL NUTRITIONAL NEEDS IN CONVALESCENCE

It is no fault of the general hospitals that many of the patients they discharge to convalescent homes are actually in a state of subnutrition or malnutrition. In fact it is the correction of these inevitable nutritional deficiencies that is an essential part of what we mean by convalescence. These deficiencies are inevitable because they are the unpreventable aftermath of acute illness, operation, or injury. Here are some examples.

Calorie-deficiency (Subnutrition) Following Fevers

Loss of appetite is a common complaint in many acute febrile diseases. In the old days the doctor used to aid the process by denying his feverish patients all food, except perhaps an occasional cup of meat extract (devoid of calories) and a sliver of desiccated toast. The patient with a long-continued fever, such as typhoid, might recover from the infection only to die in the end of starvation. The first opponent of this mistaken regimen was the great Irish physician Graves, who asked that his tombstone should be inscribed with this epitaph: "He fed fevers." But for many years he had few followers. Today we try to coax the feverish patient to take as much food—as many calories—as he will accept by feeding him fluids and semi-solids of high energy value; not meat extract and "ice-creams" made of seaweed, but sustaining soups in which a whole meal is concentrated and made tasty, and puddings containing plenty of milk or concentrated milk-protein.

The advent of the antibiotics has undoubtedly greatly reduced the extent of subnutrition and starvation resulting from long febrile illnesses, because they have curtailed the number of days on which the patient is unable to eat. Even so, I suspect that there are still many patients recovering from fevers who have a great deal of nutritional leeway to make up. A familiar example is the child who has ceased to grow during an attack of whooping-cough, through losing calories by recurrent vomiting.

Malnutrition (Deficiency of Specific Nutrients) Resulting from Injury

Loss of nitrogen.—It is now generally recognised by surgeons that the common process of putting a patient to bed, giving him a general anaesthetic, and making a simple skin incision—no more than that—is enough to put him into "negative nitrogen balance." In other words his tissues begin to break down, liberating protein which is katabolised. The nitrogen liberated by this katabolism is excreted, so that more nitrogen appears in the urine than is taken in the food and a state of negative balance ensues. If, in addition, there is serious injury the negative balance will be correspondingly severe. Many surgeons have attempted to check this biological reaction to injury by giving heroic quantities of protein immediately, either by mouth in the form of concentrated milk-protein, or by intravenous infusion of protein hydrolysate. But the general opinion now seems to be that the effort is doomed to failure because it is impossible to arrest, at the time, this reaction involving the destruction of protoplasm. It is only during the stage of recovery—during convalescence—that the lost protoplasm can be replaced.

Loss of ascorbic acid (vitamin C).—Recent work has drawn attention to the relatively enormous amounts of ascorbic acid that may vanish from the body immediately after an injury, such as a fracture or burn. The body, when fully saturated with the vitamin (which few British people are) may contain 6 g. of the vitamin; as much as 4 g. may disappear overnight after an accident. It seems likely that the corticotrophin discharged from the anterior pituitary gland in such

* Lecture delivered on April 24, 1954, to a conference on Convalescent Homes arranged in London by King Edward's Hospital Fund.

circumstances, is responsible for this rapid disappearance of ascorbic acid; the liberation of this hormone from the anterior pituitary is known to be one important aspect of bodily reactions to damage. This loss of ascorbic acid must be made good during the period of recovery, and the diet must supply it because man, like the guinea-pig but unlike the rat, cannot make it for himself.

Loss of calcium.—A remarkable experiment carried out in America recently showed that when a normal man is put to bed immobilised in a plaster cast from chest to toes, his body goes into "negative calcium balance"—i.e., he loses more calcium in his excreta than he receives in his diet. The fact is that when for any reason any part of the skeleton is immobilised it loses calcium salts, becomes demineralised, and is thus weakened. The strength of the bones is maintained only by constant use. We know too well how elderly bedridden patients may by immobilisation lose so much calcium from their bones that, when they do get up, they break a hip as soon as they put any weight on it. The occupational therapist and physiotherapist, by providing active movements for bedridden patients, not only keep the muscles from atrophy but help to maintain the strength of the bones.

Dietary Sources of Calcium, Ascorbic Acid, and Nitrogen

By far the most valuable dietary source of calcium is milk, and the milk-protein contained in cheese. Ascorbic acid is provided by fresh fruit and vegetables, nitrogen by foods of animal origin—meat, fish, eggs, milk, cheese.

Of course all these foods are regularly provided in convalescent diets; but are they always provided in adequate amounts? Before attempting to answer that question, it is worth considering first what constitutes an adequate diet for a normal adult.

Definition of an Adequate Diet for a Normal Adult

It is impossible to predict from published tables of nutritional "requirements" just how much of each class of nutrient a patient needs: needs vary very widely and unaccountably from one individual to another. But it is useful nevertheless to have certain standards—"recommended allowances"—against which to judge the adequacy of diets. Such standards have been provided by the British Medical Association's Committee on Nutrition (1950). A normal adult should be able to maintain a satisfactory state of nutrition on the following approximate daily (intake) allowances:

Calories: 2000 to 4000 according to age, sex, and activity.

Protein: At least 70 g.

Calcium: 1 g.

Iron: 12 mg.

Vitamin A: 2500 i.u.

Thiamine: 1 mg.

Ascorbic acid: 30 mg.

What do these amounts mean in terms of actual foodstuffs? This may be learnt from a study of the reports of the National Food Survey carried out by the Ministry of Food during the 1939–45 war and after. This survey shows that the average diet of urban households has been, in recent years, sufficient to meet the B.M.A. recommended allowances. The average daily consumption of different foodstuffs¹ therefore provides a useful guide to the quantities of different foods, available on the market, necessary to provide an adequate diet for a British household. This publication also provides a valuable index of the rising cost of food.

THE COST OF FOOD

Cost of an Adequate Household Diet

Twenty years ago the British urban population was spending on average about 9s. per head per week on food. Times and costs have changed since then! We know that before the war the diets of many urban

families were seriously deficient in several respects. With the introduction of rationing during the war the average level of nutrition actually improved, while the price of food was kept low by subsidies.

For various technical reasons the figures given by the National Food Survey for the cost of an average urban diet are not strictly comparable from year to year. However, I do not think that the scientific advisers of the Ministry of Food will quarrel with me seriously when I give the following personal estimate of the changing cost of a household diet adequate to meet the B.M.A. standards, making due allowance for the relative inefficiency of the housewife in her choice of the best foods to buy:

<i>Estimated Cost of an Adequate Household Diet (per head weekly)</i>			
1942–43	11/-
1946–47	11/6
1950	16/6
1951	19/6
1953	24/-

These figures are obviously only approximate, but I think it true to say that the over-all price of food has more than doubled in the last seven years and that an average urban family would not now be able to purchase an adequate diet for much less than 25s. per head per week. Fortunately many families have enjoyed a parallel increase in wages (earned from the rising prices); but it is hard on old people with fixed incomes, and also hard on hospitals. In budgeting for hospital catering we must dismiss from our minds all former ideas about what this should cost, and accept the fact that, as regards food at least, we are living in times of inflation.

Obviously it would be foolish, without full knowledge of the economic facts, to question the wisdom of lifting the subsidised lid on food prices. There are already signs that the price of some foods is falling. But meantime it seems reasonable to express the hope that the Ministry of Health understands what the Ministry of Food is doing.

Hospital Costs and Household Costs Compared

It may be argued that a hospital should be able to provide food at much less cost than the ordinary household, by reason of wholesale purchases. This is certainly true to some extent, but against this must be reckoned certain factors that may add to the catering costs of hospitals.

Age of the patients.—The figures I have given for the cost of domestic feeding are in terms of a household budget divided by the number of members in the family, including small children whose nutritional needs are obviously much less than those of an adult. A hospital providing mainly for adults would have to purchase more food per head than the average household.

Special nutritional needs in convalescence.—I have already given some reasons why convalescent patients should have ample supplies of milk, meat, and fresh fruit and vegetables as a necessary part of their treatment.

Milk

The average household purchases about 5 pints of milk per head per week. In my opinion a convalescent hospital should provide at least 7 pints at an additional cost of about 1s. per head per week.

Meat

Meat seems to be rationed more by price than anything else now, and I suspect that many families have had to alter their eating habits and accept stews made from the cheaper cuts in place of the traditional roast. It is clearly important that convalescent hospitals should not imitate the public in this respect, and attempt to save money by debasing the quality of the food they serve. A diet, to be therapeutically useful, must be appetising. The quantity of meat purchased may look very impressive on paper, but it is useless if it is inedible.

Fruit and Vegetables

Likewise I suspect that some households now find the price of many fruits and vegetables prohibitive, particularly

¹. Domestic Food Consumption and Expenditure, 1951. H.M. Stationery Office. 1953.

in the first months of the year. The ascorbic acid which they provide is the one vitamin that is commonly consumed in insufficient amounts in Britain.

A great deal of this vitamin is destroyed in the appalling traditional ways of cooking potatoes and other vegetables. The average domestic diet contains 50-70 mg. per head per day (according to season) before it is cooked, but a large part of this is destroyed in the cooking. By American standards we are certainly all of us deficient in this vitamin. Although I doubt whether keeping the body saturated with it is really necessary for health, as the Americans think, I believe that many British people—especially in the spring—have inadequate bodily reserves of ascorbic acid. A survey of blood-ascorbic-acid levels among hospital patients would almost certainly show an important proportion with little or no measurable amount of the vitamin at this season of the year.

The average domestic household spends about 1s. per head per week on fresh fruit. I would think that a convalescent hospital ought to be spending at least twice this amount, if its patients are to recover quickly from the loss of ascorbic acid sustained as a result of surgery or injury.

VALUE OF A GARDEN

At the Astley Ainslie (Convalescent) Hospital in Edinburgh we have the inestimable advantage of well-kept gardens. These provide a pleasant environment in which patients may rest, relax, and recover. In my opinion the cost of maintaining them is money that is far more usefully spent towards the benefit of patients than the large sums sometimes expended on drugs of dubious value in hospitals less fortunate.

But more important than the psychotherapeutic amenity that gardens provide are the fruit and vegetables they produce. The Astley Ainslie Hospital has 8½ acres of land devoted to market gardening, which grows a substantial part of the requirements for fruit and vegetables for a hospital of 240 beds. Fruit and vegetables sold in the markets of large cities have often been "processed" in various ways to maintain their appearance, though not necessarily their nutritive value. The ascorbic acid content of vegetable foods deteriorates rapidly with keeping. To be able to give convalescent patients fruit and vegetables fresh from the garden, without spoilage, is a most important means of providing the ascorbic acid they need, and incidentally it is more enjoyable for them than vitamin pills.

There can be no dispute that a garden is a priceless asset to a hospital, and any attempt to reduce its productivity in the name of economy should be resisted on medical grounds.

VITAMIN PILLS

It is fashionable at the present time to prescribe multi-vitamin pills of various kinds to convalescent patients. The doctors who prescribe them have probably very little notion of what is in them. They may notice that they contain pyridoxine and pantothenic acid and think that this is all very scientific and good. But there is no evidence that the human body needs these particular vitamins in its food; in fact there are reasons for believing that pyridoxine may be injurious, if the diet is deficient in another component of the B-complex—thiamine.

Vitamin pills are no substitute for food, and personally I know of very few medical uses for them. Admittedly they are valuable in the immediate treatment of beriberi, pellagra, and scurvy, but these diseases are almost extinct in Britain. My personal view is that no convalescent patient should require synthetic vitamin pills if he is provided with proper food.

Before the discovery of the vitamins, every patient in hospital had a bottle of medicine; often it was mostly infusion of gentian or some other bitter tonic intended to stimulate the patients' appetites for the nauseous meal that they were about to receive. Fortunately the members of the British Dietetic Association, with well-trained cooks and catering officers, have so improved the

standard of hospital feeding that tonics are no longer necessary.

PRESENT COST OF A CONVALESCENT DIET

But to return to the main theme; what is the minimum cost of an adequate convalescent diet? I think that today it would be difficult adequately to feed convalescent patients on much under 25s. a week, at least at the food prices current in Edinburgh.

At the Astley Ainslie Hospital, during the first two months of this year, we were actually spending 23s. 9d. a week on food; but then we have the advantage of our own market garden. This compares with the average figure of 12s. 6d. a week that we were spending during the twelve months April-March, 1946-47.

How do we know that the diet we are providing is adequate? I have obtained the records of kitchen allocations of food at the Astley Ainslie Hospital for a sample week in March, 1954, and had them calculated in terms of calories and nutrients. I am glad to say that they meet the B.M.A. standards, even allowing for inevitable cooking losses. But there is not a great deal to spare, keeping in mind the special nutritional needs of convalescent patients.

I would be the last to suggest that we should have periodic visitations from official dietetic auditors to tot up the calories in the kitchen, along with the petty cash; but I do suggest that every convalescent home or hospital should review for itself periodically the standard of its feeding, preferably with the help of a trained dietitian, to make certain that minor economies have not been allowed insidiously to undermine the standard.

COMMENT

It is ironical that at this time, when civilian rationing is at last coming to an end, hospitals are finding it necessary to impose their own system of rationing food in order to keep down expenditure. I suggest that they ought to think very carefully before they do so. I have heard of one hospital where it was recently proposed that they should economise on their milk bill, while at the same time the medical staff was freely prescribing injections of expensive antibiotics which were sometimes given for days after the patient really needed them "just to make sure," or because no-one had remembered to cross the order off the treatment sheet. If economies must be made, I suggest that we scrutinise first the drug bill—and especially the bill for synthetic vitamins.

Good food is an essential part of proper convalescent treatment. It is obviously false economy to employ an expensive staff to look after convalescent patients whose recovery is postponed and delayed because they are not getting proper food.

AN AMERICAN IN BRITAIN

Dr. J. H. Cort, a citizen of the U.S.A. who is lecturer in physiology in the University of Birmingham, was ordered last week to leave Britain by June 30.

Dr. Cort issued the following statement:

I came to this country for the second time in June, 1951, directly after completion of medical school at Yale University. My research interests at Yale had been in electrolyte metabolism and renal physiology, and I was awarded a research fellowship for two years with R. A. McCance at Cambridge. For two years, while a medical student, I had been a member of the American Communist Party. My sole political activity during that period was as a member of the Association of Internes and Medical Students, advocating health insurance and a national health service in the United States. This political activity ceased after medical school, and I have now no political affiliations or activities. I left the U.S. lawfully, with a valid passport, in May, 1951. In November, 1951, the American Embassy in London demanded the return of my passport and my immediate return to the United States. I

asked the reason for this request, but was told only that the State Department had issued the request and that no reason could be given. I was very loth to comply since I had only been in my fellowship for three months, and I had also registered as a research student at Cambridge. My legal adviser informed me that there was no legal compulsion in the request, and since I had very little reason to expect that scientific employment would be available for me under present conditions in the U.S. I did not comply with the request. In June, 1952, my passport expired. I applied for renewal of permit to stay, and the Home Office granted this with full knowledge of my status.

In the course of the next year, the Congressional Committee on Un-American Activities began investigating "subversive activity" in American universities, and, in the course of their hearings at Yale and in Boston, many of my old acquaintances were asked if they knew me, I being identified as a member of "a secret Communist cell" at Yale. These identifications were publicly printed, appearing in some detail in at least a dozen American newspapers. All of my friends who refused legally to testify were dismissed from university posts except one at Harvard. There, the university refused to dismiss him, but the Massachusetts authorities have indicted him for violating his oath to the university and the State, even though the university is not the complainant, and he is awaiting trial at present. Later, the U.S. Army began a loyalty oath programme, under which all candidates for call-up and commission were required to list all political organisations with which they had been connected. If membership of any organisation on the official "subversive list" was admitted, past or present, or if the candidate legally refused to fill in the form, he was called up as a private, regardless of medical qualifications or experience. Two of my friends so inducted have subsequently undergone court-martial for subversive activity supposedly undertaken before military service, and one has been dishonourably discharged. Last month, the U.S. Army's policy was changed, so that former and present Communists and "subversives" are not allowed into the armed Services at all.

Because of these considerations I considered that I would find it impossible to continue my scientific and medical career in the United States, and I applied in December, 1952, for a lectureship in physiology at the University of Birmingham, a permanent position. This post was awarded to me in February, 1953. In March, 1953, I received an order to appear for examination and induction into the U.S. Army either in America or Germany. I again took legal advice, and was informed that under British and international law I could only receive notice of intention, but that no legally binding notice could be served on me by a foreign government in the United Kingdom, and that my only legal obligation was to report for service upon returning to the jurisdiction of the demanding authority. I therefore did not report as ordered. The order was repeated several times, despite the fact that my parents informed the U.S. authorities of my legal position. After taking up my duties in Birmingham, the Home Office again renewed my permit to stay.

In December, 1953, I was called to the criminal investigation department of the Birmingham Police to have a message from the U.S. Embassy read out to me and to have a reply taken. This message stated that :

- (1) I was a delinquent, and had violated American Law.
- (2) I had left the U.S. without permission.
- (3) I had refused to obey legally binding call-up orders.
- (4) I had left the U.S. for the purpose of evading National Service.

The wording of (4) was important since the message went on to say that, under the McCarran Law, this last charge would be used to remove my U.S. citizenship. I was unable to get any legal advice here that professed competence in U.S. law, so that I was forced to give an official answer that merely stated that I denied the charges, and that I refused to give a detailed statement to the U.S. authorities through the agency of the criminal investigation department of the British Police, but that should the Home Office require any information I should be happy to furnish it. For the purpose of this statement, may I state in answer to the charges :

- (2) I left the U.S. with a legally valid passport. I registered with the army authorities before I was legally required to do so in order that I might be able to travel in time to take my position at Cambridge. I asked the army authorities and the University (Yale) consultant on military service whether there were any formalities in

leaving for my post, and I was told that there were none, and that I should leave.

- (3) These orders were not legally binding.
- (4) In addition to the facts stated in answer (2), I would only point out that I left the U.S. over two years before I received any induction notices, and I never had advance knowledge of these notices.

I was then notified by the Home Office that they were consulting with the U.S. Embassy on this matter. The Home Office did not request any information from me. In March, 1954, the Home Office informed me that if my citizenship were revoked they would cancel my permit to stay, and that they would not renew it under this circumstance in June, 1954.

The Home Office was approached by the Vice-Chancellor of the University of Birmingham, by Professor A. V. Hill, F.R.S., and by A. Wedgwood Benn, M.P., who supported my request to be allowed to remain in the U.K. Mr. Benn stated that he considered that I should be granted political asylum.

The Home Secretary replied that :

- (1) It would be a dangerous precedent to allow me to remain here.
- (2) Political asylum is only considered when life is endangered.

- (3) I would not be allowed to remain here after June 30.

The penalties that I face, apart from lack of employment, if forced to return to the U.S., are loss of citizenship and 5-10 years in prison.

My own wish is to settle down quietly in the U.K., and to continue my scientific work. I firmly believe that my legal and moral position is quite justified and clear.

Up till last Tuesday neither the Home Office nor the United States Embassy had commented in detail on Dr. Cort's case; but the Embassy described the statutory obligation of U.S. nationals liable to National Service to obtain a permit from their selective service board before leaving the U.S.A., and, if they remained long abroad, to report for medical examination or induction when so required. Dr. Cort declared (*Manchester Guardian*, June 15) that he was cleared by his local draft board when he left the U.S.A. in May, 1951; it was only after his name had been mentioned in investigating committee hearings that he had refused to return for enlistment.

BIRTHDAY HONOURS

The list of honours published on June 10 contains the names of the following members of the medical profession :

Baronet

Sir RUSSELL BRAIN, D.M. Oxf., LL.D.

President of the Royal College of Physicians of London; physician to the London Hospital.

C.H.

WILLIAM SOMERSET MAUGHAM, D.LITT. Oxf., M.R.C.S.

Author and dramatist.

Knights Bachelor

RUSSELL CLAUDE BROCK, M.S. Lond., F.R.C.S.

Surgeon, Guy's Hospital and Brompton Hospital, London.

ALEXANDER PATERSON MURPHY, M.C., M.D. Sydney, F.R.C.P.

President of the Royal Australasian College of Physicians.

HERBERT HENRY SCHLINK, M.B. Sydney, F.R.A.C.S., F.R.C.O.G.

Consulting gynaecological surgeon, Royal Prince Alfred Hospital, Sydney.

C.B. (Military)

Major-General WILLIAM ALEXANDER DUNNARD, C.B.E., F.R.C.S.

Major-General RICHARD MURPHY, C.B.E., M.B. Dubl., Q.H.S.

C.M.G.

ROBERT SAMUEL FLEMING HENNESSEY, M.D. Dubl., F.R.C.P.I.

Director of medical services, Uganda.

ANDREW TOPPING, T.D., M.A., M.D. Aberd., F.R.C.P.

Dean, London School of Hygiene and Tropical Medicine.

C.B.E. (Civil)

CHETWYND JOHN PERSHALL GROSVENOR, M.A., M.B. Camb.
Principal medical officer, Ministry of Pensions and National Insurance.

JOHN LEWIS ANDERTON GROUT, M.C., F.R.C.S.E., F.R.F.R.
Senior consultant radiologist, Sheffield United Hospitals.

MICHAEL SHAW JONES, M.D. Edin., M.R.C.P.E.
Director, social rehabilitation unit, Belmont Hospital, Sutton, Surrey.

NEVILLE LANGDON LLOYD, M.B. Lond., M.R.C.P.
Chief medical officer, Ministry of Supply.

PHILIP PATRICK LYNCH, M.D. N.Z., F.R.A.C.P.
Pathologist, Wellington, New Zealand.

ARTHUR JOHN METCALFE, M.B. Sydney.
Director-general of health, Commonwealth of Australia.

CECIL JULIAN MANNING WALTERS, M.B. Sydney, F.R.A.C.S.
Member of the medical board and of the board of health, New South Wales.

O.B.E. (Military)

Surgeon Commander GEORGE LUSH FOSS, V.R.D., M.A., M.D. Camb., R.N.V.R.
Brevet-Colonel MARK JOHN LINDSEY, M.C., T.D., M.B. Lond., R.A.M.C., T.A. (now T.A.R.O.)
Lieut.-Colonel HERBERT CLIFFORD SERASINGHE, E.D., L.M.S. Ceylon, Ceylon Army Medical Corps.
Lieut.-Colonel ROBERT ALEXANDER STEPHEN, M.D. Aberd., F.R.C.S., R.A.M.C.

O.B.E. (Civil)

RICHARD FRANK BOLT, M.R.C.S.
Chairman, Willesden (No. 4) medical recruiting board.

NOEL HAWLEY MICHAEL BURKE, M.R.C.S.
Lately medical superintendent, Cell Barnes Hospital, St. Albans.

EDWARD ALFRED COCKAYNE, D.M. Oxf., F.R.C.P.
Consulting physician, Middlesex Hospital, London; for services to entomology.

JOHN EDGAR DAVIES, M.C., M.R.C.S.
Senior medical officer (Wales), Ministry of Pensions and National Insurance.

MICHAEL GELFAND, M.D. Cape Town, F.R.C.P.
Physician, Salisbury Native Hospital, Southern Rhodesia.

Lieut.-Colonel DESMOND GEORGE McCULLY, M.B. Dubl.
Medical officer for the Trucial Coast, Persian Gulf.

IAN GREGOR MACGREGOR, M.B. Edin., F.R.C.S.E.
Senior specialist, Nigeria.

EUGENE PIERRE LARNACH MASSON, M.B. Edin.
Superintending medical officer (specialist), Mental Hospital, St. Ann's, Trinidad.

EVERARD ARNOLD MILLS, M.B.
Professor of bacteriology, Royal College of Medicine, Bagdad.

DOUGLAS WILLIAM LEIGH PARKER, M.B. Sydney, M.C.H.(ORTH.) Lpool, F.R.C.S.E., F.R.A.C.S.
Director, orthopaedic services, Tasmania.

BERNARD THOMAS SQUIRES, D.M. Oxf.
Medical officer, Bechuanaland Protectorate.

ROBERT STANLEY STEEL, M.B. Sydney, F.R.A.C.P.
Commissioner, St. John Ambulance Brigade, New South Wales.

JAMES TAYLOR, M.B. Glasg.
Director of medical services, Seychelles.

ARTHUR WOO WAI-TAK, M.B. Lond., F.R.C.S.
For public services in Hong-Kong.

M.B.E. (Military)

Surgeon Lieut.-Commander STANLEY GEOFFREY FOX LINTON, M.R.C.S., R.N.
Major JOHN FOSTER FENTON ROONEY, M.B. Camb., R.A.M.C.

M.B.E. (Civil)

GERALD HENRY COORAY, M.D. Lond.
Professor of pathology, University of Ceylon.

ISABEL MARY AGNES DOEG, M.B. Edin.
Lady medical officer, Bahrain government.

GOPAL KONDOPANT JOSHI, L.C.P.S.
Senior sub-assistant surgeon, medical department, Nyasaland.

Queen's Commendation for Valuable Service in the Air
Squadron-Leader IAN HECTOR MERCER, L.M.S.S.A.

Public Health

Q FEVER IN GREAT BRITAIN
SHEEP AS A SOURCE OF INFECTION FOR MAN*

B. P. MARMION †
M.D. Lond.

BACTERIOLOGIST, PUBLIC HEALTH LABORATORY SERVICE

J. STEWART
M.R.C.V.S.

P. RICHMOND
M.R.C.V.S.

From the Ministry of Agriculture and Fisheries, Animal Health Division, Kent

H. BARBER
B.A. Camb., M.R.C.V.S.

M. G. P. STOKER
M.D. Camb.

WELLCOME FELLOW OF THE HUDDERSFIELD LECTURER
ANIMAL HEALTH TRUST IN SPECIAL PATHOLOGY
DEPARTMENT OF PATHOLOGY, CAMBRIDGE UNIVERSITY

A PREVIOUS report (Marmion et al. 1953) described some aspects of the epidemiology of human cases of Q fever in Great Britain but drew no final conclusions about the animal sources of infection in this country.

Attention was drawn to the larger number of clinical cases of Q fever which had been detected in Kent compared with several counties in East Anglia (see table I). Tests of sera from healthy blood-donors living in these two areas also suggested an uneven distribution

TABLE I—Q FEVER AND STOCKING IN DIFFERENT COUNTIES

County	Human population per sq. mile		Animals per 100 acres of crops and grass			% of herds of cows infected†	% of blood-donors serologically infected‡	Clinical cases of Q fever of 1949-51
	Total	Rural*	Cattle	Sheep	Pigs			
Kent	990	678	19.7	65.9	10.9	8.2	3.29	72
Norfolk, Suffolk, Cambridgeshire, Isle of Ely, and Huntingdonshire	266	205	15.4	6.1	12.6	0.24	0.8	0

* Population per square mile, excluding towns with more than 50,000 inhabitants.

† Herd-milk samples containing *R. burnetii* demonstrable by guineapig inoculation.

‡ Percentage of blood-donors' sera which contained complement-fixing antibody at a titre of 1/10 or above (Hemzlerling antigen 1950-51 survey).

of infection, because complement-fixing antibodies for *Rickettsia burnetii* were found in 3.29% of Kentish donors compared with 0.8% of those in the eastern counties. Although the factors causing this uneven prevalence of human infection are not yet clear, it is felt that differences in the numbers and species of domestic animals available as sources of human infection in the two areas might be partly responsible.

Table I shows that the density of stocking with cattle in the two areas is about the same: 15-19 cows per 100 acres of crops and grass. Infection with *R. burnetii* appears to be commoner in Kentish cattle, judged by tests of herd-milk samples: 8.2% positive in Kent against 0.24% in the eastern counties. This difference may contribute to the relative prevalences of Q fever in man in the two areas. However, apart from infection in the cattle, the areas differ strikingly in numbers of sheep (table I).

* This work was done from the Department of Pathology, Tennis Court Road, Cambridge, as part of an investigation of Q fever in Great Britain supported jointly by the Medical Research Council and the University of Cambridge.

† Seconded for the purpose of this investigation.

That infection of sheep with *R. burnetii* takes place in Nature was shown by Caminopetros (1948), who isolated the organism from the milk of sheep in Greece. Infected sheep have also been found in North California (Lennette et al. 1949), in Italy (Baldelli 1950, Caporale 1950), and in Portugal (Fonseca et al. 1951). The results of epidemiological investigations in all these places suggest that sheep can be responsible for human infection.

If in Kent sheep were infected, as well as cattle, this would be an additional explanation for the prevalence of the disease in that county. For this reason Kentish sheep were investigated, and in a certain area of Kent with particularly large numbers of sheep infection in both human beings and sheep has been found. This finding introduces a new element into the epidemiology of Q fever in Great Britain.

Methods

CHOICE OF AREA FOR INVESTIGATION

In many parts of Kent cattle and sheep are found together in the same areas in numbers which complicate identification of one or other animal as a source of human infection. Because of this it was decided to search for human cases of Q fever and infected sheep in Romney Marsh. This is well known as a traditional place for the breeding and fattening of sheep, and its pastures carry a very large number, particularly during the summer. Romney Marsh is a small area about 31,000 acres (48.4 sq. miles). The number of sheep is large (about 287 per 100 acres of crops and grass) compared with the number of cattle (10 per 100 acres of crops and grass). The human population of the Marsh is sparse (9247) and mostly found in the towns of Lydd, New Romney, Greatstone, Littlestone, and Dymchurch. Except in 1 person who lived at Lydd, no cases of Q fever had been recognised in the area during the earlier investigation from 1949 to 1951.

DETECTION OF Q FEVER IN MAN

Two methods were used. First, a list of persons notified to the medical officer of health as having had "pneumonia," "primary pneumonia," or "influenza pneumonia" in 1949-53 was obtained through the kindness of Dr. J. Marshall, M.O.H. for the area. Secondly, with the help of the medical practitioners in the area, a number of persons who had had a febrile illness in 1949-53 but had not been notified as having "pneumonia," were collected. These two groups of patients, with the exception of children aged less than 10 years, were then visited, their co-operation was sought, and a sample of their blood was tested for complement-fixing antibody to *R. burnetii* (Nine Mile strain antigen). Those persons who both had had a clinically suggestive illness and had a complement-fixing antibody titre of 1/40 or more were considered to have been cases of Q fever and were investigated epidemiologically. Serological tests of healthy volunteers among inhabitants of the Marsh were also made to provide both a standard against which the serological results of the patients could be interpreted and an indication of the degree of exposure of Marsh residents to *R. burnetii*.

INVESTIGATION OF SHEEP IN KENT AND ROMNEY MARSH

At the beginning of the investigation, when it was still uncertain whether sheep in Kent were infected at all, specimens of blood were collected as animals were slaughtered at various Ministry of Food abattoirs in Kent. These sheep had been kept in various parts of Kent but were of differing age, sex, and breeding history. After the detection of human cases of Q fever in Romney Marsh and when the epidemiological investigation implicated sheep, particular flocks of these animals were examined. 5-10 ml. of blood was collected from the jugular vein of the ewes. The sera from these blood samples were tested for complement-fixing antibodies to *R. burnetii*. The complement-fixation test using the Nine Mile strain of *R. burnetii* as antigen was applied at first, and later many sera were retested with Henzerling strain antigen because this was found to be more satisfactory with sera from Kentish sheep. A suspension of murine-typus rickettsiae was used as a control antigen in all the tests, and only those sera which reacted with *R. burnetii* and did not react with this antigen were considered to contain specific antibody.

Further investigations are being made in Romney Marsh to find out more about clinical and subclinical infections in man and their relation to infection among sheep and cattle. Corresponding investigations, as a control, are also being made in a geographically similar area of the Fenlands near Cambridge, which has a human and cattle population resembling that of Romney Marsh but differs considerably from it in its numbers of sheep.

Results

Q FEVER IN MAN IN ROMNEY MARSH

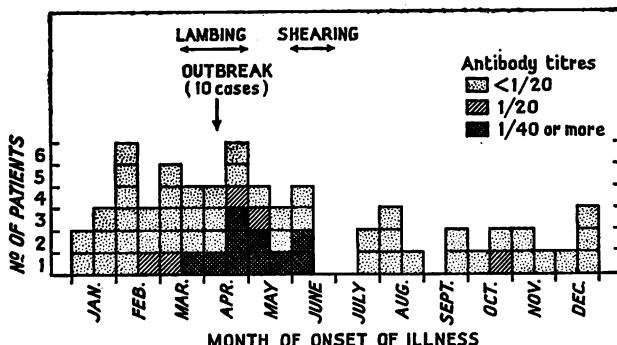
From February, 1949, to August, 1953, 90 persons were notified as having "pneumonia." This represents a "pneumonia-rate" of about 2.4 per 1000 of the

TABLE II—FREQUENCY DISTRIBUTION OF TITRES OF COMPLEMENT-FIXING ANTIBODIES TO *R. burnetii* IN SERA OF SICK AND HEALTHY PERSONS IN ROMNEY MARSH

Group investigated	Number of persons with complement-fixing antibodies to <i>R. burnetii</i> at titres of							Total
	< 5	5	10	20	40	80	160	
"Pneumonia" or febrile illness	35	7	5	5	1	3	6	62
Controls (see text) ..	76	8	14	1	1	0	0	100

population per year. Of these 90 persons 27 were children aged less than 10 years, who have not yet been investigated. 38 of the remaining 63 patients notified as having "pneumonia," &c., and 24 persons who had had unexplained febrile illness according to medical practitioners' records, making a total of 62, have been tested serologically. Of this group 10 (16%) have provided complement-fixing antibodies to *R. burnetii* at a titre of 1/40 or greater. Sera from 17 persons in the group gave lower complement-fixing antibody titres from 1/5 to 1/20, and 35 were negative at < 1/5 (table II).

It is important to know how often complement-fixing antibody at a titre of 1/40 or above would be found in healthy persons living in the Marsh, because there might be merely a chance association between the occurrence of illness and the presence of antibody in any particular person with pneumonia or fever. Examination of sera from 100 healthy controls showed that, though complement-fixing antibody is commonly found in Marsh inhabitants (16% of sera reacted at a titre of 1/10 or greater), levels of 1/40 or greater were more often found in the sera of "pneumonia" and "fever" patients (16%) than in those of the controls (1%) (table II) ($\chi^2 = 11.5$; $p = < 0.001$). Our supposition, therefore, that persons with antibody at titres of 1/40 or greater who had had clinically suggestive illness had probably had Q fever is not unreasonable. Accordingly, for



Relationship between antibody levels to *R. burnetii* in patients with "pneumonia" or with pyrexia of obscure origin and time of year of onset of illness. Times of lambing and shearing are also shown.

convenience, these persons are referred to below as patients who had had Q fever.

The accompanying figure shows the titres of antibody in the sera of the "pneumonia" and "fever" patients in relation to the month of the year when their illness began. It can be seen that the 10 patients with complement-fixing antibody at titres of 1/40 or over—the patients who had had Q fever—began their illness during the period from the second half of March to the first half of June. This is the period of the year when there is much activity with the sheep on the farms, including lambing (March and April) and shearing (June). In addition to these 10 sporadic cases, an outbreak of 10 cases of Q fever was identified in retrospect among the cast of a religious play held at a small village in the central part of the Marsh. This happened during the lambing period (see figure).

Q FEVER IN KENTISH SHEEP AND ITS RELATION TO HUMAN INFECTION

Serological Infection-rates in Kentish Sheep

906 sera from sheep killed in Kent slaughter-houses were examined for complement-fixing antibodies, the Nine Mile strain of *R. burnetii* being used as antigen. 15 (1.6%) had antibody titres of 1/10 or greater.

Epidemiological Investigation of Human Q Fever and Sheep in Romney Marsh

Five flocks of sheep associated with three groups of Q-fever patients were examined.

Flock 1 was on a large farm where two agricultural workers had had Q fever in March and April, 1952.

Flocks 2, 3, and 4 were pastured on various sides of the village where the outbreak of Q fever had occurred in April, 1949, and there was subsequently another case, Mr. A, in 1952. Flock 3 is of special interest because it had lambed in a field at the back of the row of houses where Mr. A lived.

Flock 5 is likewise of special interest, because it was associated with a patient who developed Q fever during the investigation—a fact which enabled a current, rather than retrospective, investigation of a flock to be made. For this reason the episode is described in more detail:

Mr. B, aged 26, who had not previously worked on the land, left the Royal Navy in September, 1952. In October, 1952, he was engaged as shepherd for flock 5. He was in good health until April 27, 1953, when he felt listless and alternately hot and cold. Next day he developed a severe headache and pains in the limbs, profuse sweating, and pyrexia (101°–102°F). He was ill for about a week in all. Tests of specimens of serum taken on the fourth and twentieth days of illness showed complement-fixing antibody titres of <1/5 and 1/160 to *R. burnetii*. A mild attack of Q fever was diagnosed.

The sheep in flock 5 are pastured on an isolated farm, where there are no cattle, goats, or pigs. Mr. B had not had contact with cattle, sheep, goats, or pigs on other farms at the time (April 4–14) when he probably acquired his infection. Lambing started in flock 5 on March 28 and was most frequent during the first week of April, about twenty days before the onset of Mr. B's illness. During the lambing period Mr. B was naturally much occupied with the delivery of the ewes and care of the lambs. Mr. B used in his household raw milk from a local dairy. Milk supplied by this dairy was tested and did not contain *R. burnetii* demonstrable by guineapig inoculation. The herd of cattle from which it had come did not give serological evidence of infection with the organism.

From table III it can be seen that 7.7% of the sera from sheep in flock 5 had complement-fixing antibody at titres of 1/10 or above when tested with Henzerling-strain antigen. The facts that this flock was infected; that it had lambed at a time (about twenty days before the onset of illness) when Mr. B must have acquired his infection; that Mr. B was not exposed to other

TABLE III—RESULTS OF TESTING SERA FROM SHEEP FOR COMPLEMENT-FIXING ANTIBODY TO HENZERLING STRAIN OF *R. burnetii*

Source	No. tested	Distribution of antibody titres					% positive at 1/10 or over
		<10	10	20	40	80	
<i>Ewes:</i>							
Flock 1*	92	88	2	1	1	..	4.3
Flock 2	88	86	1	2.3
Flock 3*	95	63	12	10	6	4	33.7
Flock 4	64	63	..	1	1.6
Flock 5*	143	132	5	4	1	1	7.7

* Flocks associated with a case or cases of human Q fever.

possible sources of infection, such as parturient cattle or goats, or infected milk from these animals, are all in accord with the view that he was infected from his sheep.

Similarly, serological evidence of infection was found in flocks 1 and 3 associated with the other cases of Q fever. In flock 3 the high figure of 33.7% positive was obtained. This figure was considerably higher than that observed among ewes in flocks 2 and 4, which were rather more distant from Mr. A's house (table III).

Discussion

The epidemiology of human Q fever due to infection from sheep has a suggestive pattern, of which one feature is the limited seasonal incidence of cases. Thus in North California human Q-fever is commonest from February to May (Clark et al. 1951), the months just after lambing and when sheep are being castrated, "docked," shorn, and generally much handled and moved. The epidemiological importance of parturition in sheep and the period immediately following it has been emphasised by several observers (Lennette 1950, Caporale 1950). *R. burnetii* has been found in large numbers in the placenta (Welsh et al. 1951), birth fluids (Abinanti et al. 1953), and faeces (Winn et al. 1953) of parturient sheep. It is also excreted in the milk (Caminopetros 1948, Lennette et al. 1949) after parturition, but this is probably of less epidemiological significance than parturition as such, except perhaps in countries where sheep's milk is widely drunk or made into cheese.

This sudden and intense excretion of rickettsiae at parturition, together with the increased farming activity and, perhaps, meteorological conditions favouring dissemination in dust, lead to a sharp seasonal prevalence of human Q fever.

Some features of the pattern have been found in the Romney Marsh. Q fever appears to be fairly common in the inhabitants of the area. About 16% of a group of patients who had had pneumonia or obscure fever had serological evidence of infection with *R. burnetii*, suggesting that they had had Q fever. Subclinical infection of the Marsh inhabitants also appears to be common, because a similar percentage (16%) of healthy persons tested had antibody but at lower titres than the patients who had probably had Q fever. Serological examination of sheep in the Marsh shows them to be infected, and there is suggestive evidence that this infection is responsible for that of human beings in the area. Thus, infected sheep have been found in the vicinity of human cases of Q fever—e.g., in the incident of Mr. B and his flock—and the onsets of illness in the patients with Q fever are closely grouped in time and related to lambing and shearing (see figure).

The possibility that some other domestic animal is the primary source of Q fever in the Marsh is being further explored. There are only a few pigs and an occasional goat in the area; so cattle seem to offer the only likely alternative to sheep as a source of infection. It is improbable, however, that cattle are commonly the source of the human infections. If the birth of young,

with its attendant dissemination of rickettsiae, is directly or indirectly the occasion of human infection, the number of births in either cattle or sheep during the relevant period will determine the importance of the species as a source of human infection, provided that infection-rates in the two species are not grossly disproportionate, and that parturition takes place in similar environments. In the Marsh from March to June, in which season the human cases of Q fever occurred, about 20,000 lambs and 300 calves are usually born. There is no evidence that cattle in the area are commonly infected; hence the sheep seem to be the more important on this numerical basis. In addition to this, from July to February about 400-500 calves were born, but no cases of Q fever were detected (see figure).

Lastly, dissemination of infection from cattle by their milk, which would give an effect out of proportion to their numbers, also would not completely explain the findings. Consumption of an infected milk-supply would account for the infection of only 3 of the 10 sporadic cases and is unlikely to have been the cause of the outbreak of 10 cases.

In the studies of sheep as a source of human Q fever in North California Lennette et al. (1949, 1951) have pointed out that a greater proportion of serologically positive sheep are usually found in flocks associated with cases of Q fever than in those coming to slaughter at abattoirs. It is indeed reasonable to expect such differences between flocks in which infection is active and, where as a consequence, there would be a greater probability of man being infected, compared with a sample of the sheep population at large.

In the present investigation serological infection-rates in sheep in flocks 1, 3, and 5 were from three to five times as high as in sheep at Kentish slaughter-houses. (All the sera were tested with the same—Nine Mile—antigen.)

However, the validity of such comparisons needs further assessment, for they must be influenced in addition, and to an unknown extent, by differences in the age, sex, breeding-experience, and time of testing of the two populations which are being compared.

The levels of complement-fixing antibody to *E. burnetii* found in the sera of sheep we have tested were mostly low (table III), but the finding of some sera with antibody at titres of 1/40-1/80 in the absence of reaction with the control murine-typhus antigen is considered to be a demonstration of specific antibody and evidence of infection of the sheep with *E. burnetii*.

The fact that sheep in Kent are both numerically common and infected may, as already stated, go some way to explaining the frequency of human clinical and subclinical infection in this county. Infection of man from sheep does not appear to provide the entire explanation, however, because at least 35% of our original series of sporadic cases of Q fever in Kent as a whole, in contrast to Romney Marsh, occurred at times of the year or in circumstances where infection from sheep was unlikely.

Summary

Tests of sheep in Kent have shown them to have serological evidence of infection with *E. burnetii*.

Investigation of a small area of Kent heavily stocked with sheep has shown that clinical and subclinical Q fever is common in the community and that sheep give serological evidence of infection.

Some evidence is presented that infection of sheep is responsible for infection of man in this area.

We are indebted to general practitioners in the Romney Marsh area for information about and permission to visit their patients. Dr. P. M. Vicary and Dr. E. Leiser Lonbay gave much-appreciated help with bleeding of patients, and in addition Dr. Vicary undertook the bleeding of the healthy volunteers. Dr. J. Marshall, M.O.H. for the area, and his

staff have helped us with local information and advice. We are grateful to the Ministry of Food and the slaughter-house managers at Ashford, Canterbury, Hythe, Ramsgate, Rochester, Sandwich, Sittingbourne, and Woolwich for collecting specimens of blood from sheep. Mr. A. J. Beeson, the divisional veterinary officer, advised us on the investigation of animals in the field, and his staff, in particular Miss M. J. B. Wheatley, helped us to bleed the sheep and cattle. We received valuable information about agricultural statistics from Mr. R. Duncan and Mr. T. Kimmings of the Agricultural Executive Committee, Maidstone. Lastly, we are grateful to the various farmers in the Marsh who gave us unstinted help during the bleeding of their sheep, and to Miss F. M. Callaby, Miss Z. E. Page, and Mr. P. C. Collings who did the laboratory work.

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General Practitioner and Health Visitor

Dr. J. F. Warin, medical officer of health for Oxford, in his annual report for 1953 remarks that lack of correspondence between the districts covered by individual general practitioners and health visitors had made it difficult to organise liaison between them. He met the general practitioners in groups, and thereafter each was allocated a health visitor who worked in his area. The object of this arrangement was to enable every practitioner to know personally a health visitor whom he could approach for help with any problem in his practice. It is too soon, says Dr. Warin, to comment on the result of this arrangement; but a closer understanding between family doctor and health visitor is already apparent.

Dr. Warin remarks on the excellent liaison between the staff responsible for the care of the mother in the lying-in period and the health visitor, who receives a written report on the mother's discharge from the care of hospital or midwife. One of the health visitors goes every week to the lying-in ward of each of the maternity departments, and wherever possible domiciliary midwife and health visitor meet in the mother's house. Health visitors also attend paediatric sessions at local hospitals.

Epidemiology of Poliomyelitis

In his annual report for 1952, Dr. J. Stevenson Logan, medical officer of health for Southend-on-Sea, describes a serious outbreak of poliomyelitis which began in June of that year and continued for twenty-seven weeks, involving 98 cases—41 paralytic and 57 non-paralytic. The lack of an admission unit at the infectious-diseases hospital makes it necessary for patients to be visited, before removal to hospital, either by the hospital superintendent or by a doctor from the public-health department. Thus general practitioners in the area have become accustomed to notifying suspected cases promptly; and the information about the poliomyelitis cases is unusually complete—with 1 exception the diagnosis of the non-paralytic cases rested on changes in the cerebrospinal fluid.

In investigations of the chains of contacts one striking feature was the frequency with which school-teachers were encountered; but there was no proof that the teachers' households were unusually prone to infection. The families of medical practitioners entirely escaped the disease.

In England Now

A Running Commentary by Peripatetic Correspondents

As a morbid anatomist, I have acquired a certain degree of occupational anosmia, but even my experienced hippocampus reacted to my fellow passenger. I took a sidelong glance; she was an old woman with the face of starvation, the bright and abstracted eye of lunacy, and a tangle of grey and filthy hair. She was surrounded, rather than clad, by a series of ancient garments, culminating in an incredibly patched coat, gaping at the shoulders, with many pins (non-safety) trying in vain to bring the edges of the rents together. On her knees was an old string-bag and some newspaper wrapped round a single shoe. Here at least, I thought, was unusual company, dilapidation of a Dickensian extravagance.

The portress on the platform screamed: "Mind the doors!" The doors closed. As the train moved off, my companion turned to me and observed, in the accent and intonation of a university drawing-room, "These station women have such raucous voices, haven't they?" Startled into incoherence, I could only mumble "Yes" and await further revelations. But the oracle had spoken, and finally. She mused contentedly over her pronouncement for a few minutes, then took out her false teeth, laid them carefully on her lap with the shoes and string bag, and went to sleep. I felt rather guilty when I had to waken her to let me get out at my destination, but she was very affable.

What a life-saving drug our snobbery can be—surely not a sin or a virtue, but a great gift from a kindly Heaven.

* * *

The art of reading in a bath, according to 'Q.' is rarely attained, but my great toe has now been trained to turn the hot and cold on and off. Reprints are excellent material; or, if I am already saturated with medical matters, an *Everyman* edition is well supported; and what better than *The Diary of Samuel Pepys*. But even he sets me thinking about medical matters when he writes of the plague. In those days all seemed to be attributed to it. On April 8, 1666 (Lord's Day):

"The Court full this morning of the news of Tom Cheffin's death, the King's closet-keeper. He was as well last night as ever, playing at tables in the house, and not very ill this morning at six o'clock, yet dead before seven; they think, of an imposthume in his breast. But it looks fearfully among people now-a-days, the plague, as we hear, encreasing every where again."

I fell to wondering whether a modern coroner might not bring in a different verdict, and so to bed.

* * *

In my own neighbourhood my people still refer to me as "the doctor," and, despite increasing years, in my own mind I am still active, alert, and quite a young man. But the other day on holiday in a remote village where I was a complete stranger, and not the well-accepted figure lately retired from a busy practice, I popped into the local for a glass of beer. Apart from the landlord, behind the bar, there was only another man in the room—an ancient, dilapidated fellow with unshaven red cheeks and watery eyes. A real old chronic, I thought, and nothing much to talk to.

"Good morning," I said, embracing them both in my cheery salutation.

"Good morning, Sir," said the landlord.

"Good morning, Dad," said the ancient.

Dad! Dad! Dad! The word had a sinister ring about it, coming from such a source. "Good gracious," I thought "am I as old-looking as all that?" I felt hurt; the beer didn't taste at all good; there was something undoubtedly wrong—even with having a holiday. Out in the sunshine, however, I reflected how often I had myself told people to remember they were getting older and that they should "ease up." Had I perhaps unwittingly hurt them, just as the old man in the pub had hurt me?

"Dad," he had said. Oh, yes, I would remember. I would remember that, just as ageing is usually a

gradual, slow-moving, gentle process, so giving advice about it should be tempered with great kindness, patient understanding, and quiet dignity.

* * *

Théré is no rest-house in the little village where I spent Easter, and I slept under a tree not far from the chief's compound. They warned me that the sheep and goats were not locked up at night and that I might be visited, so before retiring I made a pile of stones convenient to the hand beside my camp bed.

I was indeed visited, and after several misses one stone got home with a satisfying thud—followed by an extraordinary noise, like a mad trombone moaning to the wild west wind. Investigation showed that a goat had put its head right into the large earthenware waterpot provided for me by the chief. In its confusion after being caught in the short ribs by a stone it was waltzing dizzily, partnered by the pot, with its chin and horns impacted at the brim.

A spinal application proved ineffective, and was an ill-judged procedure, especially as the operator was of course wearing only light bedroom slippers. However, manual version without anaesthetic was fairly easy, though when the goat's head was (necessarily) pushed under water the trombone noise gave place temporarily to that of a French horn that has been turned over and over too few times. The pot was unhurt, and the goat showed no sign of birth palsy as it decamped; quite the reverse, I never saw a less spastic goat. Bannister himself would have had difficulty in following up the case.

* * *

How lucky we were to have our firstborn in the spring! Lovely, sunny days for drying the nappies and for putting baby out in the garden in her pretty little frocks. It must be so difficult in the winter with a house full of damp washing and waking up in the bitter chill of night to feed her. So many are the disadvantages of winter births that I am surprised that humans, like other more sensible mammals and birds, have not developed a breeding season confined to the spring and summer months. Of course obstetrics would then be a seasonal occupation with a mad rush in the summer followed by unemployment in the winter. The obvious answer would be to practise obstetrics in the spring and summer and paediatrics in the autumn and winter when all last year's production would be getting their coughs and colds. By the time that the last whoops were dying away the first cries of the new crop of babies would be heard in the land. The Royal College could offer a cup for the first delivery of the season.

* * *

Unsatisfied, perhaps, with my efforts, the editorial board of the *Ruritanian Journal of Abstracts* has sent me a list of abbreviations. Most of them are plain sailing. I am happily familiar with ml, ecg, i.v., and many others; i.r. (infra-red) nearly sent me to a dictionary until I realised that a hyphen was missing. But the best is C-R (crown-rump). Please, nobody tell me what crown-rump means. Rump is easy, and the C.O.D. confirms my opinion, but crown . . . Is crown a noun? Hardly, for it is apparently applied to the wrong end. Is crown a verb? If so I might arrive fairly soon at a reasonable conclusion. I shall spend many happy hours puzzling it out.

* * *

I had to go to the hospital last Sunday so I decided to give our small daughter her first glimpse of white corridors. We set off grandly in the old Riley, which has just celebrated her 19th birthday, and luckily arrived in time for coffee on the ward. Afterwards I handed Frederica over to sister children's and set off on my brief round. About forty-five minutes later we were bowling along home looking forward to our roast lunch but in deep silence; the young mind was obviously impressed.

About a week later Frederica and I were discussing the more serious side of life, which included why it wouldn't be a good thing to take out James's appendix with the carving knife even though he is too young to resist, when she suddenly looked up at me and said: "Daddy, when you go to work in the hospital every day, do you stay in bed all the time too?"

Letters to the Editor

THE POSITION OF NEUROLOGY

SIR.—I am grateful to Sir Francis Walshe for his support in the campaign of the Royal College of Physicians for an adequate neurological consultant service, but I should like to carry his diagnosis a little further. I have no doubt that the economic factor he mentions is one reason why sufficient neurological consultants are not being appointed. But how does it operate? The difficulty arises in connection with regional hospital board appointments and not in the teaching hospitals. The reason is that in a teaching hospital the needs of different departments are discussed in an influential medical committee where all are represented, and the resulting recommendations are normally accepted by the board of governors. But regional hospital boards obtain their advice from an S.A.M.O. and a medical committee which is appointed by themselves and is not representative of all the important branches of medicine. How many such committees include a neurologist? Regional neurological committees may exist, but these are ineffective if they are not represented at the centre. Their advice may not be taken or even sought.

I know that the medical committees of regional hospital boards are devoted and hardworking bodies, but I believe that a medical service cannot be effectively planned unless its organisation includes a comprehensive and representative medical committee at regional hospital board level. This lack is one of the major defects of the present system.

London, W.1.

W. RUSSELL BRAIN.

THE PLIGHT OF SENIOR REGISTRARS

SIR.—In recent issues of *The Lancet* there have been several letters from registrars about the problems of their group. It is a sad commentary on the present state of affairs that most of the writers should have had to remain anonymous. They must feel that their own positions are so insecure and their future so uncertain that they cannot risk being dubbed as "political agitators." This thought must be influencing many registrars, who, as individuals, are surprisingly unvocal about the disastrous position which still confronts them.

There has been a comparative lull in official thought about senior registrars because of the Ministry decision¹ to allow them to re-apply for their own posts and to permit retention of "transitional posts." This does not mean that there has been any real improvement in the situation. If illustration is needed, the case of the Bournemouth obstetrics post can be cited. For this post—recently advertised—there were 108 applicants of less than consultant status. We can reasonably assume that all these applicants have their M.R.C.O.G. When these numbers are set against the 36 posts in obstetrics that have been advertised in the past two years it is clear that the word "disastrous" is not too strong to apply. In some specialties affairs are better arranged, but the over-all situation is just as grave as that in obstetrics.

For several years sporadic attempts have been made, alternately by the Ministry and by the profession, to solve the senior-registrar problem. The measures so far taken have been only of a temporary nature, but as they have avoided the large-scale dismissal of senior registrars they have been acceptable to regional boards, consultants, and registrars alike. The junior staffing of hospitals is now suffering, partly because young doctors see the mess that their predecessors are in, and will not commit themselves to a similar uncertain future. This is the moment for the Ministry and the profession to agree on a solution to the senior-registrar problem which

will at one stroke set right the wrongs of the present generation and prevent any recurrence of the muddle.

To understand the present position it is necessary to recall briefly some historical points:

1. Towards the end of the war some senior members of the Royal colleges recalled their own struggles after the 1914-18 war. A willing Ministry of Labour was persuaded to give ex-Service grants; the Ministry of Health encouraged the training of large numbers of specialists; willing consultants took on extra staff, and the positions later designated as senior registrar and registrar were rapidly filled.

2. In 1950 the Ministry saw the troubles ahead and attempted to halve the number of senior registrars. The method of doing this and the lack of alternative plans for doing their work caused a political storm and the rejection of the scheme. In its object, however, it was sound.

3. The problem was discussed between the Ministry and the Joint Consultants' Committee, and in 1951 a revised establishment of 960 senior registrars was agreed.² In accepting this figure the Ministry, the consultants, and the registrars made a fundamental mistake. This large number was agreed because it seemed necessary to provide a certain amount of competition for each available consultant post. In addition, the senior registrar was regarded as essential to the working of the hospitals. Here I must quote the words of the joint committee on this subject: "In view of the fact that the senior registrar is a key member of the medical staff . . . the number of posts should not be related too closely to the number of possible openings for consultants, and besides being related to hospital needs they should allow for a proper measure of competition on the Senior Registrar/Consultant level."³ It was estimated that approximately 150 permanent specialists' posts would be available each year, and it was therefore reasonable that something over 200 doctors should be available to compete for them ("the annual outflow"). In theory, the surplus of unlucky senior registrars then disappeared and the following year a new batch, again over 200 strong, were available for the next 150 posts; and so the thing was to go on year after year. In reality, at any given moment and for any given post there are competitors from senior registrars in their 3rd, 4th, and subsequent years, from research-workers, from S.H.M.O.S., and from university lecturers. This false concept of the numbers needed to provide competition has led directly to the present state of affairs. It is now clear that even if the 960 senior registrars were the only competitors there would be far too many to provide fair competition. This is the main error that must be corrected.

Before proposing a solution we must examine the work being done today by senior registrars. No-one can deny that in many cases this is of consultant nature; often the senior registrar has complete control of beds in all but name. It is obvious that a numerically inadequate specialist service is being supported by a grossly exaggerated body of senior registrars. The only possible excuse for getting this work done by men of less than consultant status is to say that they are "training"; but, in fact, we now know that they are training for non-existent positions. This employment of senior registrars in excess of training needs is the main source of cheap specialist labour in the hospital service.

Quite apart from the intense personal problems of the present senior registrars it is essential to the future of the hospital service that this anomaly should be removed. The actions needed are these:

1. The real training needs should be re-assessed in the light of the "competition" fallacy exposed above. The co-operation of the universities should be sought in arriving at a reasonable figure.

2. All positions surplus to the real training needs should be re-assessed. It will be found that the majority of these should be consultant posts. They should be reorganised and re-advertised as such. It might well be acceptable if most of them were made full-time posts with an option of transfer to part-time work after a stated period.

This proper balance between senior registrars and consultants must be such that any man who in future

1. *Brit. med. J. suppl.* 1953, i, 243.

2. *Ibid.* suppl. 1951, ii, 47.

3. *Ibid.* suppl. 1951, i, 24.

becomes a senior registrar can be reasonably certain of getting a consultant post within the foreseeable future. The real selection of future consultants must take place at the registrar/senior-registrar level.

The present crisis in hospital junior staffing provides for the first time a separate and vigorous stimulus for solving the senior-registrar problem. Registrars and consultants alike must hope that reason will prevail and swift action follow.

St. Mary's Hospital for Women and Children, Manchester. R. M. FORRESTER Chairman, Manchester Regional Registrars' Group.

SIR.—My problem is that of a very large number of senior medical and surgical registrars throughout the country. Many of us qualified before September, 1939; we saw the war start and we saw it finish; we took off our uniforms and, since specialists were to be needed in the new health service, we sacrificed some further years in acquiring higher medical and surgical degrees; in this we were most kindly aided by Government grants which fed our families and paid some of the rent.

From then onwards we began to emerge with specialist qualifications. We got registrar posts and we climbed to senior-registrar posts; but this, to most of us, now growing middle-aged, has been the end of all progress and hope. We are extraordinarily well qualified, both by examination and experience, for consultant posts, but such posts are fantastically rare and, unless one has acquired a prominent backer or is known personally to a member of a selection committee (I say this with resignation and not rancour), one has, for practical purposes, no chance at all.

I should like to ask two definite questions:

1. Is it intended to do anything about our plight, or are we to be left until despair and financial hardship have successfully reduced our numbers and thus solved the problem?
2. If the answer to (1) is Yes, can something be expected within twelve months? What may this be?

Two explicit answers here would at least salve some of the heartsickness caused by hope deferred for so many years.

Secondly, I have three suggestions to make in the hope that something can be done quickly:

1. Senior-registrar posts should be made permanent, with protection on both sides, so that the registrar and his family can settle without being uprooted every few years.
2. Their pay should be increased, according to qualifications and experience, by annual increment if necessary, so that it more nearly approximates to that of the most junior consultant or that of the general practitioner or any other responsible doctor.
3. Appointments to consultant posts should conform to some recognisable national plan.

SENIOR REGISTRAR.

SIR.—I have only just seen the letter from "Senior Registrar's Wife" (May 8). Unfortunately there is little likelihood that her appeal will register with those who could help, since through long exposure to such *cris de cœur* they have developed an attitude of uneasy laissez-faire. I refer of course to the consultants. It is distressing to have to criticise senior colleagues whom in other respects one holds in esteem, and I should like to excuse in advance the outspokenness of my ensuing remarks on the grounds of desperate urgency.

The present so-called surplus of senior registrars is an isolated phenomenon based on a series of factors so well known as not to need recapitulation, and which we all hope will not recur. The pressure from below has ceased, and it seems likely that the situation will have responded to the law of supply and demand in a few years' time. In the meantime, however, there exists an unfortunate group of some hundreds of senior registrars, many of them excellently trained and qualified, who are unable

to find permanent positions. It is difficult to understand, rationally, why this should be so. Can there really be a surplus of senior registrars when most of them are still doing a full day's clinical work? Is it not possible for them to continue to do that work under conditions of security of tenure? In my opinion two factors contribute greatly to the magnitude of the registrar problem.

The first is that too much specialist work, especially in surgery, is still being done by general practitioners.

I know personally of several such instances. I have the highest regard for the G.P. as a G.P., who has a full-time job calling for special skills and knowledge. Few, however, have had adequate surgical training by modern standards, and fewer still work in an environment in which surgical knowledge and technique can be kept at top efficiency. At a time when some hundreds of competent surgeons face professional extinction there can be no place for such surgical dabbling by privileged amateurs. Only the senior consultants, however, could put an end to this abuse. The reasons why they do not do so are obvious to those in contact with the situation, and are not particularly creditable. Most consultants whom I know personally agree in private that G.P. surgery is undesirable, but they are anxious not to offend the often influential men who practise it. The approach employed seems to be the "tactical" one of allowing the G.P. surgeon to die a natural death. Unfortunately we senior registrars face an even more imminent demise.

The second factor is the inertia which obstructs any move to increase the specialist force.

Lack of money is the extremely disingenuous excuse often given. Can anyone believe, however, that the Government, if so urged by the consultants, would balk at the relatively small financial outlay involved in promoting a series of fourth-year senior registrars to part-time consultants? Most hospitals with which I am acquainted could well substitute one or two extra consultants for an equivalent number of senior registrars. Such a move, if applied generally, would virtually solve the registrar problem. Some regional boards, to their everlasting credit, have already taken such steps. Others are lagging, and in our unfortunate position we registrars cannot entirely rid ourselves of the suspicion that the established consultants are influenced in certain cases by a desire to avoid competition in the restricted field of private practice. It would be charitable to assume that this motivation, where it exists, is subconscious.

The ball is with the consultants, many of whom would do well to consider how they themselves might fare, today, if they were applying for their own posts. We senior registrars are not mendicants or misfits. We do not ask for feather-bedding, or for automatic Army-style promotion. All we seek is a fair chance to build our careers.

I dislike unsigned letters, but since my name is at present before committees I would ask your permission, Sir, to remain anonymous.

TRAVELLING FELLOW.

EFFECT OF CONTROLLED HYPOTENSION ON CEREBRAL FUNCTION AND CIRCULATION

SIR.—The elevation of the head in a tilted or upright position reduces the blood-pressure in the brain by 2 mm. Hg for every inch of vertical height above heart level. When vertical, the cerebral blood-pressure in the average adult is approximately 30 mm. Hg lower than at heart level.

In your issue of June 5 Dr. Saunders claims that cerebral function in conscious healthy adults is only slightly impaired when the blood-pressure in the erect posture falls to 60 mm. Hg (presumably measured on the arm at heart level). In two subjects pressures lower than this (45–50 mm. Hg) were apparently without effect on cerebral function. As the cerebral blood-pressure in these subjects must have been in the region of 20–30 mm. Hg during these observations, it is evident that the brain has an enormous safety margin in its vascular supply.

From these figures it is reasonable to assume that the tilted position employed by some anaesthetists for controlled hypotension is reasonably safe, particularly when associated with the decreased cerebral oxygen consumption of anaesthesia.

London, W.1.

G. E. HALE ENDERBY.

SYNDROMES OF RHEUMATOID ARTHRITIS

SIR.—Dr. Kersley's article last week is one of the most useful that has appeared in this field for a long time. My clinical experience is in close agreement with his.

I have had a similar proportion of cases which at the outset clinically resembled the classical picture of rheumatic fever more closely than that of rheumatoid arthritis, but eventually developed into typical rheumatoid arthritis. I have not found the therapeutic test of giving salicylates useful, as some of the cases responded well to salicylates at first.

I agree that monarticular cases of rheumatoid arthritis do occur and that the differential diagnosis from tuberculous arthritis is difficult on clinical grounds. The diagnosis is a dangerous one, and should not be made until the chest has been radiographed and a synovial biopsy done; even then the diagnosis should be kept under continuous review. I was recently consulted by a patient who had been attending a rheumatic clinic for some months with so-called monarticular rheumatoid arthritis. At the first consultation a chest radiograph revealed a miliary appearance in the lungs. The patient has since died.

I have also seen several cases of advanced rheumatoid arthritis without pain. Possibly these cases are commoner than Dr. Kersley's experience and my own would lead us to expect, as the patients consult their doctors late in the disease and may pass their lifetime without attending a hospital clinic. Two of my cases were seen in domiciliary practice, for other general medical causes, on their death-beds. Although I agree with Dr. Kersley's general impressions of these fascinating cases, I cannot agree with his argument that because two cases developed pain late in the disease therefore any question of the general pain threshold playing a part is ruled out. In the single case reported by Clark¹ the cutaneous pain threshold was measured and found to be greatly elevated. I have not been able to collect enough cases to form a reliable assessment. It would be interesting to hear the experience of others, and especially to hear of any cases in which the general pain threshold has been measured. This is a most fascinating problem both from the point of view of discovering the fundamental mechanism of the phenomenon, and from the point of view that these cases reveal one of the many fallacies in using tenderness as a test for assessing therapy in rheumatoid arthritis unless the general pain threshold is measured at the same time.

Dr. Kersley's article adds to the belief that astute and careful clinical observation still has a large contribution to make in the elucidation of fundamental problems in rheumatism.

Filmwell, near Wadburst,
Sussex.

G. E. LOXTON.

SIR.—I have read with interest Dr. Kersley's article and particularly his account of cases with acute onset resembling rheumatic fever.

As a cardiologist I have always held the opinion that true rheumatoid arthritis does not lead to rheumatic endocarditis (mitral or aortic valvular disease). I note that in Dr. Kersley's series of 750 cases of rheumatoid arthritis only 1 developed carditis resembling that of rheumatic fever.

In this case which he describes (case 1) mitral and aortic disease was noted four months after the development of acute rheumatism and pericarditis at the age of 25.

1. Clark, C. J. M. *Ann. rheum. Dis.* 1951, 10, 105.

Dr. Kersley does not state whether the mitral disease was mitral stenosis. If this was so it is most unlikely that the valvular disease arose from the acute rheumatic infection four months previously, as mitral stenosis usually takes much longer before it becomes manifest—usually two to five years at the earliest. The valvular disease is much more likely to have originated from an old rheumatic endocarditis in childhood. There may be no history of rheumatic infection at that time, and a rheumatic endocarditis often passes unrecognised and unsuspected until valvular disease becomes manifest years or decades later, as is well known. A further attack of acute rheumatism, as in Dr. Kersley's case, will often make it manifest. The commonest age at which rheumatism attacks the heart is from 5 to 15 years and it very rarely does so after 20 years.

Rheumatoid arthritis is a not uncommon disease in young people in the 20–40 age-group, and this is also the age-group when rheumatic endocarditis is likely to become manifest following a rheumatic infection in early life. It would, therefore, be expected that rheumatoid arthritis with endocarditis will be found in some cases, but this does not at all imply that the endocarditis is the result of the rheumatoid arthritis. I quite agree with Dr. Kersley that "rheumatoid arthritis and rheumatic fever are normally quite distinct, being completely different in clinical course, cardiological complications, prognosis, and therapy"; but I do not agree that "occasional border-line cases should make us wary of regarding them as separate entities." I still believe that they are separate entities, though they may co-exist.

Blackpool.

MAURICE NEWMAN.

VOMITING AND REGURGITATION DURING ANAESTHESIA

SIR.—I was very interested in last week's article by Dr. O'Mullane on the foot-down tilt during the induction phase of anaesthesia for the patient who may have a full stomach. This is a technique that I have found very safe and satisfactory, and I would press for its wide adoption as a standard method for this type of case.

The method as described by Morton and Wylie¹ depends for its effectiveness on the prevention of: (1) active vomiting, by the administration of thiopentone and a relaxant; and (2) passive regurgitation, by ensuring that the pharynx is well above the level of the stomach. In my opinion this method is the safest way of inducing anaesthesia in patients with intestinal obstruction or other causes of the full stomach.

In one respect only would I differ from the observations of Dr. O'Mullane—namely, that vomiting may occur after sleep has been induced but before the relaxant has had time to take effect. Thiopentone depresses the central nervous system so rapidly that the patient is carried below the stage of vomiting before it has had time to develop, and provided the airway is kept completely clear there is no danger of aspiration of gastric contents into the hypopharynx.

The traditional method in these cases—namely, nitrous oxide, oxygen, and ether—possesses two main disadvantages: (1) a relatively low oxygen content in the inspired mixture; and (2) a highly irritant vapour which may on occasions, particularly in inexperienced hands, lead to laryngeal spasm. This in turn may cause aspiration of gastric contents into the hypopharynx, usually aggravated by the head-down tilt adopted at such times, and a very vicious circle is initiated. The resultant anoxia may be highly dangerous to an elderly, ill patient with hidden coronary artery disease and a myocardium ill suited to such an insult. Surely it is more rational to ensure that the gastric contents never reach the pharynx than to rely on the natural reflex ability of the cords to prevent foreign material being aspirated into the lungs—a reflex which may in itself be dangerous.

1. Morton, H. J. V., Wylie, W. D. *Anaesthesia*, 1951, 6, 190.

This method does not absolve the anaesthetist from ensuring as far as possible that the stomach has been emptied through a suitably wide tube, but even with the utmost care some material may remain in the stomach. One important point must be borne in mind when using the method: it is more important than ever that the anaesthetist should be fully aware of the danger of inducing hypotension in the shocked or oligæmic patient by giving too large a dose of thiopentone.

Newcastle General Hospital,
Newcastle upon Tyne.

P. HEX VENN.

MERIT AWARDS

SIR.—The council of the Regional Hospitals' Consultants and Specialists Association is aware that throughout the country there is considerable disquiet at the manner in which merit awards are distributed. This disquiet is no doubt due in the main to the overt secrecy which enshrouds the subject. Since the early days of the National Health Service there have in many regions been no local consultations and little or nothing is known of how recommendations are made or considered. In many areas local advisory committees have not been further consulted and, indeed, in some cases have been summarily dissolved.

At its meeting on June 3 the council of this association accepted the following resolution put forward by one of its constituent bodies:

"The Council of the Regional Hospitals' Consultants and Specialists Association is of opinion that in the granting of Distinction Awards the Awards Committee should consult local medical opinion, and that this could best be done through small Regional Advisory Panels of Consultants elected by the Consultants in each Region."

45, Lincoln's Inn Fields,
London, W.C.2.

JOHN SIMONS
President.

HYPERTHYROIDISM AND MYASTHENIA GRAVIS

SIR.—In their interesting article (May 8) Dr. Maclean and Dr. Wilson refer to the antagonism between these two disorders where they co-exist. They note that appropriate treatment for the thyrotoxicosis aggravates the myasthenia gravis, whereas in patients with myasthenic symptoms produced by thyrotoxicosis these symptoms are relieved by such treatment.

They suggest that thyrotoxic myasthenia may be due to the rapid destruction or defective production of cholinesterase at the neuromuscular junction, possibly as the result of a high blood-thyroxine content. Elsewhere they make the apparently contradictory suggestion that a high blood-thyroxine level may cause deficient production or too rapid destruction of acetylcholine.

Does the first of these suggestions provide a clue to the phenomena observed? If in thyrotoxicosis acetylcholine is present in excess owing to the absence of adequate amounts of cholinesterase, might not the myasthenia that may supervene in such a case be due to the persistent effects of unhydrolysed acetylcholine producing neuromuscular blocking? Feldberg¹ found that an excess of acetylcholine produced a spread of the depolarisation current from the motor end-plate to adjacent parts of the muscle-fibre. Might the tendency to persistence of acetylcholine, though in less amounts than would produce neuromuscular blocking, account for the fine tremors of the voluntary musculature in thyrotoxicosis?

On this hypothesis the alleviation of symptoms of myasthenia gravis in thyrotoxicosis would be explained by the relatively small amounts of cholinesterase at the nerve-endings sparing the acetylcholine to some extent.

Royal Mental Hospital,
Aberdeen.

H. C. S. MACLEAN.

1. Feldberg, W. *Brit. med. J.* 1951, i, 967.

PERIPATETIC PRACTITIONERS

SIR.—May I strongly endorse Dr. Forbes's advice (June 5) about the importance of doctors keeping their defence societies and the General Medical Council informed of a change of permanent address?

There is another disadvantage in failing to do so which he does not mention. The Medical Protection Society sometimes hears of impending litigation which may involve a member whose present whereabouts are unknown to us, and delay in establishing contact with him at an early stage may later seriously prejudice his legal position or that of his colleagues as the action matures.

The difficulty in tracing a woman practitioner may be further increased when she does not inform her defence society or the Registrar of the G.M.C. that she has changed her surname as well as her permanent address!

Medical Protection Society,
Victory House,
Leicester Square, London, W.C.2.

ALISTAIR FRENCH
Secretary.

MENTAL CARE

SIR.—The articles by Dr. Bickford (May 1) and Dr. Ling (May 29) and your leader (May 29) raise many important issues for the planning of the mental health services. While with enthusiasm and well-directed effort much can be done to improve the situation, neither the well-known and already widely practised methods of rehabilitation so eloquently presented by Dr. Bickford nor the highly successful approach devised by Professor Querido will entirely solve the problems which mental illness presents. One does not want to be pessimistic at this stage, but it is important to realise the limitations imposed by the clinical, social, and cultural complexities inherent in the problems of mental illness. The mental hospitals' deficiencies do not always account for not achieving the desired complete remission of all symptoms. One must agree with Dr. Bickford, however, that most patients with psychiatric disorder show a very high capacity for social rehabilitation and an ability to live with their symptoms. More research is required into the causes of our successes and failures before we can say what results can be expected from this new approach.

Faced with the serious overcrowding, which burdens and often almost paralyses the proper functioning of the mental hospitals, my colleague, Dr. D. H. Bennett, and I paid a visit to Professor Querido and his colleagues in Amsterdam a little while back. We have spent some time and thought on the problems that could arise, for our own mental hospital and the community it serves, with the introduction of such a scheme as that outlined in Dr. Ling's article and your leader.

The Amsterdam scheme was developed and is operated by the local health authority, of which Professor Querido, a psychiatrist, is also the chief medical officer of health. The mental hospital under these circumstances remains without its own outpatients and other aftercare services, and we came to the conclusion that this conception was not entirely satisfactory. We therefore suggest that the scheme will require modifications in this respect. For our population area of 600,000 we should require for such a twenty-four-hour psychiatric service, apart from transport, about six additional psychiatrists and six psychiatric social workers. Even with this increased number of staff, if these were available, the saving not only in the adult mental health field but also in the departments of child care and education would be very considerable.

All this might sound unduly cautious. It is, however, certain that many of the new principles at present under discussion, adapted to this country's needs, will yield promising results. We do not mean to leave your readers

under the impression that no more capital need be spent on the mental hospitals, whose buildings are out of date and whose equipment is inadequate to meet the needs of patients. Without extra staff or resources it has, however, proved possible in our own case, by applying some of the principles of the Amsterdam scheme, to reduce the overcrowding to an extent which encourages us to plead for a fuller and realistic development of preventive and after-care services. Whilst this cannot be offered as a solution to the problem of the cause and cure of mental illness, it would undoubtedly improve the pattern of psychiatric care.

Netherne Hospital,
Coulson, Surrey.

R. K. FREUDENBERG
Physician-superintendent.

PREOPERATIVE ANÆSTHETIC OUTPATIENT CLINIC

SIR.—The interesting article by Dr. Loder and Dr. Richardson (June 5) draws attention once again to a leading advantage of such clinics; the number of surgical beds available is increased by preliminary investigations and treatment in the outpatient department.

Glycosuria can be stabilised, dental sepsis cleaned up, the anaemic patient given a normal haemoglobin level by simple therapy, and a report obtained from the chest physician on the patient with tuberculosis. A history of angina of effort or coronary occlusion can at least be noted, putting the anæsthetist on his guard, while in non-urgent cases the advice that the operation should be postponed may prevent a catastrophe.

Less important functions of the clinic include the treatment of obesity by low-calorie diet, with frequent supervision and encouragement (or censure of the uncooperative). I have seldom met a surgeon, and never an anæsthetist, who does not prefer a reasonably thin patient to a fat one. When thyroidectomy is contemplated, we examine the vocal cords by indirect laryngoscopy. It is wise to record the fact that both cords move normally before anaesthesia and operation.

I notice that some hospital authorities are encouraging the formation of these clinics within the existing establishment. This is asking a good deal of the anæsthetists, and seems a little unrealistic. The work, like all outpatient work, is time-consuming and fatiguing, and requires at least one whole session weekly.

In conclusion I should like to re-emphasise the medicolegal responsibility of the anæsthetist to his patient. Thorough pre-anæsthetic investigation and examination gives the anæsthetist an assurance which is most valuable and may be of great importance if anything goes wrong. Sometimes when feeling somewhat paranoid I think of Dr. Johnson :

"It is the fate of those who toil at the lower employments of life to be exposed to censure without hope of praise; to be disgraced by miscarriage or punished for neglect when success would have been without applause, and diligence without reward."

As anæsthetists we should take all reasonable steps to ensure that everything is done to make the anæsthetic and operation as safe as humanly possible.

General Hospital,
Southend-on-Sea.

J. ALFRED LEE.

SIR.—Dr. Lee is to be congratulated on his foresight and enterprise in initiating in 1949 the idea of an anæsthetic outpatient clinic.¹

It has been said that a new idea is the most potent antigen known to science, and it is not surprising that as yet relatively few of these clinics are in existence. It was refreshing to read in January, 1952, of the clinic established at St. George's Hospital, London, by Green and Howart,² and in your issue of June 5 of the one run by Dr. Loder and Dr. Richardson at the Peterborough

Memorial Hospital. This was referred to as a pre-operative clinic; but, having had a similar type of clinic one afternoon a week at the Hull Royal Infirmary for the past three years, I find it is also of value in seeing patients postoperatively, particularly those on whom one has done diagnostic and therapeutic nerve-blocks and those subjected to specialised techniques such as controlled hypotension.

The principle of the anæsthetic outpatient clinic is sound; it can be managed successfully, and I believe one should form an integral part of every anæsthetic department.

The anæsthetist of the future must be not merely a technician but also a physician, and it is already possible to obtain the M.R.C.P.E. with anaesthesia as the special subject and the F.R.C.P.(C.) with emphasis on anaesthesia.

Hull.

W. N. ROLLASON.

SECULAR HUMANISM

SIR.—Dr. Joseph Walker (May 15) seeks to discredit humanism by saying it is incompatible with Christianity, in much the same way that McCarthy has succeeded in discrediting liberalism by insinuating that it is un-American. Just as American liberals must now cast about for another word to describe the man who conceives his own political interest as bound up in that of society as a whole, so will humanists, if Dr. Walker's "smear" sticks, have to find another word for the deliberate rational quest of human welfare. Thus is our language littered with the untouchable corpses of contaminated words, like the mounting waste of material and tools rendered permanently and lethally radioactive in the production of the bombs.

In maintaining that Communist society is a natural outcome of the humanist tradition he confuses the latter with materialism. The deliberate quest of human welfare does not produce cruel systems, such as Russian Communism or the Spanish Inquisition, which arise from the enforcement of a creed ostensibly in the interest of the majority but in reality out of hatred for the minority. Hatred of the bourgeois is disguised as concern for the proletariat, hatred of heretics disguised as concern for their souls.

By using a revered word, Christianity, with which he tells us humanism is incompatible Dr. Walker seeks to darken the meaning of the latter. Unfortunately he does not tell us whether by Christianity he means the teaching of Christ or that of the Church. Humanism in no way conflicts with the former, but it is of necessity secular—i.e., free of the Church—for it hopes to influence Hindus, Moslems, Christians, Jews, in fact humanity. If by Christianity he means the teaching of the Church then he can hardly expect its firm espousal, which he recommends to the West, to be followed with enthusiasm by our brethren in Asia and Africa. Unencumbered with the elaborations of Alexandrian and European theologians, the teachings of Jesus, an individual and incidentally an Asian, stand far greater chance of acceptance.

Humanism preaches the need for universal love and the conquest of hate but it does so through the method and terms of science, partly because science is one of the few products of Western culture which command universal respect. But more important is the fact that science is the method of securing maximum agreement, with its appeal to the evidence of this world rather than to the authority of dead theologians conjecturing about the next.

The Christian Church has had many hundreds of years in which to persuade mankind to accept its doctrines, yet its failure to do so is continually blamed on mankind (a product of God) rather than on the Christian Church (a product of men). It is hardly likely to succeed in the few decades that are left to us to choose between total destruction and a deliberate rational search for agreement

1. Lee, J. A. *Anæsthesia*, 1949, 4, 169.

2. Green, R. A., Howart, D. D. C. *Ibid*, 1952, 7, 40.

among all men, at present divided by their adherence to man-made religions, philosophies, and nationalities.

The appeal of the Church is waning because of its insistence that man must adapt to its doctrine rather than vice versa, because of the denial of the biological nature and needs of man involved in much of its mythology and ethics, because of its circumvention rather than incorporation of the scientific attitude, and lastly because of its complacency towards the problem of overpopulation—almost as urgent a danger as are the bombs.

Saskatoon, Saskatchewan,
Canada.

A. G. RICHARDS.

SURGICAL TREATMENT OF ACUTE OSTEITIS IN CHILDHOOD

SIR.—By describing a simple but possibly very useful modification of technique as “abandoning the method so strongly recommended” Professor Trueta suggests (June 5) that I have been disillusioned in my early preference for aspiration of pus in osteomyelitis as opposed to open operation. Far from it: to improve a technique is not to abandon it, and the use of lavage through two (not several) needles may prove to be a way of getting over the main disadvantage of aspiration, the need for frequent repetition in some cases. The results continue to be as good as before, that is to say as good as those reported from Newcastle seven years later.

The demand for an “objective” report of our late results is reasonable enough. So as to avoid any suspicions that our accounts of our cases may be subjective Professor Trueta is hereby given an invitation to join Dr. Bodian and myself in a review of them at any date that suits him.

As to our original argument, those interested in medical polemics will find it rewarding to look up the correspondence.¹ It ended with an unanswered challenge to state in what ways the final results of open operations are better than those of aspiration; it is obvious enough in what ways they are worse.

London, W.1.

DENIS BROWNE.

EARTHING ELECTROCARDIOGRAPHS

SIR.—A rising water-main is usually considered the most efficient earth for electrocardiographs that require earthing, but one is not always readily available; in such cases the earth-wire of a three-pin plug is often a satisfactory alternative. It is an advantage to be equipped for using any of the several standard-size plugs and I have found the following arrangement useful:

The earth-pin of a three-pin 2-amp. plug top is fitted with a single wire about 6–8 in. long, the other end of which is fitted with a crocodile clip with screw terminal. This is connected with the earth-wire of the electrocardiograph. The other two pins of the three-pin 2-amp. plug top are fitted with two wires (twin flex) to carry the A.C. supply to the instrument and with a terminal (5-amp. two-pin socket or bayonet cap) that can be connected with the terminal of the A.C. supply wire of the cardiograph. This arrangement makes it possible to use a three-pin 2-amp. plug for providing the A.C. supply and earthing of the instrument.

By adding a 5-2-amp. three-pin adaptor, a 5-amp. three-pin plug can be used, and by the further addition of a 15-5-amp. three-pin adaptor (M.K. standard, protected by a 5-amp. fuse) a 15 amp. three-pin plug can be used.

With this outfit, which can be put together easily and cheaply, one is equipped to use any of the three standard sizes of three-pin plugs (15-amp., 5-amp., 2-amp.) for providing the A.C. supply and the earthing. This arrangement, however, cannot be used with the more recent 13-amp. square plugs, which are fitted in some new houses, but a plug top of these square plugs can easily be fitted with the necessary wires and terminals.

London, W.1.

A. SCHOTT.

1. *Brit. med. J.* 1947, i, 757 et seq.

THE DISABLED

SIR.—In your leader of June 5 you state that the Central Council for the Care of Cripples finds that some employers make up their quota of disabled by engaging people whose disability does not hamper them for the work in hand. Surely it is just this that needs to be done. The more disabled people that are in jobs congenial to both themselves and their employers, the smaller the problem of employing disabled people.

In occupational health it is necessary to achieve a harmony between the individual and his working environment. A deaf man is better suited to work in a boilermakers' shop than one with acute hearing (in this instance the disability is a positive advantage). A person with a history of bronchitis should not be employed in a silica brickworks or as an electric-arc welder but will probably be well suited to assembly work in a toy factory as long as there is no soldering involved. With a little training a blind person is perfectly able to operate a telephone switchboard.

The essence of employing disabled people is to achieve this harmony, and the only way it is likely to be achieved is by studying the problems and applying the results in the factory. In medicine generalisations are never satisfactory, and in the last resort these problems always boil down to the individual case and one or two possible jobs in any particular factory. It should always be remembered that the main function of industry is to produce, and good production results from the intelligent use of men, machinery, and materials. If industry uses disabled men intelligently it adds an important social function to its main purpose.

Dunvant,
near Swansea.

G. G. MATHEW.

SIR.—In your admirable leading article there is one statement with which I do not find myself in agreement. You say, in the sixth paragraph, “a bank clerk with a gastric ulcer . . . is not disabled and should not count towards the quota.”

Why not? Surely the intention of the Act was to safeguard our weaker brethren. Where mechanical aids decimate staffs (as, I am informed, may happen), will not some remote managing director in the city say: “Yes, now we'd better get rid of Jones in the Littletown Branch first, he's lost a fair amount of time in the last few years.” And so poor Jones, unprotected, goes and his ulcer increases another few millimetres in diameter. Or perforates.

Again, “the regulations might well be tightened . . .” This is a fair comment, but how is it to be done? Those of us in industry know that registration under the Act does not represent a true picture of the extent of disabilities. We can all think of workers whose justification for registration is slight; we know that the motives which cause a man to register are many and various. But, by and large, the definition of a disabled person is fair, just, and reasonable, and if it be interpreted in the liberal spirit of the Act no injustice will be done.

It seems to me that the more practical approach would be to raise the quota for industry generally or to apply differential quotas. The latter solution may not appeal because of the inevitable controversy and dispute which it would arouse.

Finally, Sir, one of the functions of the industrial medical officer is to fit the disabled worker, where possible, into a job in which his disability is of no account and he can work on equal terms with his fellows. But that does not mean to say that the disabled worker has the same potential mobility as his fit colleagues. Should hard times come again, the mobility of labour is going to be much more important than it has ever been since the far-off days of 1939.

Rotherham.

R. McL. ARCHIBALD.

DIET AND CORONARY DISEASE

SIR.—After reading Professor Duguid's riposte to Dr. Leitner and Mr. Daw I turned to the very next page of your June 5 issue to find the photograph of the late Sir James Spence and, opposite, his words: "Techniques have their place in medicine, but they are not medicine."

Surely neither Professor Duguid in his laboratory experiments, nor Dr. Leitner in quoting statistics, presume to do more than stimulate speculation on this subject by "techniques" which in both instances could be used to confound their own deductions.

To a practising clinician coronary disease and atherosclerosis spell ageing—wear and tear of the cardiovascular system: "A man's as old as his arteries." He may be mystified why patients with similar heredity, habits, and environment should present at times vastly different rates of ageing, but he does come to see and know as a clinical fact that cardiovascular wear and tear is associated with the seven fat years rather than the seven lean ones, that the seven fat years do not mean merely increased fat percentage of total calories, but increased percentage of mechanical transport, sedentary occupation, and nervous as opposed to physical exertion. On this broader base-line Dr. Leitner's graph assumes a more clinical flavour.

Likewise it is of remoter significance to know how a certain lesion is laid down or how it can be mimicked in dog or rabbit than to appreciate why such a lesion means myocardial infarction in one and not in another—a problem that Professor Wenckebach's series of 5000 necropsies leaves unanswered.

London, W.1.

W. PINNINGTON JENSON.

APPOINTMENTS SYSTEMS

SIR.—Your annotation last week on the "reasonable, practical, and kindly duty of arranging appointments systems for outpatients" maintains that failure to provide such a system is due to lethargy. There are, however, under certain circumstances valid arguments against an appointments system, and as such apply to one of the hospitals in Leeds Group A, I would like to indicate them.

Ideally appointments are the perfect system. In practice when such a system is instituted the consultant decides the maximum number of patients he can see at each session compatible with giving each a really comprehensive examination. Inevitably in some departments this number is less than was seen in the pre-appointment days, and as a result a waiting-list is soon built up and the patient may have to wait several weeks or even months for an outpatient appointment. There are two possible ways of preventing a waiting-list accumulating. More consultants could be appointed, but this does not seem likely to happen in the near future. Alternatively the consultants could see sufficient numbers of patients at each session to clear the list of patients wanting appointments each week. This would lead to a lowering of the

standard of work but would be counterbalanced by the patient being seen within a few days.

In Leeds there are two main outpatient departments: the General Infirmary, where an appointments system has been working very efficiently for some years but where, at times in some departments, outpatients may be kept waiting several weeks for an appointment; and the Public Dispensary, which maintains the "open door" system whereby patients are sent up without a previous appointment and seen if possible the same day (occasionally on very big days they may be referred to the next session). Pressure has been brought to bear on the dispensary to adopt an appointments system. Before any action was taken the local medical committee was consulted and was strongly opposed to any appointments system. The general practitioners maintained that for many patients it was much less deleterious to wait an hour or two on a given day in outpatients than to wait several weeks for an appointment before they ever go to the hospital. The patients appreciated this when it was explained to them.

It is obvious that in Leeds we are lucky in having the two systems working side by side. Where a case is not urgent and the general practitioner wants to send him to a special consultant at the infirmary he can have an appointment. On the other hand for non-acute but relatively urgent conditions the patient can go at once to the dispensary, though he may have to wait a bit when he gets there. For subsequent visits appointments are made at both hospitals.

This letter is a plea against generalisations, emanating from a central authority, which, though excellent in theory, may in certain circumstances do the patient more harm than good.

F. F. HELLIER

Chairman of the Medical Advisory Committee,
Leeds Group A Hospitals.

ACTION OF ISONIAZID AND ANTIBIOTICS ON NOCARDIA MADURÆ

SIR.—The effect of antibiotics on several human pathogenic fungi has lately been reported.^{1,2} We should like to report a study of the effect of antibiotics in vitro, against *Nocardia madurae* (previously known as *Actinomyces madurae*), the causative organism of Madura foot, which is prevalent in parts of Southern India. Antibiotics have been used in the treatment of this disease but results have been inconclusive.

In our experiments a strain of *Nocardia madurae* was grown in Ashby's mannitol broth (medium A) and glucose-peptone broth (medium B),³ and assay was made by the serial-dilution method. The assay tubes, each containing 10 ml. of the final broth, were incubated at 37°C for up to three weeks, and the activity of the antibiotics was determined from measurements of growth. The results given in table I indicate the potency of different antibiotics in varying

1. Bieberdorf, F. W. *Antibiotics and Chemotherapy*, 1953, 3, 513.
2. Waksman, S. A., Romano, A. H., Lechevalier, H., Raubitschek, F. *Bull. World Health Org.* 1952, 6, 163.
3. Ashby, S. F. *J. Agric. Sci.* 1907, 2, 38.

TABLE I—EFFECT OF DIFFERENT ANTIBIOTICS ON *Nocardia madurae*

Concen- tration (μg. per ml.)	Streptomycin		Chloramphenicol		Aureomycin		Penicillin		Actidione		Patulin		Polymyxin		Penicillic acid	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
0	++++	++++	++++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
10	+++	+	++++	+++	-	-	+++	+++	+++	+++	+++	+++	+	-	+++	±
25	+	±	+++	++	-	-	+++	+++	+++	+++	+++	++	++	-	-	++
50	-	-	++	±	-	-	+++	+++	+++	++	++	++	-	-	+	-
75	-	-	-	-	-	-	+++	+++	+++	++	++	-	-	-	±	-
100	-	-	-	-	-	-	+++	+++	+++	++	+	-	-	-	-	-

++++ = good growth. +++ = medium. ++ = poor. + = very poor. ± = doubtful. - = no growth.

TABLE II—EFFECT OF ISONICOTINIC ACID HYDRAZIDE AND STREPTOHYDRAZIDE ON *Nocardia madureae*

Concen- tration (mg. per ml.)	Isoniazid		Streptohydrazide	
	A	B	A	B
0	++++	++++	++++	++++
0.25	+++	++++	-	++++
0.50	+	++++	-	+++
1.0	-	++++	-	++++

concentrations against the test organism. All experiments were carried out in triplicate and the mean values recorded.

Isoniazid and streptohydrazide (a condensation product of isoniazid and streptomycin) were similarly tested, but limiting concentrations were much higher than those used in the case of antibiotics. The same experiments were carried out, and the results are given in table II.

It was shown that streptomycin and aureomycin might be successful in clinical use and that polymyxin is also worth clinical trial. Actidione and patulin, two anti-fungal agents, had no promising inhibitory action while penicillin, although widely used, had practically no action against test organism. Streptohydrazide was effective in concentrations of 0.25-1.0 mg. per ml. and isoniazid inhibited growth only at concentrations of 0.5-1.0 mg. per ml.

The absence of inhibition by isoniazid and streptohydrazide in medium B, is difficult to explain on the available data, and further work on this point will be reported elsewhere.

Our thanks are due to Dr. A. Chakravorty, of the School of Tropical Medicine, Calcutta, for the strain of *Nocardia madureae*, and to Messrs. Chas. Pfizer for pure samples of antibiotics.

A. K. BANERJEE

Microbiological Laboratory,
Bose Institute,
Calcutta, 9.

G. P. SEN
P. NANDI.

ARTROPLASTY v. ARTHRODESIS

SIR.—It is very wrong of Sir Reginald Watson-Jones (June 12) to use such a phrase as "the results [of arthroplasty] can be good if the operation is done well, and most recent failures have arisen not because the operation was bad but because the operation was done badly." Surely he does not really mean thus to insult those of us who have had reason to doubt the efficacy of recent methods of arthroplasty of the hip-joint. The investigations reported by Dr. Margaret Shepherd,⁵ are based upon work carried out in half a dozen centres by a number of competent surgeons in 500 cases. The conclusion is that too high a proportion of cases have results which do not stand up long enough to stress of normal character. The operation and after-treatment, which costs the State at least £200 and has only a 50% chance of giving satisfaction for five years, must be regarded with the gravest doubt. It is probable that the results are even worse than my figures suggest. Such would not be tolerated by any general surgeon treating hernia or gastric ulcer.

To say that the bad results of surgery are the results of bad surgery is a half-truth that can be quite untrue. Many surgeons regard gastro-enterostomy as a bad operation even though it has produced some excellent results with a low mortality; but their opinion is not based upon the fact that occasionally the operation was badly done. What right has Sir Reginald to stigmatise the work of his professional brethren, when unsuccessful, as "done badly"? If the result of such criticism should be to prevent other surgeons from allowing an honest inquiry into their results, he will have done surgery a disservice.

Exeter.

NORMAN CAPENER.

4. Pennington, F. C., Guerico, P. A., Solomons, I. A., J. Amer. Chem. Soc. 1953, 75, 2262.

5. See *Lancet*, May 29, 1954, p. 1113.

SURGERY OF THE THYMUS GLAND

SIR.—In his article last week Mr. Geoffrey Keynes refers to some of the evidence for the existence in myasthenia gravis of a circulating curare-like substance, and suggests the thymus gland as a source.

The established neuromuscular block of myasthenia undoubtedly has the properties of a competitive inhibition or curare type of block. Thus, it is reversed by substances having only an antagonism for competitive block in common (e.g., neostigmine, adrenaline, and tetraethylpyrophosphate), it is potentiated by *d*-tubocurarine, and it is greater on higher (tetanic) rates of nerve discharge.

It is, however, a far cry from establishing the presence of a competitive inhibition block in myasthenia to suggesting a circulating curare-like substance of thymic origin as the cause of it, particularly as this would not explain many of the clinical and experimental findings peculiar to myasthenia. For instance, it is difficult to see how the circulating curare-like substance alone could produce weakness confined to isolated peripheral muscles such as occurs in some forms of myasthenia. Further, it can be observed both clinically and electromyographically that myasthenic weakness, unlike that produced by *d*-tubocurarine, is a progressive type of transmission block, requiring a period of exertion to produce it, and reversing on relaxation.¹ In fact, the whole clinical and electromyographic picture is that of a cumulative neuromuscular block dependent on the arrival of nerve impulses and totally unlike the effect of the administration of muscle relaxants of either the competitive inhibition or depolarising type to conscious human subjects.

Similarly, experimental evidence does not support the concept of a circulating curare-like substance as the cause of myasthenic weakness. Neither measurements of the relative sensitivity of different myasthenic muscles to *d*-tubocurarine² nor the reactions of such muscles to decamethonium salts³ lend support. The latter consists in either tolerance to or the production of a competitive inhibition block by decamethonium iodide, a substance which normally acts as a pure depolariser. This phenomenon is explicable only in terms of local changes at the motor end-plates of myasthenics.

Finally, attempts to obtain direct evidence of the presence of a substance in the serum or thymus tissue of myasthenics, capable of depressing nerve-muscle preparations, have been numerous⁴ and as contradictory as the results of thymectomy appear to be. In this connection, we note that Mr. Keynes states: "these thymus glands can be made to yield a potent extract which repeats on the laboratory bench the nerve-block effect ordinarily obtained with tubocurarine." In fact, according to the publication he quotes,⁴ thymus extracts, while capable of depressing the response of nerve-muscle preparations to indirect stimulation, have not been shown to leave the response to direct stimulation unaffected, nor to produce a depressed response capable of reversal by neostigmine or worse on high rates of nerve stimulation. Thus, thymus extracts from myasthenics have not been shown capable of producing the competitive inhibition or curare-like neuromuscular block which is characteristic of the condition.

In summary, we suggest that the available clinical and experimental evidence indicates that the weakness in myasthenia gravis is due to local changes at the motor end-plates, and is not due to a circulating curare-like substance of thymic origin.

London.

H. C. CHURCHILL-DAVIDSON

A. T. RICHARDSON.

1. Denny-Brown, D. Amer. J. Med. 1953, 15, 368.

2. Jarrett, P. S., Eaton, L. M., Lambert, E. M. Amer. J. Physiol. 1948, 155, 3.

3. Churchill-Davidson, H. C., Richardson, A. T. J. Physiol. 1953, 122, 252.

4. Wilson, A., Obrist, A. R., Wilson, M. Lancet, 1953, ii, 368.

Obituary

ANGELO LOUIS PETER PEENEY M.R.C.S.

Dr. A. L. P. Peeney, director of the clinical pathological service of the Queen Elizabeth and General Hospitals, Birmingham, died in the Queen Elizabeth Hospital on June 10 at the age of 50.

He was a son of the late John Peeney of Blackpool, and he studied medicine at Manchester University, qualifying in 1928. After holding appointments as house-physician at the Manchester Royal Infirmary and the Brompton Hospital, London, he became a member of the staff of the Royal Infirmary laboratory, and later of the public-health laboratory, in Manchester. In 1936 he was appointed clinical pathologist to the Queen's Hospital, Birmingham. Two years later, when the Queen's ceased to be a general hospital, his laboratories were transferred to the new Queen Elizabeth Hospital, where he remained in charge of pathology and haematology until his death. In 1946 he was given supervision also of the corresponding laboratories at the General Hospital, and was appointed an honorary lecturer in his subject at Birmingham University.

Shortage of staff and the steady increase in routine work gave him little time during the earlier years for research, but when these burdens were eased he made valuable contributions to his special subject, notably on the action of the antibiotics and the blood picture in the sprue syndrome. His descriptions of this blood picture are some of the earliest and most accurate that have been given. But the bare outline of his career and the short list of his publications go little way towards accounting for the influence and esteem which Peeney enjoyed in his hospitals and outside them. H. M. S., a member of his staff, writes: "Peeney's papers bear only a token relation to his knowledge, acuteness, and industry. He did not confine his interests to one type of disease, leaving the rest to his juniors and to laboratory routine, and for all cases he set the most exacting standards of investigation. He saw patients himself; he learnt every detail about them; he considered their problems with an anxious care which was often prolonged far into the night. This diligence and his natural shrewdness gave him an almost divinatory power of diagnosis far beyond his own field, and he seemed to be consulted by everyone about everything. In later years the unceasing stream of doctors seeking for his help took up the greater part of his day, but it is safe to say not one of them ever received the impression that Dr. Peeney was sparing his time with reluctance. Another great host of visitors was his patients. Among them, his warm personal interest, his kindness, and his courtesy commanded extraordinary respect and affection. Those who came up regularly for routine examinations still wished always to see Dr. Peeney, if only for a moment, and were inclined to go away dissatisfied if for once they did not succeed. His attitude of universal kindness was not unallied to an amused penetration into the characters of others. His staff can affirm that his tolerance of their faults was due to charity and not to blindness. Nor was his devotion to his work due to narrowness of interests. He had a full appreciation of all the good things of life. Of sport, particularly cricket, he was a keen follower, and his knowledge of its annals appeared to have no limits."

T. L. H. looked upon Peeney's department as the pivot on which the medical activities of the hospital turned; "and the man measured up to the stature of his work. Humility, charity, wisdom, and humour were his in full measure and he held malice towards none. Nothing was too much trouble, and even when beset with the many cares of his office he was always available in his laboratory or in the wards for consultation. The reports from his department were models of lucidity, and when difficulties arose they were invariably followed by Peeney himself in an attempt to clarify an obscure problem—and I recall with gratitude and pleasure many fruitful conversations over morning coffee. When the history of the early years of the Queen Elizabeth Hospital comes to be written the name of Angelo Peeney will hold an honoured place. Meanwhile the hospital mourns the

loss of a devoted servant, and his colleagues that of a lovable man. His memory will remain unforgettable and unforgotten."

Dr. Peeney is survived by his wife and a son.

DOUGLAS NOEL HARDCASTLE M.R.C.S., D.P.M.

Dr. Noel Hardcastle, physician to the London Clinic of Psycho-Analysis, died on May 17 at the age of 62.

He was born in Brighton, the son of S. B. Hardcastle, and he studied medicine at St. Mary's Hospital, London, qualifying in 1915. He joined the R.A.M.C. almost at once and the following year went to France with the 60th London division. From 1920 to 1921 he served as a neurologist in charge of "shell-shock" wards at Ministry of Pensions hospitals in Edinburgh and Manchester.

After his return to civilian practice he took the D.P.M. in 1922 and was appointed to clinical assistantships at Bethlem Royal Hospital and in the psychiatric department at St. Mary's Hospital. He also continued to act as a specialist for the Ministry of Pensions at their London neurological clinic and to serve on their boards. During these years he served for a time on the staff of the Tavistock Clinic. In 1927 he was appointed to the staff of Moorcroft House under Dr. G. W. B. James, but in 1929 he gave up this post to spend three years of postgraduate study in the United States at child-guidance clinics in Philadelphia and Los Angeles. After his return to this country in 1932 he gave most of his time to this growing specialty. His work as the founder and director of the Fulham clinic quickly won recognition, and when child guidance was started by the Herts County Council, under the directorship of Dr. W. J. T. Kimber in 1934, Hardcastle was appointed psychiatrist to take clinical charge of the Hill End Hospital nerve clinic at St. Albans. He established the child-guidance service in Hertfordshire but resigned in 1938 because of ill health.

During the second world war he served as a psychiatrist with the Emergency Medical Service, first at Haymeads Emergency Hospital at Bishop's Stortford and later at Wharncliffe neurosis centre in Sheffield. Since 1943 he had been in consultant practice at Bishop's Stortford; he was also a physician on the staff of the London Clinic of Psycho-Analysis.

W. H. writes: "Dr. Noel Hardcastle was a keen thinker and observer of everything relating to the development and conflicts of children, and as the years went by he felt more and more the need to look for what was not on the surface. Uncompromising as he was, he underwent psycho-analytic training shortly before the second world war, and despite his age he insisted on seeing it through. In these last years, by combining work as a psychiatrist and psycho-analyst in a small provincial town with the pleasures of family life, he had found a solution for which other colleagues, perhaps with greater professional rewards, may silently envy him."

Dr. Hardcastle married Miss Kitty Duguid, who survives him with their three children.

SERGEI YUDIN Hon. F.R.C.S.

Professor Yudin, chief surgeon of the Sklifosovski Hospital for Traumatic Diseases in Moscow and director of the surgical clinic of the Moscow Postgraduate Medical School, died on June 14 at the age of 64. He received the honorary fellowship of the English College in 1943.

Before the war Professor Yudin was chiefly known in this country for his use of stored cadaver blood for transfusion. As the central hospital for emergency surgery in Moscow the Sklifosovski Institute received many patients in urgent need of transfusion, while many severely injured people died in its receiving-rooms. Convenience may thus have led Yudin to use, and later to store, cadaver blood for the copious transfusions which he advocated, but he also believed that it had certain advantages over blood from a living donor—notably that it did not need the addition of an anticoagulant. A not unnatural repugnance had to be overcome, but in 1937 he was able to describe in our columns¹ an organisa-

1. *Lancet*, 1937, ii, 361

tion which he had built up over ten years, and to record that in over 1000 cases transfusions had been successfully given.

Yudin was also well known as a resourceful abdominal surgeon—he numbered his gastrectomies by the thousand. But during the war he turned his attention to the treatment of compound fractures. As his work on blood-transfusion showed, he believed in examining an urgent problem afresh, and the technique he advocated for these war injuries was different from the practice of most Western surgeons. He did not limit his intervention to casualties reaching operation within six to twelve hours, and he excised all necrotic tissues, making a large hole into the limb, and keeping it wide open by suturing the skin to the deep fascia not only in the primary wound but in any counter-opening that might be needed to secure free drainage.

When a British surgical mission visited Russia in 1943^a they were struck by the vast scale on which surgery is done in the U.S.S.R., and one of the occasions of their wonder was to find their newly elected honorary fellow doing three operations in one day for the replacement of permanently obstructed oesophagus by jejunum, working with an astonishing rapidity and ease of technique.

SIR JAMES SPENCE

Few men have the qualities of heart and mind required of a great teacher, but Sir James Spence possessed them in abundant measure. It was inevitable that young men were attracted to work with him, for he was a master of his subject, and, possessing a sensitive human philosophy of life, he liked helping and stimulating young men. From many parts of the United Kingdom and British Commonwealth of Nations men sought training with him, and as an Australian I had the honour and privilege of serving as a member of his team. My association with him developed into a warm friendship over the years, for it was characteristic of him to maintain an interest and help those who had worked with him.

In addition to his outstanding ability as a teacher James Spence made two great contributions to paediatrics. The first was his work on the care of children in hospital, the second in the field of clinical science. His wide knowledge of medicine and society, together with a humanitarian philosophy, were responsible for his revolt against the common and often rather inhuman practice of segregation of infant and child from its mother both in obstetric and children's hospitals. The principles of his practice of mother-child care in hospitals have now been widely accepted, and have done much to improve the care of the infant and child while in hospital and to abolish parental and child anxiety. In the field of clinical science Spence adopted the study of the whole individual and his environment. He maintained that this approach had been largely neglected and that there was much to learn, especially in children's illness. His departmental study of the illnesses and environment of a thousand families is an outstanding model and contribution towards understanding common family problems and illnesses.

He built his house well, for those young men whom he inspired and taught will carry on his work.

Melbourne, Australia.

H. W.

Dr. A. O. F. ROSS

E. E. P. writes: "A. O. F. Ross was not only one of the most distinguished venereologists of the day, but a man with an exceptionally broad background of knowledge. His enthusiasm and burning zeal were contagious and he shone as a teacher. He had unfailing sympathy and understanding, and generations of seafarers have reason to be grateful for his care and attention. He was a great doctor and a delightful host, and his great sense of humour made him a most amusing correspondent. He endeared himself to all; our hearts are heavy at his going."

2. *Ibid.*, 1943, ii, 198.

Births, Marriages, and Deaths

BIRTHS

MANN.—On June 5, at Brighton, to Joy, wife of Dr. Trevor P. Mann—a third son.

Diary of the Week

JUNE 20 TO 26

Monday, 21st

UNIVERSITY OF LONDON

5 P.M. (University College Hospital Medical School, University Street, W.C.1.) Prof. B. T. Mayes (Sydney): Postpartum Haemorrhage.

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. Brian Ackner: Psychiatric Problems during Pregnancy and the Puerperium.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

2 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Prof. J. Louw (Cape Town): Pelvic Inflammation.

Tuesday, 22nd

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2

3.45 P.M. Prof. R. J. Last: Pectoral Girdle. (Arnott demonstration.)

Wednesday, 23rd

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1

5 P.M. Section of Endocrinology. Dr. G. W. Thorn (U.S.A.): Diagnosis and Treatment of Disturbance in Adrenal Cortical Function.

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. H. Haber: Acantholysis.

Thursday, 24th

UNIVERSITY OF OXFORD

8.30 P.M. (Nuffield Orthopaedic Centre, Wingfield-Morris Orthopaedic Hospital.) Prof. C. G. Rob: Present Status of Blood-vessel Grafting.

HONYMAN GILLESPIE LECTURE

5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Mr. D. L. Savill: Ankylosing Spondylitis.

Friday, 25th

POSTGRADUATE MEDICAL SCHOOL OF LONDON

2 P.M. Mr. T. McW. Millar: Surgical Experiences in Treatment of Obstructive Jaundice.

4 P.M. Dr. E. G. L. Bywaters: Collagen Diseases.

ROYAL SOCIETY OF MEDICINE

8.15 P.M. Section of Obstetrics and Gynaecology. Professor Mayes: Cesarean Section and Management of Subsequent Pregnancy and Labour.

INSTITUTE OF CARDIOLOGY

5 P.M. (1, Wimpole Street, W.1.) Dr. Graham Hayward: Pulmonary Oedema. (St. Cyres lecture.)

INSTITUTE OF LARYNGOLOGY AND OTOLGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Mr. K. G. Rotter: Otitis Media in Children and Infants.

Appointments

BYRNE, UNA B., M.B. Belf., D.A.: anaesthetist, Fermanagh H.M.C.

DOWNING, D. M., M.B. Belf., D.A.: anaesthetist, North Antrim group of hospitals.

FLOOD, J. J., M.B. N.U.I., D.P.M.: senior asst. R.M.O., The Priory, Roscommon, S.W.15.

• HEFFLESTON, J. D., M.B. Manc., DIP. PATH.: consultant pathologist, South Cheshire Hospital centre.

JUSTICE, J. J., M.B. B.Sc. Glasg., D.P.M.: consultant psychiatrist and medical superintendent, St. Mary's Hospital, Stannington.

LAURIE, ALEXANDER, M.B. Glasg., D.P.H.: asst. county M.O.H., Derbyshire, and M.O.H., borough of Ilkeston and urban districts of Alfreton and Ripley.

RAMSAY, CHRISTINE M., M.B. Lond., D.A.: anaesthetist, Royal Cancer Hospital, London.

SIDDLE, J. L., M.B. Durh., D.P.H.: asst. county M.O., Durham (No. 4 area), M.O.H., urban and rural districts of Chester-le-street.

Appointed Factory Doctors:

CADENHEAD, R. MCN., M.B. Aberd.: Lerwick, Shetland.

KILVERT, E. E. K., M.B. Birn.: Clevedon, Somerset.

ROWNTREE, J. K., M.R.C.S.: Grantham, Lincoln.

The Bethlem Royal Hospital and the Maudsley Hospital:

HOBSON, R. F., B.A., M.D. Camb., D.P.M.: physician.

HOFFER, WILLI, M.D., PH.D. Vienna, L.R.C.P.E.: physician.

REES, W. L. L., M.D., B.Sc. Wales, M.R.C.P., D.P.M.: physician.

South-Western Regional Hospital Board:

AZAM, M. A., M.B. Punjab, F.R.C.S.E.: surgical registrar, South Devon and East Cornwall Hospital, Plymouth.

BALMFORTH, G. V., M.B. Lond., D.O.BST.: medical registrar, Gloucestershire Royal Hospital, Glos.

COLE, PAULINE, M.B. Lond., D.C.H.: paediatric registrar, South Devon and East Cornwall Hospital, Plymouth.

DUTTON, J. E. M., M.B. Durh., F.R.C.S.: senior registrar, department of neurological surgery, Frenchay Hospital, Bristol.

GERRARD, JEAN O., M.B. St. And.: anaesthetic registrar, Bath group of hospitals.

HOY, C. H. A., M.B. Lond.: surgical registrar, Torquay and Newton Abbot hospitals.

Welsh Regional Hospital Board:

CORRADO, H. A., M.D. Malte: asst. chest physician (S.H.M.O.).

Caernarvon and Anglesey H.M.C.

COSGROVE, P. C., M.B. Dubl., F.R.C.P.I., D.T.M. & H.: asst. chest physician (S.H.M.O.), Swansea.

SEAL, R. M. E., M.B. Wales, M.R.C.P.: consultant pathologist, Sully Hospital.

* Amended Notice.

Notes and News

AN APPEAL FOR THE RHEUMATIC

THE British Rheumatic Association has prepared a five-year plan including the setting up of special hostels, the promotion of medico-industrial reablement, village and home treatment, and measures to help the sufferer to help himself. To get this plan going an appeal is being made for £75,000 in the first year and £150,000 in subsequent years. At a luncheon held in London on June 10 Mr. Tom Williams, who presided, said that there were so many sufferers from rheumatism that the disease was often taken for granted; but the country could not afford to take it for granted any longer. Lord Horder, as "the father of the Empire Rheumatism Council," said that the council had primarily taken on the function of research, but at the same time had tried to make people understand how widespread and painful and costly the disease was. Ten years ago, in "A Plan for National Action," he had hammered on the doors of the Ministry of Health; and these had opened a little way—only alas to shut again. He hoped that the British Rheumatic Association would (1) do something to make early diagnosis easier, and (2) do something for patients after they had been treated in hospital. Here they would be undertaking work that the Empire Rheumatism Council could not undertake. And he hoped that they would mobilise public opinion, which could be done only by voluntary effort. When public opinion was mobilised, the official doors would open again.

Sir Walter Puckey explained that the association's scheme would be of direct value to industry. Rheumatism stood very high on the list of causes of absenteeism and loss of production. It was estimated that the disease caused the loss of some three million working weeks every year, and in terms of sickness benefit, medical care, and production loss the cost was put as high as £250 million a year—all this apart from the human suffering. As chairman of the Pioneer Hostel established at Bracken Hill House, Northwood, by B.R.A. Homes Ltd., of which he is chairman, Sir Walter expressed the hope that many other hostels of the same kind would be set up. Dr. Francis Bach said that rheumatism was not taken seriously enough in the early stages either by the sufferer, by the manager, or by the doctor. Also there should be more understanding of the importance of the relation between the man, his employer, and his work. Four stages of disability could be recognised: some patients regained full working capacity; a second group, though handicapped, could also carry on. A third group, however, required sheltered conditions and these ought to be provided. Many people, though called cripples, still could fill an important place in industry: if the kitchen does not suit one's wife, one does not change one's wife but modifies the kitchen—and similarly industrialists should modify their industrial processes. Work could be provided, too, for the home-bound. All this required careful planning; and at present, though the majority of rheumatism patients were fit to go back to work of some kind, it was extremely hard to get them replaced in industry.

The association's address is 11, Beaumont Street, W.1.

WELFARE FOODS

WHEN the local offices of the Ministry of Food close at the end of June, welfare foods—liquid milk, National dried milk, cod-liver oil, orange juice, vitamin tablets—will still be available for expectant mothers and young children, but the following changes will be made in the system:

Distribution.—From June 28 the foods themselves (except liquid milk) will be distributed by the local health authority at welfare clinics or other convenient centres. Liquid milk will continue to be distributed by dairymen.

Entitlement Documents.—Until the end of October, when a new system will start, existing ration books will continue to be used as proof of entitlement for expectant mothers, babies, and young children. These books should, therefore, be preserved carefully when food rationing ends in July. New applications for entitlement documents should be made to the local office of the Ministry of Pensions and National Insurance or, in some places, the Ministry of Labour and National Service.

SYMPOSIUM ON TUBERCULOSIS

THE latest issue of the *British Medical Bulletin*¹ contains a symposium on tuberculosis covering a large field stretching from laboratory research to the organisation of chest clinics. The quality of the articles varies widely. Some are outstanding, especially those on vaccination with the vole bacillus, the relationship between the host cell and the parasite, the action of cortisone and certain surface-active agents on

the tuberculous animal, and the detection of pulmonary tuberculosis in a community. The article on drug resistance may possibly confuse but will certainly stimulate the reader; and the importance of this subject to the clinician is admirably discussed by Dr. J. G. Scadding, the scientific editor. It is a pity that a few contributors seem to have forgotten that the *Bulletin* is intended primarily for foreign readers. A didactic style and criticism of the health and social services in this country are out of place in it.

SLEEP HABITS OF SCHOOL-CHILDREN

We do not know how many hours of sleep any person needs, or (which is a different thing) how many he could use with advantage, given the opportunity. The need, in any case, varies from person to person, and in the same person over a lifetime.

Dr. G. P. McLauchlan² has made a small study of the sleep habits of children, aged 10½–11½, attending county primary schools in Guildford. All the children were examined physically and "no child with any defect likely to interfere with his wellbeing was included in the survey." The sleep habits of the 250 accepted for study were established by questioning them and their mothers. Their bedtimes varied widely, one of them going to bed at 6.30 P.M. and three at 10 P.M.; the largest number, however, went to bed at 8 o'clock. Most of them awoke or were awakened between 7 and 8 A.M. though one boy regularly wakened at 5. But going to bed is one thing and going to sleep is another; and McLauchlan took the precaution of finding out how long they stayed awake after getting there. An estimate based on the answers of the mothers and children suggests that one child was having as little as 7½ hours' sleep while three were getting as much as 12½ hours. The largest number got 11 hours, and some five-sixths of the total were having 10–11½ hours.

Sleep, however, varies in quality as well as quantity; and he quotes the work of Davis et al.³, who distinguished, by electro-encephalography, five depths of sleep, merging into one another: (1) a stage of dropping off to sleep when one is neither asleep nor awake; (2) a stage of light sleep; (3) a deeper stage in which one can yet be easily disturbed; (4) sound sleep, in which the patient is not easily disturbed; and (5) really deep sleep. The depth of sleep varies in the course of the night, and in children the variation follows a fairly definite pattern. Depth of sleep increases rapidly from the moment the child falls asleep, and reaches a maximum by about the end of the 1st hour. Sleep then becomes progressively lighter until about the 6th hour, after which it again deepens, to reach a second period of great depth at the 8th or 9th hour. After that it becomes lighter again until the child wakes, or dozes until called. McLauchlan draws the conclusion, which may or may not be justified, that if a child is hard to waken in the morning he has not completed his sleep cycle, and so has not had as much sleep as he needs. Of his 250 children, 184 (three-quarters) wakened of their own accord, 53 wakened easily on being called, and 13 were difficult to waken.

He noted, too, that 43 of the children had a poor appetite for breakfast, a symptom which is also thought to be associated with a sleep deficiency; and indeed 7 of the 43 were among those difficult to waken. There were thus 49 children, who, judged by these standards, might be going short of sleep. But—unless their requirements were much above the average—the deficiency for most of them was not in quantity: for four-fifths of them were in bed by 8.30 and all but 5 were getting 10–12 hours' sleep. Some of them took longer to go to sleep than the other children studied, only slightly over half of them being asleep 30 minutes after going to bed, as against four-fifths of the rest. Reading in bed cannot be blamed, for only 9 of them enjoyed this privilege. Neither sharing a room nor sharing a bed seemed to interfere much with their sleep, and in any case more than two-thirds of them had a bed to themselves. Presumably their sleep deficiency was therefore a matter of quality rather than quantity; but it is hard to be sure from this study that these 49 children really were suffering from a lack of sleep. If they were, it had evidently not affected their health seriously, or they would not have been included in the survey. Their inability to waken easily and their lack of appetite for breakfast are interesting symptoms, certainly, but they are surely susceptible of other explanations besides a lack of sleep.

1. *Med. Offr.*, 1954, 91, 261.

2. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., Hobart, G. J. *Neurophysiol.* 1937, 1, 24.

SPECIAL DIETS

THE Hospital Catering Advisory Service of King Edward's Hospital Fund for London has issued a useful booklet for the guidance of catering officers, kitchen superintendents, and housekeeping and nursing sisters at smaller hospitals where there is no trained dietitian.¹ The essentials of a balanced diet are explained, and, on the basis of this, various special diets are described: for diabetes; for reducing weight; gastric diets; bland low-residue diets; diet for occult-blood test; high-protein and low-protein diet; low-fat diet; salt-free diet; and gluten-free diet. A specimen kitchen sheet is given, and there are recipes for gastric diets, for sauces for fat-free diets, and for using gluten-free flour.

University of London

Dr. C. B. B. Downman, senior lecturer at St. Thomas's Hospital Medical School, has been appointed to the readership in physiology at the Royal Free Hospital School of Medicine.

Among those on whom the university will confer honorary degrees to celebrate foundation day on Nov. 26 is Sir Rudolph Peters, F.R.S., who will receive the degree of D.Sc.

University of Durham

Mr. D. J. Tibbs, first assistant in the department of surgery, has been appointed reader in surgery in the Newcastle division.

Royal College of Surgeons of England

The directors-general of the medical services of the Armed Forces attended a meeting of the council held on June 10, when the following medals were presented:

The Sir Gilbert Blane medal to Surgeon Commander J. L. S. Coulter; the Mitchiner medal to Lieut.-Colonel H. D. Chalke; and the Lady Cade medal to Squadron-Leader R. R. L. Pryer.

Mr. R. S. Handley (Middlesex Hospital) was admitted to the court of examiners, and Mr. D. M. E. Thomas (Sully, Glam) and Mrs. Dorothy Campbell (Coventry) were admitted to the fellowship.

The following were co-opted to the council for the year 1954-55 representing various branches of practice:

Dr. O. C. Carter (general practice), Prof. A. M. Claye (gynaecology and obstetrics), Mr. Myles L. Formby (otolaryngology), Dr. Bernard Johnson (anaesthetics), Mr. A. B. Nutt (ophthalmology), Dr. E. Rohan Williams (radiology). Prof. F. C. Wilkinson was invited to act as the representative of dental surgery.

The following examiners were appointed for the ensuing year:

Fellowship.—Ophthalmology: E. A. Blake Pritchard. Anatomy: D. N. Matthews, Mary F. Lucas Keene, Lambert C. Rogers, R. J. Last. Applied Physiology and Pathology: Geoffrey Hadfield, Albert Hemmings, J. L. D'Silva, H. A. Magnus. Diploma of L.R.C.P., M.R.C.S.—Elementary Biology: Alan Fisk, G. E. H. Foxon. Anatomy: Thomas Nicol, E. W. T. Morris, A. J. Heriot. Physiology: C. C. N. Vass, Esther M. Killick. Midwifery: R. G. Maliphant, W. R. Winterton, H. H. Fouracre Barns, Ian Donald. Pathology: L. E. C. Norbury, Joseph Bamforth, A. C. Cunliffe, V. C. Pennell.

Diplomas of fellowship were granted to the following:

F. L. Davies, M. J. May, H. F. McG. Bassett, A. L. T. Easton, N. C. Rees, M. J. Gilkes, W. J. Gall, F. E. Weale, A. L. Levene, I. L. Macfarlane, M. A. Brennan, W. F. W. Southwood, A. A. Eley, Gerald Keen, O. L. Thomas, † A. G. Ackery, Pamela M. Moody, F. H. Haine, Daya Shankar Kaicker, Anand Narain Razdan, † D. R. Scorgie, A. S. Dawson, Joseph Hirshstein, † J. S. Martin, Kamel Mohamed Said, Michael Salvaris, Phillip Goldstein, G. N. Perera, E. A. M. Ryan, *T. A. S. Boyd, P. F. Early, Catherine N. McRobert, Chimbanhai Jiawabhai Patel, Pesi Bharamsha Bharucha, J. L. Edmondson, P. D. Hill, N. H. Birch, Ben-Ami Eilenberg, John Kirk, Chimbanhai Cheturbhai Patel, Nader Mohamed Soualem, Tarun Kanti Banerjee, *J. D. Brosman, J. R. Dickson, Michael Kugler, M. E. Leake, T. D. H. Perera, † B. H. Pickard, Khalid Abdul Aziz Qassab, Piyasiri Rathnayaka Walpita, J. A. M. White, Mohamed Yassef Ahmed Alyan, I. M. Cran, Ahmed Refaat El Mazny, Colm Galvin, J. G. Hamilton, † Akkinapalli Badri Narayan, Rao, J. S. Roarty, † H. W. H. Sheppard, H. F. R. Story, † T. P. Cannon, Sukumar Das, M. J. Gallagher, J. E. Howson, J. F. Lee, Alexander McCaister, Tassaduddin Hussain Moghul, Bernard Murphy, J. P. O'Neill, † P. B. O'Neill, D. N. Robinson, E. F. Soothill, R. T. Todd, W. F. Walker, Kadirbukhsh Yar Mohammed Ansari, R. A. Bailey, S. C. Baker, A. J. Davies, J. K. Francis, F. C. Hoyte, W. J. Metcalfe, Charles Miller, L. J. Opit, N. H. Porter, † Noel Roydhouse, Hassouna Mahmoud Saba, L. A. Wells, T. G. Lorentz, Maqbool Ahmad, Krishna Kant Bhatnagar, J. H. Kettle, Sarinder Man Singh.

* In ophthalmology. † In otolaryngology.

The fellowship of the faculty of anaesthetists was granted to B. H. Smith, and a diploma of membership of the college to H. N. Baylis.

1. Memorandum on Special Diets. 1954. Obtainable from King Edward's Hospital Fund for London, 10, Old Jewry, London, E.C.2. Pp. 36. 1s. post-free.

Royal College of Physicians of London

Dr. E. B. Verney, F.R.S., will deliver the Bertram Louis Abrahams lecture on Thursday, July 8, at 5 p.m., at the college, Pall Mall East, S.W.1. He is to speak on Renal Excretion of Water and Salt.

Royal College of Surgeons in Ireland

At a meeting of the college on June 7, the following officers were elected:

President, Ian Fraser; vice-president, A. B. Clery; other members of council, J. F. L. Keegan, R. A. Stone, Henry Stokes, J. F. Devane, William Pearson, A. A. McConnell, T. O. Graham, William Doolin, Frederick Gill, T. G. Wilson, M. P. Burke, C. H. G. Macafee, R. R. Woods, S. F. Heatley, J. H. Coolican, T. A. Boucher-Hayes, N. A. Kinnear, E. W. L. Thompson, J. M. McA. Curtin.

Royal College of Physicians of Ireland

At a meeting of the college held on June 4, with Dr. Edward Freeman, the president, in the chair, the following were admitted to the fellowship:

Alan Proctor Grant, Rex St. John Lyburn (in absentia).

The following were admitted to the membership:

H. T. F. Barniville, Mary E. Bewley, F. R. Counihan, C. K. Heffernan, Ferdinand Hillman, M. J. Lalor, A. J. MacDonald, Hugo McVey, Samuel Miller, W. A. Norris, A. P. H. Randle, Charles Reid, D. S. Wilson.

Lady Tata Trust

The trustees of this fund announce that they have made the following awards for research on leukaemia and allied diseases, in the year beginning next October:

Grants for research expenses.—Dr. Astrid Fagraeus and Dr. Bo Thorell (Stockholm); Dr. Jo Nordmann (Paris); Dr. Arunachala Sreenivasan (Bombay).

Senior research fellowship.—Dr. Jørgen Kieler (Copenhagen).

Scholarships.—Dr. Ragna Rask-Nielsen (Copenhagen); Dr. Roger Robineaux (Paris); Dr. Flemming Kissmeyer-Nielsen (Aarhus, Denmark); Dr. N. A. Stenderup (Aarhus, Denmark); Dr. Jørgen Ringsted (Copenhagen); Dr. Jørgen Rygaard (Copenhagen).

Part-time scholarship and grant for research expenses.—Dr. Maxime Sellmann (Paris).

A special scholarship awarded to Dr. Gayino Negroni (Italy), for work at the Imperial Cancer Research Fund Laboratories, will continue until April 30, 1955.

Mackenzie Industrial Health Lecture

Dr. W. M. Goldblatt will give the Mackenzie lecture on Tuesday, July 13, at 2.30 p.m. in the Library Theatre, Manchester. He will speak on Research in Industrial Health in the Chemical Industry.

North of England Society of Anaesthetists

On May 21 Dr. E. J. Millar, the president, presented the registrar's prize to Dr. F. Sorrell for his essay on bronchospasm. Dr. M. H. Armstrong Davison was elected president for the coming session, and Dr. E. I. Tate was re-elected hon. secretary.

Northern Ireland Health Services

Sir George Henderson, Mr. J. V. S. Mills, and Mr. H. G. Tanner (chairman) have been appointed to advise minister of health and local government on the health services in Northern Ireland. Dr. G. C. Kelly and Mr. N. Dugdale will act as joint secretaries to the advisers.

Wellcome Research Laboratories

Colonel H. W. Mulligan has been appointed head of the biological division of these laboratories, in succession to Dr. J. W. Trevan, F.R.S., who retired last year.

After graduating M.B. from the University of Aberdeen in 1923, Colonel Mulligan joined the Indian Medical Service. He was posted to its medical research department in 1928 and he remained in this branch, except for three years on active service during the war, ultimately becoming consultant malariologist, Persia and Iraq Command. Among the appointments he held in India were those of director of the Pasteur Institute, Coonoor, and later of the Central Research Institute, Kasauli, where he had earlier been in charge of the serum and vaccine department. When the I.M.S. was disbanded in 1947 he went to West Africa to set up the African Institute for Trypanosomiasis Research. Colonel Mulligan is the West African representative on the Scientific Council for Africa, and a member of the International Scientific Committee for Trypanosomiasis Research and of the World Health Organisation expert panel on parasitic diseases. During the last three years he has shared in planning the West African Council for Medical Research, which was established a few months ago.

CORRIGENDUM.—The late Prof. J. B. Buxton, whose death we recorded last week, was president of the Royal College of Veterinary Surgeons in 1932-33, and in 1936 he became principal of the Royal Veterinary College.

**REMARKS ON THE
ÆTILOGY OF BRONCHOGENIC
CARCINOMA ***

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PROBABLY everyone here is aware of the claim that bronchogenic carcinoma is a much more common condition than it was thirty or thirty-five years ago. Although there are still a few who, like Smithers of the Brompton Hospital, are sceptical of this claim (Smithers 1953), the overwhelming majority of those who have studied the question are thoroughly convinced. There has been a striking increase in the incidence of the disease which cannot be explained by the greater longevity of people nowadays or by better diagnosis. Few realise, however, that the very remarkable increase is unique in the field of cancer. Probably never before in medical history has a cancer of a particular organ shown so rapid an increase. Other common cancers with which we are familiar are showing either no change or perhaps even a slight decline in incidence (fig. 1). Cancer of the respiratory system in the United States, and I believe in the United Kingdom, has now jumped to the leading position, superseding cancer of the stomach for first place.

One other generality that should be mentioned here is that the condition is much more frequent in men than in women. Various ratios are given in the literature. An average of them shows that bronchogenic carcinoma is about six times more frequent in males than in females.

* From the second Sir John Fraser lecture delivered at the University of Edinburgh on May 11, 1954.

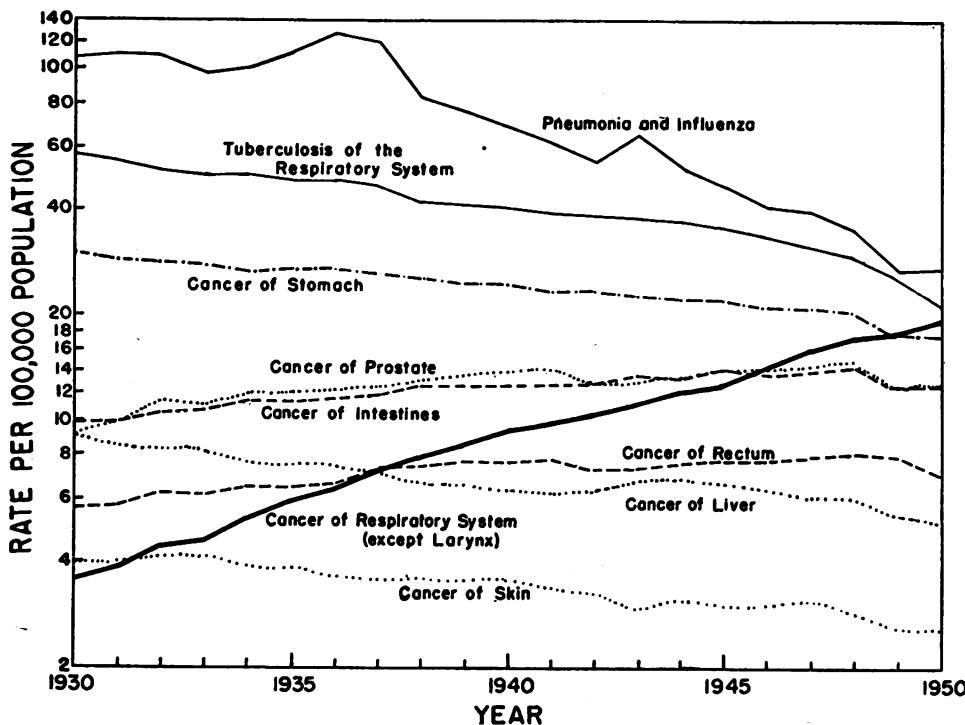


Fig. 1.—Death-rates for selected respiratory diseases and sites of cancer among white males, United States 1930-50. (Rates standardised for age on the 1940 population.) Showing the rapid rise in the curve of incidence of cancer of the respiratory system in comparison with the nearly straight lines of other common cancers. (Prepared by Dr. E. Guyler Hammond, chief statistician of American Cancer Society, and reproduced with his permission.)

This fact in itself arouses curiosity because there is no reason whatever for assuming that there is any anatomical or physiological difference between the lungs of the two sexes.

If we accept these facts it behoves us to try to find an explanation for them. Immediately of course the idea occurs that the explanation of the very rapid increase in incidence must lie in something pertaining to our culture or habits in the last thirty-five years which differs from those of a previous time. At once the possibility of some factor connected with the motor-car comes to mind, since this is the motor age. In a study, however, of 857 cases of bronchogenic carcinoma by Wynder and myself (1951), with special reference to industrial exposures as possible aetiological factors, we found no significant increase of this cancer in garage men, automobile mechanics, chauffeurs, and oil-field workers. Certain other occupational exposures are known to be associated with a greater risk of developing lung cancer than the risk run by the general population. The most striking examples are the well-known studies made on the Schneeberg and Joachimsthal miners with incidences of 40% and 48% respectively of deaths from lung cancer in the two places. Lorenz (1944) has published an admirable review of this subject. Also, more recently, it has been found that workers in the chromate industry have a higher death-rate from pulmonary cancer than does the general population (Mancuso and Hueper 1951). These industrial exposures, however, could not possibly explain the large increase in the incidence of lung cancer, because so few people are involved. Also, despite the fact that small amounts of carcinogenic agents have been found in the atmospheric "smog" of some cities, as, for example, in Los Angeles by Kotin (1954), it would be difficult to explain the lower incidence of the disease in the women who inhale the same atmosphere as the men.

Relation to the Tobacco Habit

As long ago as 1912 Adler, of New York, who wrote the first monograph on bronchogenic carcinoma, at a time when the condition was relatively rare, suggested that perhaps tobacco-smoking might be of some importance in the aetiology. Since that time the list of those who have made the same suggestion has become a long one. The difficulty, however, has been that in most instances only the suggestion was made and nothing was done to try to find out. What was needed was a statistical study on a sufficiently large number of patients to make the results significant.

In May, 1950, Wynder and I published such a study, based on 684 proven cases. Nearly all the patients were in the Barnes Hospital, St. Louis, but they came from many places in the Middle West and Southwest of the United States. They were interviewed about their

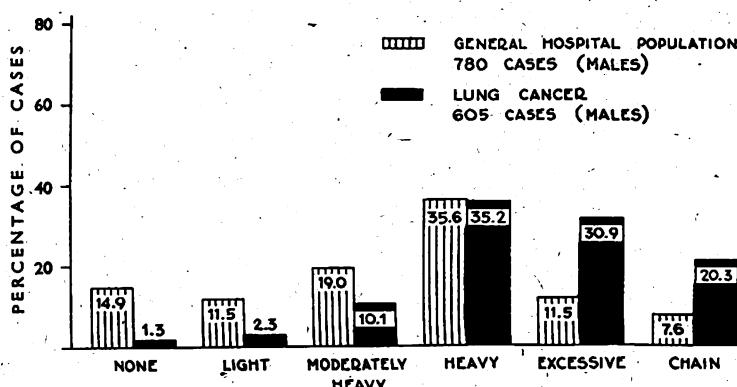


Fig. 2.—The amount of cigarette-smoking in 605 male patients with proven bronchogenic carcinoma as compared with 780 males over 35 years of age without cancer of the lung (Wynder and Graham 1950).

The arbitrary classifications of smoking are as follows: Non-smokers (less than one cigarette per day for more than twenty years); light smokers (up to one-half pack per day for more than twenty years); moderately heavy (one-half to three-quarters of a pack); heavy smokers (three-quarters to a whole pack); excessive smokers (one to one-and-three-quarters packs); chain smokers (more than one-and-three-quarters packs).

smoking habits by one of three young women who used a standard questionnaire. In our study we found that of 605 men with bronchogenic carcinoma, other than adenocarcinoma, no less than 86.5% had smoked from about a pack to more than two packs of cigarettes a day for at least twenty years †; and among these men with the two common types of carcinoma (epidermoid and undifferentiated) only 1.3% were non-smokers. Of a control group of 780 men without lung cancer 54.7% had a similar history of heavy smoking of cigarettes, and 14.9% were non-smokers (fig. 2). We found also that no less than 72% of the men with lung cancer stated that they had smoked for from thirty to fifty years. Another important finding concerned the smoking habits of women. Although it is commonly stated that women smoke at least as much as men, if not more, the findings of our study of 552 women patients without lung cancer and above the age of 35 revealed the rather astonishing fact that 79.6% of them were non-smokers, as compared with only 14.9% of men in a similar control group (fig. 3). It is clear, therefore, that, at least in the United States, it is not true that women in general smoke as much as men. It is the young women and the girls who do the heavy cigarette-smoking, not the women of the cancer age. Moreover, the young women have not been smoking for the period of more than twenty years which seems to be necessary in order to develop a cancer of the lung.

In September of that year appeared in England the well-known statistical study of Doll and Hill (1950). Although it happened to be published a few months after ours it was begun about the same time and was carried on entirely independently of ours. It was based on about the same number of patients, who were interrogated in about the same manner as ours. Their results also closely resembled ours. For example, of 649 men with cancer of the lung only 0.3% were non-smokers. A high proportion of the patients with lung cancer were in the heavier-smoking categories. Doll and Hill conclude that their figures "suggest that, above the age of 45, the risk of developing the disease increases in simple proportion with the amount smoked, and that it may be approximately 50 times as great among

those who smoke 25 or more cigarettes a day as among non-smokers."

Actually, in addition to our own (Wynder and Graham 1950, 1951) and that of Doll and Hill (1950) ten different statistical studies have been reported (Breslow et al. 1954, Dungal 1950, Gsell 1951, Kouloumies 1953, Levin et al. 1950, McConnell et al. 1952, Mills and Porter 1950, Sadowsky et al. 1953, Schrek et al. 1950, Wynder and Cornfield 1953). Some are less significant than others because the numbers of cases were too small. Nevertheless, all the studies reported point in the same direction in showing a probable relation between excessive cigarette-smoking and the production of bronchogenic carcinoma. No study has failed to show a relation.

Carcinogens in Tobacco Smoke?

Although the statistical studies suggest very strongly that excessive cigarette-smoking plays an important part in the aetiology of lung cancer, it is obvious that experimental production of cancer with cigarette

smoke would make the evidence stronger. The literature on this subject is long. It has been carefully reviewed in a recent article by Wynder, Croninger, and myself (1953). For the most part the results have been negative, though a total of seven epidermoid cancers of the skin have been reported as having been obtained in mice with products of cigarette smoke, out of many animals used. Most workers who have attempted to incite experimental cancer with tobacco products have used rabbits. Roffo (1939) reported the successful production of carcinoma in rabbit ears after painting them with a distillate of tobacco, but Sugiura failed in his attempt to reproduce Roffo's results. Also Flory (1941) succeeded in obtaining only "carcinomatoids" in rabbit ears after application of a tobacco distillate.

It seemed to us, after studying the literature, that the occurrence of cancer in the experimental animals was so rare that it offered little if any conclusive evidence beyond that produced by the statistical studies. Moreover, little was known or stated about the strains of mice used. This is a very important matter because, for the experiments to have value, a strain of mice must be used which is known not to develop spontaneous cancers of the skin. Accordingly we undertook an experimental study to determine whether we could produce cancer by

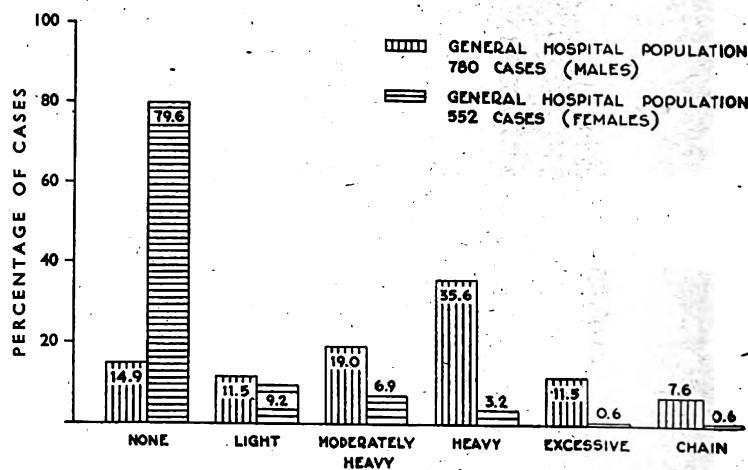


Fig. 3.—This chart (Wynder and Graham 1950) refutes the common belief that women smoke as much as men, at least in the St. Louis area. The statistics were obtained by questioning 780 male and 552 female patients in the Barnes Hospital. None of the patients had a bronchial carcinoma and all were more than 35 years old.

† A pack contains 20 cigarettes.

painting the skin of mice of a suitable strain with tar collected from cigarette smoke. For our purpose we used mice belonging to the inbred strain known as CAF₁, which is free from spontaneous tumours of the skin. This strain has been developed in Dr. C. C. Little's laboratory at Bar Harbor, Maine.

We devised a machine with which we smoked 60 cigarettes at a time by means of a small motor. The smoke was drawn into flasks which were cooled with dry ice. The sudden cooling of the smoke resulted in the precipitation of the tar from the smoke. This tar was dissolved in acetone and the solution was painted on the skin of the mice. Thrice-weekly paintings of a solution of one part of tar to one part of acetone were used. The acetone proved to be an inert substance which failed to produce even any irritation of the skin of control mice which were painted with that substance alone.[†]

Of 81 tarred CAF₁ mice, 59% (26 females and 22 males) developed papillomas. Of these papillomas, 8.6% regressed. More important, however, was the fact that



Fig. 4—Carcinoma induced in mouse by painting with tobacco tar ($\times 50$).

of the 81 tarred mice 44.4% (or 36 mice) developed epidermoid cancer of the skin (figs. 4 and 5). In most instances there was only one cancer but in several cases there were two, and in one mouse actually three cancers appeared on the painted area. In view of the preponderance of incidence of lung cancer in the human male it is of interest that in the experimental animals 25 of the cancers occurred in females and 11 in males.

Several of the cancers produced in the mice have been successfully transplanted into other mice. In one example, successful transplantation was carried out for twenty generations.

One of the striking results of the experiments was the fact that the average time of appearance of a cancer was after seventy-one weeks of painting. This period of time represents a little more than one-half the average life-span of the mouse, which is ordinarily a little more than two years. The duration of painting required to produce a cancer in a mouse is thus equivalent to the approximate thirty to fifty years of smoking in the human required to produce a bronchogenic carcinoma; for that period is a little more than one-half the life-span of the human.

[†] For details of the experimental work the reader should consult our original article (Wynder, Graham, and Croninger 1953).

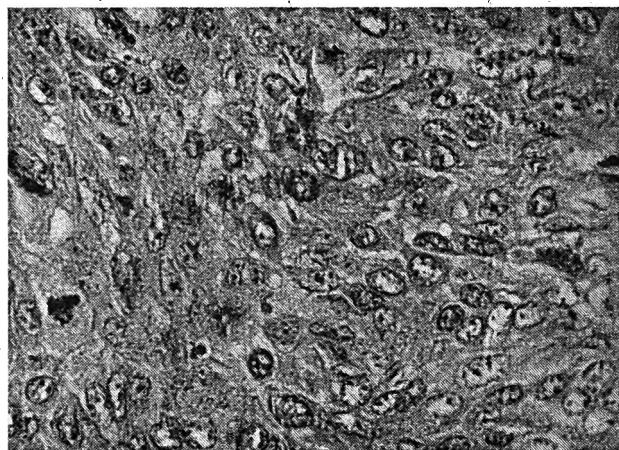


Fig. 5—Same lesion ($\times 200$).

These experimental results demonstrate that there is something in the smoke of cigarettes which is capable of producing carcinoma of the skin of mice.

Significance of the Findings

What is the significance of the findings? We find that many thoughtful people believe that our experimental results bring to the statistical studies additional convincing evidence of an aetiological relation between excessive cigarette-smoking and bronchogenic carcinoma. There are others, however, who remain unconvinced. These "die-hards" state that so far no proof of the relation has been presented. One must grant that indeed no absolute proof has been offered. But what sort of proof is called for? To satisfy the most obdurate of the die-hards it would be necessary to take the following steps:

- (1) Secure some human volunteers willing to have a bronchus painted with cigarette tar, perhaps through a bronchial fistula.
- (2) The experiment must be carried on for at least twenty or twenty-five years.
- (3) The subjects must spend the whole period in air-conditioned quarters, never leaving them even for an hour or so, in order that there may be no contamination by a polluted atmosphere.
- (4) At the end of the twenty-five years they must submit to an operation or an autopsy to determine the result of the experiment.

I will say to those who wish to volunteer for such an experiment, "please form a queue to the right; no crowding please."

Perhaps the animal experiments might be somewhat more convincing if the cancers had been produced in the bronchi instead of in the skin; but there can be no doubt that we have demonstrated the presence of a carcinogenic factor in cigarette smoke. The technical experimental difficulties in the attempt to produce a cancer of the bronchus in a mouse are very great. Long-term inhalation experiments for the most part have been fatal because the mouse is relatively intolerant to nicotine. Indeed, after the cancers had ulcerated, we were compelled to use denicotinised tar in the painting of the animals because fatal amounts of nicotine were absorbed through the raw surface of the ulcer. If larger animals are used, in order to create bronchial fistulae more easily, the experiment must be carried on for a much longer time in view of the apparent rule that the contact with the tar must be for approximately one-half the life-span of the animal. Actually for a period of two and a half years we have been painting some bronchial fistulae in dogs, but we expect to have to continue the experiment for about three years longer.

Different Kinds of Carcinoma

One source of the disagreement among those who are interested in this subject is, it seems to me, the common opinion that bronchogenic carcinoma, or primary cancer of the lung, is a single entity. (The statisticians, who know little, if anything, about pathology, are especially likely to fall into that error.) Actually, there is much evidence that there are at least three distinct varieties of this disorder, differing from each other so much that they may be regarded as three distinct diseases, with different aetiological factors.

I fully realise that one should not place too great reliance on differences and classifications based on the morphological appearance and arrangement of cells. As a rule there is no great difficulty in distinguishing between a typical epidermoid (or squamous) carcinoma and an adenocarcinoma, but there are a good many cases in which there is very little differentiation. Usually in such examples it is possible to recognise a tendency towards the development of an epidermoid carcinoma, and we are therefore accustomed to speak of cancers showing such characteristics as undifferentiated epidermoid carcinomas.

We are inclined, then, to recognise as the three principal varieties of bronchogenic carcinoma (1) the epidermoid or squamous, with its subhead of undifferentiated carcinoma, (2) the adenocarcinoma, and (3) the so-called alveolar-cell carcinoma. The tumour which you British often designate as the oat-cell carcinoma is not regarded by us as a separate variety.

That which goes by the name of alveolar-cell carcinoma is rare in comparison with the other varieties, but from year to year more cases are recognised. It closely resembles the disease of sheep known as "jagziekte," and there is good reason to believe it is due to a virus.

In our experience by far the most common bronchial carcinoma is the epidermoid, with its variant the undifferentiated type. It constitutes more than 90% of the cases in our series. It is this variety which is apparently associated with excessive cigarette-smoking and it is found much more often in the male than in the female.

The typical adenocarcinoma has many characteristics, both clinical and pathological, which set it apart from the epidermoid cancer. Statistically it seems to have a much less close relation to smoking. For example, in our series, out of 39 men with adenocarcinoma no fewer than 4 (or 10%) were non-smokers, whereas among the other 605 men with bronchogenic carcinoma the proportion of non-smokers was only 1.3%. More striking is the fact that of 15 women with adenocarcinoma 13 were non-smokers. Another difference noted is that the very great preponderance of incidence of epidermoid carcinoma in the male sex does not hold to the same degree for the adenocarcinoma. Again, as shown by Olson (1935) and others, the primary carcinoma of the lung occurring in the younger age-groups is nearly always adenocarcinoma. Indeed Olson states that of 576 cases of lung cancer compiled from the literature by Brunn in 1926, 12% were in the age-group 20-29, and all of them were adenocarcinoma. All these characteristics seem, therefore, to suggest that the adenocarcinoma is a different entity from the epidermoid cancer. In 1938 Womack and I called attention to the malignant potentiality of the so-called bronchial adenoma. At first the idea was not generally accepted but now apparently there are few who doubt it. When this tumour does become malignant the arrangement of the cells is often of a pattern to suggest an adenocarcinoma. In some cases of adenocarcinoma, therefore, the cancer has probably originated in a so-called bronchial adenoma which has undergone malignant transformation.

Many of the die-hards who are unwilling to concede that there is any causal relation between cigarette-smoking

and cancer of the lung base their objection on the ground that they have known people to develop lung cancer who had never been smokers. If it is realised and admitted that different varieties of the condition are separate entities with different aetiologies it becomes easier to understand that, for example, a high percentage of non-smokers may be found among the group of adenocarcinomas but a low percentage in the group of epidermoid carcinomas. Again, of course, nobody would be foolish enough to state that cigarette-smoking is the only cause of bronchogenic carcinoma. As I have mentioned, the high incidence of lung cancer in the Schneeberg and Joachimsthal miners, as well as in workers in the chromate industry, suggests that some carcinogenic substance was inhaled by the workers in those industries. Moreover, for any malignant transformation to take place, there must be a reaction of the host's cells to the carcinogenic agent. After all, in our animal experiments with cigarette tars, only 44% of the mice developed carcinoma: the other 56% did not respond to the stimulus in the same way.

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INFECTION WITH DRUG-RESISTANT TUBERCLE BACILLI

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PROFESSOR

WHEN streptomycin was given alone in pulmonary tuberculosis, the bacilli became drug-resistant in a high proportion of patients from whom positive cultures were obtained after the third month of treatment. It was found that once the bacilli from a patient had become consistently streptomycin-resistant they usually remained so indefinitely. It was often pointed out that there was a danger that such a patient might infect others with his drug-resistant organisms. Harold (1951) has collected from published reports 9 cases in which tubercle bacilli isolated before treatment were found to be streptomycin-resistant. In most a source of infection could be identified. He added 2 further cases of his own, making 11 in all. Of these cases 6 were

pulmonary tuberculosis, 2 were tuberculous pleural effusions, 2 were tuberculous meningitis, and 1 was a primary tuberculous complex in the lung. In addition Debré et al. (1951) have reported 4 cases of tuberculous meningitis in which the bacilli were streptomycin-resistant before treatment was begun.

Similar dangers presumably exist when either *p*-aminosalicylic acid (P.A.S.) or isoniazid is given alone. The emergence of isoniazid-resistant bacilli in a high proportion of cases has been established by the Medical Research Council (1953a), but isoniazid has been used for a relatively short time, and we are not aware of any reports of the transmission of resistant organisms to new cases apart from 1 accidental laboratory infection (Borgen 1953). The emergence of P.A.S.-resistant bacilli when P.A.S. is given alone has received little attention in this country, but there is no doubt that it is a real danger. When tests for P.A.S. resistance have been made, resistant tubercle bacilli have been isolated in an important proportion of cases. Fresh evidence on this subject has recently been reported and the published cases have been reviewed by Turnbull et al. (1953). So far as we know, no case of infection by P.A.S.-resistant bacilli has previously been recorded.

Material and Methods

We report here cases from which tubercle bacilli resistant to streptomycin or to P.A.S. or to both were isolated but which had never received the drug to which their bacilli were resistant. Except when otherwise stated drug-sensitivity tests were made by the methods recommended by the Medical Research Council (1953b). The figures given for streptomycin and P.A.S. sensitivities are the ratio of the drug resistance of the test organism to that of the control strain H37Rv. The minimal inhibitory drug concentrations for each strain, in μg . per ml., are given in parentheses where these are known, the test strain being the numerator in each case.

Findings

INFECTION WITH PRIMARILY STREPTOMYCIN-RESISTANT BACILLI

Case 1.—A man, aged 30, was admitted to Robroyston Hospital, Glasgow, in 1951 with bilateral pulmonary tuberculosis, which probably dated from 1947. Later he developed right sacro-iliac disease with a superficial abscess, which was aspirated on numerous occasions but provided no tubercle bacilli. Tubercle bacilli cultured from the sputum in May, 1952, had a streptomycin-resistance ratio of 8 (2/0.25 μg . per ml.) and a P.A.S.-resistance ratio of 2 (0.5/0.25 μg . per ml.) and were sensitive to 0.2 μg . per ml. of isoniazid. There was no known source of infection. The patient was treated daily with streptomycin and isoniazid for three months, with moderate improvement. Cultures were negative until September, 1952 (after two months' treatment), when the sensitivities to all three drugs were unaltered. All further cultures were negative.

The history suggested that this patient had had pulmonary tuberculosis since 1947, though no radiograph was taken at that time. Streptomycin-resistant bacilli were exceedingly rare in 1947; hence this may have been a case of superinfection by streptomycin-resistant bacilli, the source of infection being unknown.

Case 2.—A girl, aged 17, was admitted to Aintree Hospital Liverpool, in April, 1952, with four months' history of cough. Radiography showed bilateral pulmonary tuberculosis. She had received streptomycin and P.A.S. for four days before admission. Culture of the sputum showed a streptomycin-resistance ratio of 128. Tests for P.A.S. resistance were not made. The patient's mother had had open pulmonary tuberculosis since 1950 and had been treated with P.A.S. alone for two months before the patient's admission; her bacilli were sensitive to streptomycin. A sister had had pulmonary tuberculosis since 1948 and had been treated both with streptomycin alone and with P.A.S. alone at different times; tubercle bacilli grown from her sputum had a streptomycin-

resistance ratio of 128. Two other sisters (twins) also had pulmonary tuberculosis, but their sputum was negative. The patient was treated with streptomycin 1 g. daily and P.A.S. 20 g. daily. Positive cultures of unaltered sensitivity were obtained one and two months after treatment began. There was moderate clinical and radiographic improvement during three months' chemotherapy but in the subsequent three months on rest in bed only she deteriorated slightly.

The patient was infected, probably by her sister, with tubercle bacilli moderately resistant to streptomycin.

Case 3.—A man, aged 26, was admitted to Aintree Hospital in April, 1952, with pulmonary tuberculosis, abnormal radiographic shadows having been present since 1947. A positive culture on admission gave a streptomycin-resistance ratio of 128 and a P.A.S.-resistance ratio of 0.5. There were two domestic contacts of the patient, neither of whom was said to have had streptomycin. The patient's wife had abdominal and pulmonary tuberculosis but had only received a month's streptomycin and P.A.S. when the patient was admitted. The patient was treated with streptomycin and P.A.S. daily for three months, with moderate clinical and radiographic improvement. Culture after the first month of treatment gave a streptomycin-resistance ratio of 128; no further positive cultures were obtained.

Since this patient was known to have had pulmonary tuberculosis in 1947 he had probably been subsequently superinfected from an unknown source with a streptomycin-resistant strain.

Case 4.—A man, aged 49, was admitted to the City Hospital, Edinburgh, in July, 1951, with chronic bilateral pulmonary tuberculosis, which had been present at least since March, 1947 (mass-radiography film). Drug sensitivities were first tested in April, 1952, when the streptomycin-resistance ratio was 8 (4/0.5 μg . per ml.) and P.A.S.-resistance ratio 16 (2/0.12 μg . per ml.); the bacilli were fully sensitive to isoniazid. The patient had been given P.A.S. alone for six months in 1949-50 but had never had streptomycin. His only son had been discovered in July, 1948, to have pulmonary tuberculosis and had died, without having received chemotherapy, in January, 1950. His wife was found to have extensive pulmonary tuberculosis in October, 1949. She received streptomycin and P.A.S. daily for forty-one days, after which P.A.S. was continued alone for five months. P.A.S. was then supplemented by streptomycin 1 g. twice weekly for a further nine months. She died four months later. Although no resistance tests were made, it seems very likely that, on the above régimes, her tubercle bacilli would have become resistant first to P.A.S. and later to streptomycin (Turnbull et al. 1953). Her husband nursed her throughout most of this illness. From April, 1952, before the sensitivity results were obtained, he was treated with streptomycin 1 g. daily and isoniazid 200 mg. daily. Twenty-five days after the start of this régime bacilli resistant to 0.2 μg . per ml. of isoniazid and with a streptomycin-resistance ratio of 64 (8/0.125 μg . per ml.) were isolated; fifty-eight days after the start the bacilli were resistant to at least 50 μg . per ml. of isoniazid. There was no clinical or radiographic response to therapy.

This patient was known to have had pulmonary tuberculosis at least since March, 1947, and was probably superinfected by his wife with streptomycin-resistant tubercle bacilli. Subsequent treatment with concurrent streptomycin and isoniazid did not prevent the emergence of isoniazid-resistant bacilli.

INFECTION WITH PRIMARILY P.A.S.-RESISTANT TUBERCLE BACILLI

Case 5.—A girl, aged 18, was admitted to Aintree Hospital in September, 1952, with bilateral pulmonary tuberculosis. She had no known domestic contacts; other patients lived in the vicinity, but none had had P.A.S. A sputum culture on admission gave a P.A.S.-resistance ratio of 64 (8/0.12 μg . per ml.). The patient was treated with P.A.S. and isoniazid daily but discharged herself before completing three months' treatment. A second culture, in December, 1952, after two months' chemotherapy gave a P.A.S.-resistance ratio of 8 (2/0.25 μg . per ml.). The culture on admission was resistant to 0.2 μg . per ml. of isoniazid, which could be regarded as within normal limits of sensitivity; after two months the bacilli were

resistant to 1 µg. per ml., probably indicating a significant rise in resistance.

The patient was infected from an unknown source with a P.A.S.-resistant strain of tubercle bacilli. By the time this was established she had been treated with daily P.A.S. and isoniazid; after two months' treatment the organisms had become slightly isoniazid-resistant.

Case 6.—A woman, aged 33, was admitted to Southfield Hospital, Edinburgh, in May, 1952, with extensive tuberculosis of the left upper lobe. She had had a left pleural effusion a year previously. There was no known source of infection. A culture on admission gave a P.A.S.-resistance ratio greater than 256 ($>32/0.12$ µg. per ml.) but was sensitive to streptomycin. Before this was known the patient was treated with daily streptomycin and P.A.S. The last positive culture, after two months' treatment, was still sensitive to streptomycin, but the P.A.S.-resistance ratio was at least 16 ($>2/0.12$ µg. per ml.). The patient subsequently made excellent progress, and laryngeal swabs were still negative a year later.

The patient was primarily infected with a P.A.S.-resistant but streptomycin-sensitive strain of tubercle bacilli. No source of infection was known. Sputum conversion took place after two months' treatment with daily streptomycin and P.A.S.

Case 7.—A boy, aged 18, with congenital pulmonary stenosis, was known to have had pulmonary tuberculosis since 1946, but had never been given P.A.S. There was no known source of infection. He was admitted to Southfield Hospital in March, 1953, with bilateral fibrotic apical tuberculosis. Tubercle bacilli cultured on admission had a P.A.S.-resistance ratio of 64 ($4/0.06$ µg. per ml.) but were sensitive to streptomycin and isoniazid. Before this was known, the patient was treated with isoniazid 100 mg. and P.A.S. sodium 5 g., both given twice daily. After two months' treatment two cultures within four days gave P.A.S.-resistance ratios of 4 ($1/0.25$ µg. per ml.) and greater than 1000 ($>64/0.06$ µg. per ml.). Such fluctuations are not uncommon with P.A.S. resistance. The first of these cultures was resistant to 50 µg. per ml. of isoniazid on solid medium. Two months later two further cultures remained highly resistant to isoniazid. There was some initial clinical and radiographic improvement.

As tuberculosis was known to have been present since 1947, this patient had presumably been superinfected with P.A.S.-resistant tubercle bacilli. The combination of P.A.S. with isoniazid did not prevent the emergence of isoniazid resistance.

Case 8.—A boy, aged 15, was admitted to Southfield Hospital in May, 1952, with tuberculous meningitis. There was no known source of infection. He was treated with daily intrathecal and intramuscular streptomycin, and daily P.A.S. The positive cultures obtained from the cerebrospinal fluid on admission, and after two days' treatment, had died before P.A.S. sensitivity was tested; these cultures were sensitive to 3 µg. per ml. of streptomycin on solid medium. The first culture on which P.A.S. sensitivity could be tested was obtained five days after treatment had begun; three tests on this culture gave P.A.S.-resistance ratios of 8, 32, and 32. The presence of P.A.S.-resistant tubercle bacilli within five days of the start of treatment suggested that the organisms were almost certainly resistant before treatment was begun. Seven days after the start of treatment a culture gave P.A.S.-resistance ratios of 4, 32, and 32 in three tests, and streptomycin ratios of 1 and 2 (probably sensitive). The patient died after about four months' treatment. Cultures obtained post mortem were resistant to 5 µg. per ml. of streptomycin on solid medium though sensitive to 10 µg. per ml.

This patient was almost certainly infected with P.A.S.-resistant bacilli, which also became resistant to streptomycin while under treatment with streptomycin and P.A.S.

INFECTION WITH TUBERCLE BACILLI PRIMARILY RESISTANT TO STREPTOMYCIN AND P.A.S.

Case 9.—A woman, aged 36, was referred from an antenatal clinic in Edinburgh in July, 1953. Bilateral apical tuberculosis had been found on routine radiography. There was

no known source of infection. Tubercle bacilli obtained on culture of the sputum had a streptomycin-resistance ratio of 512 ($128/0.25$ µg. per ml.) and a P.A.S.-resistance ratio of 256 ($16/0.06$ µg. per ml.). She was treated with rest in bed, streptomycin, and P.A.S. for two months before the sensitivity results were known. There was some clinical improvement but no radiographic change even though the lesions were of an exudative type which would have been expected to respond to chemotherapy. No further positive culture was obtained.

This patient was apparently primarily infected with tubercle bacilli highly resistant to both streptomycin and P.A.S. There was no known source of infection.

Discussion

In the light of present knowledge the proportion of patients in whom drug-resistant bacilli emerge, and who may pass these on to other people, should be small. Several of the present patients were probably infected when the dangers of giving P.A.S. alone were not generally appreciated, and when large numbers of patients were treated in this way. Others may have been infected by patients whose bacilli had become streptomycin-resistant before methods of preventing this were known. If present knowledge is sufficiently widely applied, such tragedies should become even rarer. We wish to emphasise once more the impracticability of giving one drug alone.

Our attention has recently been drawn to the possibility that at least some strains of bovine tubercle bacilli may be relatively insensitive to P.A.S. (Djang et al. 1952). The P.A.S.-resistant bacilli recorded here were not typed, because we had no reason to suspect bovine tuberculosis; but in future it would be wise to type any tubercle bacilli which appear to be primarily P.A.S.-resistant.

The controversy about the possibility and frequency of superinfection has continued for many years. Previously it could only be proved by superinfection by bovine on human infection, or vice versa. Drug resistance provides another label for the tubercle bacillus, and in 3 of the present cases (cases 3, 4, and 7) there is a strong suspicion that the patient was superinfected with drug-resistant bacilli. In a 4th case (case 1) superinfection may have taken place, but the evidence is more doubtful.

Summary

9 cases are recorded in which drug-resistant tubercle bacilli were obtained although the patient had received no previous chemotherapy with the relevant drug. In 4 of the patients the bacilli were primarily resistant to streptomycin, in 4 to P.A.S., and in 1 to both drugs.

3, and possibly 4, of the patients were known to have had tuberculosis before the relevant drug was in general use. Their original bacilli are therefore presumed to have been drug-sensitive, and it is thought that they had been superinfected with resistant bacilli.

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ADDENDUM

Since this paper was written, 6 additional cases of infection with P.A.S.-resistant bacilli have been recorded in the Edinburgh Centre.

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PRESERVATION OF ARTERIAL GRAFTS BY FREEZE-DRYING A SIMPLIFIED METHOD

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ARTERIAL grafts have been stored in several different ways, notably by refrigeration in a nutrient medium (Gross et al. 1949) and in the frozen state (Eastcott and Hufnagel 1950). Of these two methods we have preferred frozen storage because it has worked better in practice, (Rob and Eastcott 1953). The main disadvantage of "deep-freezing" for artery banking has been the need for maintaining at all times the low temperatures necessary to avoid physical and chemical changes in the grafts. Transportation in particular has been troublesome; special containers are needed, and detailed travelling arrangements have to be made.

An alternative method of preserving proteins is to dry them from the frozen state. This method is finding increasing application in the laboratory and in commerce; plasma, antibiotics, sera, and some food-stuffs can be stored readily and for a long time at room temperature in vacuum containers after freeze-drying. Arteries the surgeon can carry in his instrument bag or post to other parts of the world with as much ease as a glass ampoule can be prepared by this method.

At the National Naval Medical Center, Bethesda, Maryland, much has already been achieved in the experimental investigation of tissue banking by freeze-drying. Blood-vessels, skin, and bone have been stored in this way. Marrangoni and Cecchini (1951) and Strong (1954) have reported their results after using freeze-dried material in a large number of abdominal aortic homo-

grafting operations in dogs; they believe them to be better than those obtained with fresh homografts. Hufnagel (1954) reports that the same has been true in his experience with 12 freeze-dried aortic and peripheral arterial grafts in patients. We have used such arteries in 27 patients with satisfactory early results.

We describe here a simple method of freeze-drying arterial grafts, and report some experimental observations on the process.

Technique

PRINCIPLE

Sublimation of water vapour from the frozen state is greatly accelerated by reducing the total pressure of the surrounding atmosphere. The latent heat of vaporisation is derived from the material being dried, which is thus kept frozen. It is known that frozen solutions and suspensions must be kept below a certain temperature, which varies with the substance under examination, if separation of their constituents is to be avoided. The eutectic point of a mixed substance is the temperature above which one of its components separates out by melting; the greater part of the drying process should be done at a temperature which is below this. During freeze-drying, as the water content decreases, the temperature of the material rises towards that of its surroundings, but in other respects its composition remains constant.

METHOD

The method is based upon that used by one of us for drying purified diphtheria toxoid (Holt 1950) with much of the actual apparatus used in the early technique for small-scale production.

Grafts have been dried in the 'Pyrex' test-tubes in which they had originally been frozen, at -79°C, in several instances a year before. The rubber cap was in each case removed, and a piece of sterile gauze was secured in its place with a rubber band (to serve as a bacteriological filter when air was later readmitted to the system). The graft tubes were next placed in a glass container, attached by a standard vacuum fitting to a 2.5 or 3.0 litre glass condenser¹ (fig. 1), whose inner surface was kept at -79°C with a mixture of alcohol and solid carbon dioxide. The condenser outlet was connected by a length of 1/2-in.-bore rubber pressure tubing to a single-stage rotary vacuum pump.² A secondary moisture trap containing phosphorus pentoxide was inserted between the vacuum line and the pump to prevent any remaining water vapour from entering it. The system was found with a Pirani gauge to operate at 0.030–0.060 mm. Hg during drying. With either pump a hard note was reached in a minute or less.

1. Edwards 'Speedivac 1A' (pumping capacity 38 litres a minute) and '18.150' (144 litres a minute) were both used and proved completely satisfactory.

2. Penicillin freeze-drier: National Glass Industry Ltd.

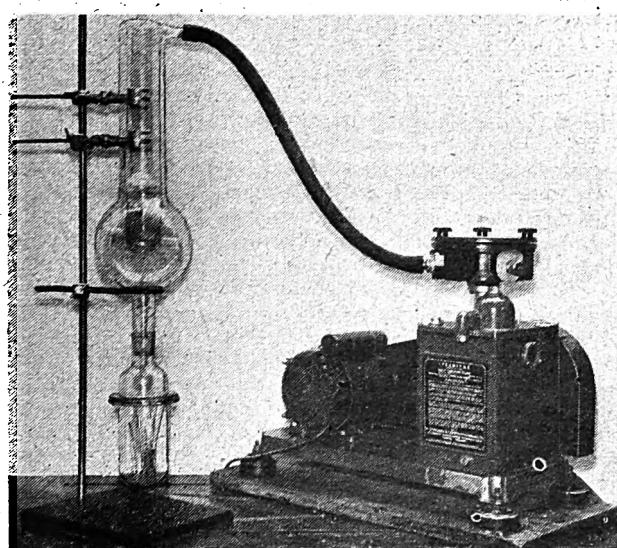
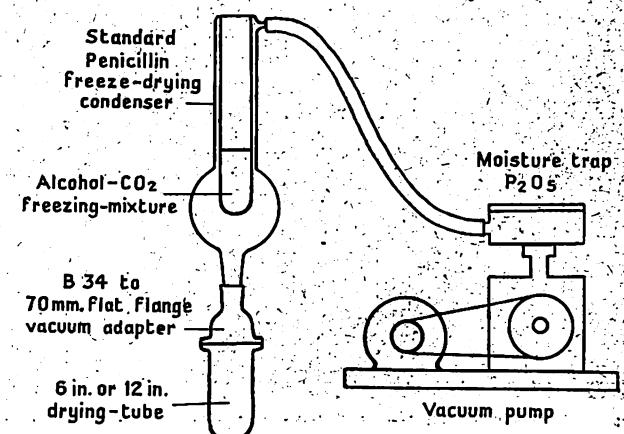


Fig. 1—Apparatus used for simultaneous primary freeze-drying of up to six arterial grafts.



Primary drying.—Under these conditions it was possible to complete the primary drying of 1-6 assorted arteries during a working day. The grafts became slightly shrunken, hard, and pinkish white, and fell free from the wall of their containers, which on removal were found to be no more than cool to the touch. A few loose fragments of dried plasma were often present. Ice accumulated on the condensing surface was recovered next morning as water and was measured.

Secondary drying.—Much of the remaining moisture was extracted by placing the grafts, still in their gauze-capped tubes, in a vacuum desiccator over fresh phosphorus pentoxide. This container was evacuated by the pump for at least twenty minutes, and the vacuum was maintained for three days or more; except with large batches, little visible change developed in the phosphorus pentoxide during this time.

Final sealing.—Close-fitting rubber caps,³ autoclaved and vacuum-desiccated, were applied to the tubes, whose gauze filters were taken off on removal from the desiccator. A sterile hypodermic needle attached to the vacuum line was next inserted through each cap in turn, and the air was thus extracted until no further increase in the vacuum obtained could be detected by the high-frequency spark tester or by the note of the pump. The needle was next quickly withdrawn, and the cap covered in melted black 'Picien' vacuum wax. In very few instances has this seal failed. Tubes have been periodically examined with the spark tester and a final check made just before each graft was reconstituted for use.

Reconstitution.—Sterile isotonic saline solution was injected through the rubber cap until the tube was full; no air was admitted until the artery had regained its

3. Baird & Tatlock Ltd. Ref. no. ZSD 4158. Suba Seal Ltd. Ref. no. 867278.

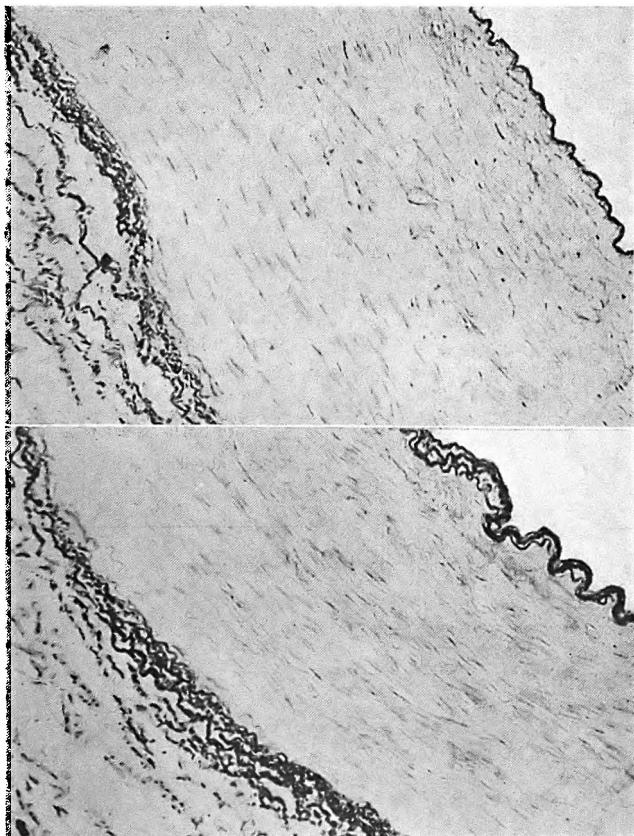


Fig. 2.—Histological appearance of same arterial graft: upper, fresh; lower, after freeze-drying and reconstitution in vacuo with isotonic saline solution.

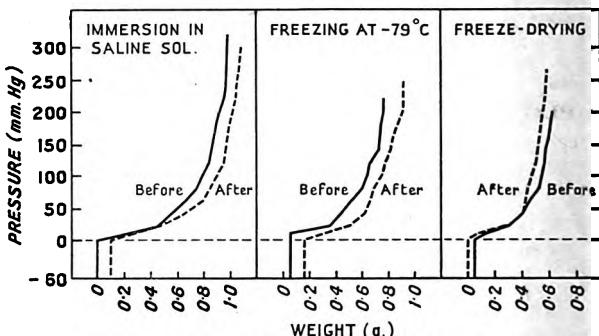


Fig. 3.—Pressure-volume characteristics of segment of same artery before and after a month's preservation by different methods. The increase in weight in g. is numerically equal to the increase in volume of the graft in ml. of injected isotonic saline solution.

normal appearance from twenty to thirty minutes later; it was then inserted into the patient or was used for the tests described below.

Experimental Observations

Bulk of Material to be Dried

An arterial tree, including the thoracic and abdominal aorta, the iliac, femoral, and popliteal arteries, and short lengths of their branches, weighed 67 g. With a large wide-necked drying tube of the type shown in fig. 1 most of the grafts prepared from such a specimen could be dried in one batch.

Examination of Condensate

Primary drying of the arteries mentioned above yielded a layer of ice on the condenser from which 37 g. of water was later recovered. This is more than the amount of water which it is practicable to remove with phosphorus pentoxide alone. For amounts greater than 15 g. a refrigerated condenser is more satisfactory but, unless mechanically chilled, needs closer attention.

Chemical analysis of the condensate showed a chloride content of 3 m.eq. per litre or less; no sodium or potassium could be detected by flame photometry. Some specimens of condensate were clear, others faintly opalescent. These were found to show a similar fluorescence on exposure to ultraviolet light to that obtained with vacuum grease.

Characteristics of Grafts after Reconstitution

Grafts reconstituted in vacuo with isotonic saline solution presented a normal fresh appearance. Histological examination showed no difference from control specimens of the same artery fixed in formalin and saline solution (fig. 2). This was true of sections stained with haematoxylin and eosin, with iron haematoxylin and van Gieson, and with elastic tissue stain.

Pressure-volume curves were constructed for three segments of human femoral artery with an apparatus constructed for us by Dr. S. Rowlands. It consisted of a mercury manometer connected by a T tap to a hypodermic syringe containing isotonic saline solution, and through a second and detachable tap to the segment of artery under examination, ligated at its free end. With each ml. of injected saline solution the increase in volume of the artery could be measured directly from its increase in weight. A curve from 0 to 250 mm. Hg was constructed for each of the three segments, and was repeated after each piece had been preserved for four weeks either by immersion in nutrient saline solution (Hanks and Wallace 1949) at 0°-4°C, or by freezing at -79°C, or by freeze-drying by the method described. The results are shown in fig. 3.

Effect of Varying Conditions of Drying

It was possible, through the co-operation of the Edwards Company, to subject three equal lengths of an

external iliac artery to the following treatment. After freezing by immersion in small capped bijou bottles in alcohol-carbon dioxide freezing-mixture at -79°C , one length of artery was dried for forty-seven hours without external cooling, the second length for six days at -30°C , and the third for fourteen days at -50°C . Each piece was then examined for residual moisture content, by the following method :

Moisture determinations.—The remaining water content of these and the other grafts examined in this investigation was extracted by a further process of freeze-drying in a micro-unit at Pirani pressures of about 0.015 mm. Hg. The vapour evolved was trapped in a narrow-bore glass U-tube immersed in alcohol and carbon dioxide at -79°C , and in equilibrium with an oil manometer in parallel with the vacuum line. The amount of ice thus condensed was next measured by closing a tap between the two limbs of the manometer and removing the cold trap, so that the ice revapourised. Its pressure thus measured was converted into terms of weight by the man-

TABLE I.—EFFECT OF TEMPERATURE VARIATION ON DRYING OF ARTERIAL GRAFTS

Temperature of drying-chamber ($^{\circ}\text{C}$)	Time of drying	Residual moisture content by final dry weight (%)	Estimated amount of original tissue water removed (%)
20	47 hr.	0.83	99.9
-30	6 days	9.32	96.5
-50	14 days	100—i.e., processed specimen still contained a weight of water equal to its final dry weight	65.5

meter scale, which was calibrated in units of 0.00001 g. H_2O . When no more water could be extracted in this way, the now totally dry specimen was quickly weighed. The percentage residual moisture content could then be calculated.

Results obtained by this method confirm that arterial tissue dries rapidly at room-temperature, but below 0°C drying-rates become progressively slower as the temperature falls (table I). Samples taken during primary drying with a thermocouple in the wall of the artery were also examined for moisture content at known temperatures in this cycle. The results of these observations are shown in table II. The final moisture content of other arteries after secondary drying for seven days over phosphorus pent-oxide in a vacuum desiccator was found to be 2% ; the transfer from desiccator to micro-drier necessarily involved a short exposure to atmospheric water vapour. This condition, however, is reproduced in the process of final sealing of grafts by the method described.

Thermometry during Freezing and Drying

The temperature of the tissue during freezing has an important bearing on its chance of physicochemical preservation, and during drying it indicates the stage which drying has reached. We have therefore recorded the temperature changes within the wall of several

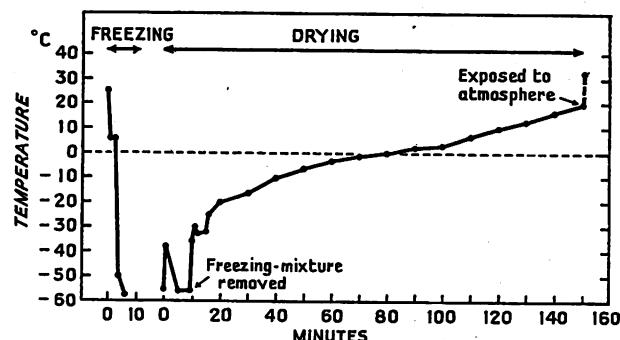


Fig. 4.—Thermocouple readings during freezing and freeze-drying of a femoral artery segment 2.5 cm. long. The peaks at the beginning and end of the primary drying cycle correspond respectively to the evacuation of the system and to the exposure of the graft to room air.

grafts throughout the cycle, using a very fine gauge thermocouple to reduce the error from conducted external heat. This confirmed what had been found by simple thermometry : freezing in an alcohol- CO_2 mixture at -79°C in an air-containing glass tube though not slow is not rapid either. A 2.5 cm. length of carotid artery, weighing 0.5 g., equilibrated with its surroundings at -58°C in five minutes, whereas a 5 cm. length of aorta, weighing 14 g., took fifteen minutes.

The same specimens were next subjected to rapid evacuation in the apparatus described, the thermocouple leads having been brought out through brass electrodes fitted into standard B.14 vacuum sockets. The results, indicated in fig. 4, prove that already frozen artery tissue

TABLE II.—MOISTURE REMOVED FROM AND REMAINING IN ARTERIAL SEGMENTS AT VARIOUS STAGES IN DRYING PROCESS

Stage of drying in chamber at $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$	Residual moisture content by final dry weight (%)	Estimated amount of original tissue water removed (%)
Specimen at -6°C in primary drying cycle	51.0	86.8
Specimen at 0°C in primary drying cycle	19.5	93.0
On reaching 20°C (end of primary drying)	4.4 5.1 5.3 specimens examined	99.2
After seven days' drying at 20°C	2.2 2.3 2.0 specimens examined	99.3

placed in the drying-chamber at a low temperature and quickly decompressed can be relied on to remain frozen by virtue of the rapid evaporation of water vapour alone. No external cooling need be used ; in fact such cooling has already been shown to slow the rate of drying. Experiments of this kind also confirmed that a moderately large batch of arteries—e.g., the whole yield from one donor—can be taken through the stage of primary drying in about ten hours.

TABLE III.—QUANTITATIVE EFFECT OF FREEZING AND FREEZE-DRYING ON BACTERIAL CONTAMINATION OF ARTERIAL GRAFTS

Control culture	Added bacteria	Method of processing graft	Result
10 segments taken aseptically ; 7 lightly contaminated with <i>Staph. albus</i> (donor with type-II nephritis)	11.8×10^4 viable coliforms between 10 segments	Freeze-dried	Average per segment 340 organisms
10 segments ; 7 contaminated with spore bearers (donor with pelvic peritonitis)	8.5×10^4 viable coliforms between 19 segments	10 Frozen and thawed 9 Freeze-dried	3×10^4 organisms 7/9 sterile 1 segment 100 organisms 1 segment 1200 organisms
10 segments taken aseptically ; 2 contaminated with <i>Esch. coli</i> (donor with carcinoma of colon)	75×10^4 <i>Staph. aureus</i> between 20 segments	10 Frozen and thawed 10 Freeze-dried	20.3×10^4 organisms 2.1×10^4 organisms

Bacteriological Studies

Many bacteria survive freezing and thawing, and some also resist prolonged desiccation. Freeze-drying is one of the accepted methods of preserving bacterial cultures. If the moisture content of a dried culture is very low, and storage is prolonged, there is a progressive loss of viable organisms; in fact, measures must be taken to protect them (Proom and Hemmons 1949).

We therefore studied the effect of freeze-drying on a known bacterial contamination of human arterial grafts. Some arteries were taken aseptically, and others contaminated deliberately with known quantities of bacteria. Control cultures were obtained, and were later repeated on equal numbers of contaminated arterial segments after freezing and thawing, and after freeze-drying and reconstituting. The effects of these procedures on measured numbers of viable coliform bacilli and staphylococci are shown in table III.

These results indicate that the freeze-drying of arterial grafts by this process is an effective means of reducing bacterial contamination. But the grafts remain infected; therefore the need for careful selection of donors and an aseptic graft-taking technique still remains.

Discussion

This method of freeze-drying, though simple, yields a product which, after reconstitution, retains most of the properties of fresh material, judged by its physical and morphological characteristics. When it is applied to other substances—e.g., penicillin and purified diphtheria toxoid—which are assayable, good chemical preservation can be demonstrated.

Tissue is usually dried for histological purposes at -40°C or less. This is necessary if certain minute structural changes are to be avoided; but such drying takes much longer (table I). Complicated apparatus is needed to maintain the refrigeration of the drying-chamber and of the condenser during this long time, particularly if fairly large amounts of tissue are being dried.

One objection to drying with the chamber at room-temperature is the possibility of changes due to eutectic separation of water and other constituents. Table II, however, shows that, as the drying temperature rises, the water content rapidly falls, with the result that at -6°C about 87% of the original water has already been removed. It is therefore unlikely that the relatively small amount of water remaining will disturb the structure of the arterial segment, and the histological appearance of the reconstituted artery confirms that by this standard the method has been satisfactory.

It is important to select donors of arterial grafts for freeze-drying with particular care. Even early evidence of intimal or medial changes preclude the use of this method, since lipoid material cannot be dried, and early changes in the tissue-proteins may lead to further denaturation during drying. We therefore apply stricter criteria to the selection of donors when the vessels are to be freeze-dried than when they are to be banked frozen.

Summary

A simple method of preserving arteries by freeze-drying is described.

Such arteries can be stored at room-temperature for an indefinite time.

In clinical practice freeze-dried transplants of large arteries have given results which in the early stage equal those of arteries preserved by other means.

We wish to thank Dr. R. D. Andrews, of the Wright-Fleming Institute, and Dr. G. W. D. Scott, of the department of morbid anatomy, St. Mary's Hospital, for their help with the bacteriological and histological studies respectively; and Dr. P. N. Cardew, of the department of medical photography, St. Mary's Hospital Medical School, for the photographs.

References at foot of next column

THE FATE OF BISMUTH CARBONATE IN THE STOMACH**A RADIOLOGICAL STUDY**

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The therapeutic value of an alkali in the treatment of peptic ulceration appears to depend on at least six factors: chemical efficiency of the alkali; the absence of any after-secretion effect; the persistence of the alkali in the stomach under varying conditions; any protective effect it may have by adhering to the gastric mucosa, thus providing neutralisation of hydrochloric acid as it is secreted; any physical or chemical protective effect that it may have by persisting in the crater of an ulcer; and the absence of undesirable side-effects. With radio-opaque alkalis radiological methods can be used to examine with some degree of accuracy three of these factors—namely, the persistence of the alkali in the stomach, any adherence to the gastric mucosa, and the persistence in the crater of an ulcer.

There has been of late revived interest in the use of bismuth carbonate in the treatment of peptic ulcer, and Kemp (1950), Croxon Deller (1952), Douthwaite (1953), and Avery (1953) have reported favourably. Hence it seemed worth while to study the fate of this alkali when it was given in therapeutic dosage under different conditions to healthy people and to patients with either gastric or duodenal ulcer. Special attention was directed to its persistence in the stomach, its adherence to the gastric mucosa, and its retention in the ulcer crater in patients with recently proved radiological evidence of peptic ulcer.

The dose of bismuth carbonate used for the test-meals was 20 g. This dose is within the therapeutic range and is the alkali equivalent of about a third of the normal 24-hour secretion of hydrochloric acid. It was given in the form of a cream by whisking the bismuth carbonate powder in 2 oz. of water for a minute or so in a high-speed electric mixer. The cream could be swallowed easily from a medicine-glass, and any remaining in the glass was scraped out with a spoon.

Methods

It was decided to make each test examination on four persons, but in one of the groups of normal subjects five were included, and one patient in one of the gastric-ulcer groups also had a duodenal ulcer and therefore also appeared as a fifth patient in one of the duodenal-ulcer groups. The people examined were unselected. Two of the normal subjects (women) were used twice for different examinations after a fortnight's interval. None of the patients with peptic ulcer appear twice in the series, except the male with a double lesion. The normal subjects and the patients were examined fasting.

Tests

The tests made on normal persons were as follows:

(1) Bismuth carbonate 20 g. was given in 2 oz. of water, the subject being prepared as for a barium-meal examination.

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(2) As in (1), but a few minutes after the bismuth had been given 6 oz. of water was drunk, and observation was continued.

(3) The bismuth carbonate was given on an empty stomach and followed by one egg beaten up in milk to a total volume of 6 oz.

(4) The bismuth carbonate was followed by an ordinary mixed meal.

(5) An ordinary mixed meal was given to the fasting subject, and then the bismuth carbonate was given.

(6) A mixture of 20 g. of bismuth carbonate in 6 oz. of milk was given.

The tests made on patients with gastric ulcer were identical with those enumerated above, except that test 2 was omitted. The tests made on patients with duodenal ulcer were limited to tests 4 and 5.

Radiological Examination

The gastric emptying-rate of bismuth carbonate, the adherence of bismuth carbonate to the gastric mucosa, and the persistence of bismuth carbonate in an ulcer crater were all likely to be affected considerably by the position adopted by the patient during the test and by the use of abdominal palpation. Accordingly it was decided to adopt the erect position throughout the examination, except for two normal subjects in test 1 and one normal subject in test 2, who were deliberately examined prone, the films being taken in that position. The patient or subject sat in a chair during the intervals between individual radiographic examinations. Abdominal palpation was deliberately avoided. The radiographic examinations were made rigidly to the time schedule previously arranged at fixed intervals of up to an hour after the start of the test. It was thought that the erect and sitting positions adopted throughout the test corresponded most nearly to those of a patient receiving ambulatory treatment for peptic ulcer. The erect position had the additional advantage that it facilitated estimation of the quantity of bismuth carbonate remaining in the stomach at the end of a given time.

At every stage of each investigation an attempt was made to assay the distribution and quantity of the remaining bismuth carbonate in the stomach, the presence of coating of the gastric rugae, and the retention of bismuth carbonate in the crater of a gastric or duodenal ulcer.

Results

Normals

In the normal subjects there was a wide variation in the degree of retention of bismuth carbonate in all the tests except test 6 (bismuth-carbonate and milk mixture), in which nearly all the bismuth carbonate was retained in each of the five people at the end of an hour. Coating of the gastric rugae was seen in those given bismuth carbonate only, in those who were later given water after their bismuth, and in three of the four people given a meal followed by bismuth, but in this last group the coating was slight. Flocculation took place in all the other tests except test 6, in which curds and not fine fragments were observed.

Gastric Ulcer

In the patients with gastric ulcer there was a lack of uniformity in all the tests in the rate of emptying of the stomach, and even test 6 showed considerable variation. Maximum retention took place in test 3, in which a mixture of egg and milk was given after the bismuth. Coating of the gastric mucosa was seen after a dose of bismuth carbonate given to the fasting patient, but did not persist for an hour in any of the four patients tested; it was infrequent in the other tests. Coating of the mucosa was only seen to persist for an hour in one of the twenty patients with gastric ulcer examined in the five different tests. Flocculation was present in

every test except test 1, in which bismuth carbonate was given alone; temporary coating was observed in this test. In fourteen of the twenty patients the ulcer crater was recognisable an hour after the test had begun, owing to the bismuth carbonate retained in it, but the amount of bismuth retained in the crater was no more than a trace in seven of these patients.

Duodenal Ulcer

In the patients with duodenal ulcer there was again a lack of uniformity in the rate of disappearance of bismuth carbonate from the stomach. The bismuth was usually retained longer in the stomach in patients given the bismuth after a meal of food than in patients given bismuth on an empty stomach. Flocculation rather than true coating of the stomach was present under the conditions of experiment. In only two of the nine patients examined was the duodenal ulcer crater recognisable an hour after the start of the test.

Conclusions

From these results it is evident that the retention of a significant quantity of a 20 g. dose of bismuth carbonate varies greatly from person to person under the same conditions. In a healthy person the retention is greatest when the bismuth is given in a milk mixture. True coating of the gastric rugae persists only to a significant extent when bismuth carbonate is given as a suspension on an empty stomach, but it may occur to a slight extent in other circumstances. Flocculation of bismuth in the stomach is more common than coating.

Ten of the twenty patients with gastric ulcer retained half or more of the bismuth in the stomach under various conditions of test for an hour, but the emptying-rate was not uniform. Coating of the rugae was exceptional at the end of an hour. Bismuth was retained in the ulcer crater in nearly three of every four patients, but in only one of every four was this retention considerable.

In patients with duodenal ulcer the rate of disappearance of bismuth carbonate from the stomach was more rapid than in gastric-ulcer patients. In the small number tested only three of the nine had half or more of the bismuth remaining in the stomach at the end of an hour. Flocculation of bismuth and not coating of the gastric mucosa took place in every patient in the two tests after half an hour. Retention of bismuth carbonate in the ulcer crater was uncommon.

It is evident that the effectiveness of bismuth carbonate as an alkali given in large dose at infrequent intervals is likely to vary considerably from patient to patient as well as with the circumstances of administration. It seems that, when the bismuth is given in milk or is followed by egg and milk, its retention in the stomach will be maximal. There is also some evidence in favour of giving it after a meal rather than before. It is clear that any protective effect exerted by direct contact with an ulcer surface is likely to be small.

Summary

Experiments are described in which radiography was used to examine the retention of bismuth carbonate in the stomach, its adherence to the gastric mucosa, and its retention in peptic ulcers.

Ten of twenty patients with gastric ulcer retained half the test dose of 20 g. of bismuth carbonate in the stomach for an hour irrespective of the method of administration. Three of nine patients with duodenal ulcer retained half the test dose for an hour.

Persistent coating of the gastric mucosa for an hour occurred only once in twenty patients with gastric ulcer, and did not occur in nine with duodenal ulcer, and is thus unlikely to be an important factor in the effectiveness of the alkali.

The ulcer crater was persistently outlined by small amounts of bismuth carbonate in fourteen of twenty patients with gastric ulcer, and two of nine with duodenal ulcer.

There is evidence in favour of combining bismuth and milk as a mixture or following it with egg and milk to prolong the retention of the alkali in the stomach. In duodenal-ulcer patients retention in the stomach is also more likely if the alkali is given after a meal.

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BOVINE ANTIHÆMOPHILIC GLOBULIN IN THE TREATMENT OF HÆMOPHILIA

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THE rational treatment of hæmophilia aims at raising the blood level of antihæmophilic globulin (A.H.G.) to the point at which coagulation can become haemostatically effective. This is usually attempted by transfusing blood or plasma or by injecting a concentrated preparation of A.H.G. In practice, therapy is hampered by uncertainty about the activity of available preparations, the minimal blood-level required, and the duration of any increase produced. All these troubles can be traced to the difficulty of measuring A.H.G. activity. Assay methods used hitherto determine A.H.G. activity from the amount of material required to correct the clotting-time, prothrombin consumption, or thrombin generation (Pitney and Dacie 1953) of hæmophilic blood. They thus depend on a supply of hæmophilic blood; and, since this is seldom continuously available in the laboratory, the tests which could be made were limited. For this reason there have been relatively few observations on the blood-levels of A.H.G. which might indicate the physiological minimum, apart from those of Brinkhous et al. (1954) who used hæmophilic dog blood. Experimental work on the purification of A.H.G. has also been greatly restricted, since at every stage the activity of the product should be tested if systematic progress is to be made.

The thromboplastin-generation test, introduced by Biggs and Douglas (1953), has removed these restrictions since it can be modified to assay A.H.G. and requires only constituents derived from normal blood. This application, which will be published later, has allowed many measurements of blood-A.H.G. levels to be made. From these findings and those of Brinkhous et al. (1954), Pitney and Dacie (1953), Graham et al. (1953), and Baserga and de Nicola (1951) it can be deduced that 30–50% of the normal amount of A.H.G. in the blood is needed for reasonable haemostatic efficiency. Usual estimates of the therapeutic level are much lower than

these (Wright et al. 1948) because restoration of the clotting-time to normal is often taken as the criterion, and 2–5% of the normal amount of A.H.G. in the blood is probably sufficient for this in most hæmophilic patients. In cases in which dosage has been controlled by determining the clotting-time the real therapeutic levels of A.H.G. have seldom been reached, and the patients have often continued to bleed. It follows that the proper treatment of a haemorrhagic episode and the prevention of bleeding after a minor operation will involve the use of much larger amounts of blood or of A.H.G. than are usually given.

In view of the limited supply of human blood we decided to investigate the possibility of using A.H.G. derived from animals. Patek and Taylor (1937) showed that plasma fractions active in correcting the clotting time of hæmophilic blood could be obtained from the blood of the sheep, ox, rabbit, and monkey. Pohle and Taylor (1938) used an ox-blood plasma fraction as a local haemostatic to control hæmophilic bleeding. Spaet and Kinsell (1953) produced a bovine A.H.G. preparation by a method based on the Cohn process but did not use it clinically. Lorand and Laki (1954) have prepared material with A.H.G. activity from dog and ox blood by adsorption on to kaolin. Our own work has also been mainly concerned with ox blood, which is available in large quantities from the slaughter-house, and which we found to have an average A.H.G. activity sixteen times that of human blood. Pig, horse, and sheep blood have been investigated but are less active.

Many experiments were made to improve methods for extracting and purifying bovine A.H.G., the results being checked by frequent assays of activity. The best material has been produced by salt fractionation, and, though losses have been unaccountably variable, enough bovine A.H.G. has been prepared to allow a study of its effects on animals, and a trial in man. Details of the method of preparation will be published in another paper. The material has an activity equivalent to about 20 pints of normal blood per g. of protein; it is far from "pure," containing a large proportion of fibrinogen. It maintains its activity indefinitely in the dried state, but quickly deteriorates in solution. When the publications by Spaet and Kinsell (1953) and Lorand and Laki (1954) appeared, the methods described by them were used in parallel with our own but were found to yield less active material.

Before bovine A.H.G. was used clinically certain investigations were necessary. The assay of activity, which had been based on the thromboplastin-generation test, was confirmed by finding the expected ability to correct the prothrombin consumption and thrombin generation of hæmophilic blood in vitro. Sterilisation of the A.H.G. in solution presented some difficulty, since it was heat-labile, lost activity on Seitz or Berkfeld filtration, and could not be passed through a gradocol membrane. Sterilisation was finally achieved by centrifuging at high speed, followed by measured exposure to ultraviolet light, the solution being contained in a rotating quartz tube. Toxicity was investigated by injecting the material into mice and rabbits. The mice each received an intraperitoneal injection of about 100 times the human dose in proportion to body-weight. 30 mice survived without obvious ill effects, but a batch of 5 died, about two weeks after injection, with kidney lesions indicating nephrosis, these 5 animals having received material which had been denatured and partially coagulated by accidental overexposure to ultraviolet light. One rabbit received 1 g. of material by intravenous injection in three doses in six weeks and showed no ill effects.

The clinical action of the material was next studied in three hæmophilic volunteers. The results were judged

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by the effect on clotting after intravenous injection and by the amount of haemorrhage after dental extraction. Since an obvious disadvantage of the use of animal protein is the development of antibodies, tests for their presence were made on all three volunteers.

Methods

The *clotting-time* was measured by a modification of the Lee and White method (Biggs and Macfarlane 1953), the normal range being 3–10 minutes. The *prothrombin-consumption index* was measured by the method of Merskey (1950), the normal range being 0–40%. *A.H.G. activity* was measured by a modification of the thrombo-plastin-generation test of Biggs and Douglas (1953), which will be published later. *Platelet-agglutination* tests were made on a mixture of the test material and human citrated blood incubated for ten minutes and then haemolysed with ammonium oxalate and observed in a counting-chamber by phase-contrast microscopy.

Results of Clinical Trial

All three patients were admitted to the Radcliffe Infirmary under the care of Dr. P. C. Mallam.

Case 1 (Reg. no. 32036).—A man, aged 43, with the family and personal history typical of haemophilia, had spent much of his life in hospital with haematuria, haematemesis, haemarthroses, and haemorrhage in the deep tissues requiring many transfusions. Previous dental extractions had led to prolonged haemorrhage and required the transfusion of 42 pints of blood in all, but on one occasion there was only slight bleeding and no transfusion was needed.

Trial.—At the beginning of the trial a skin test was made with bovine A.H.G., which gave no reaction. A small intravenous dose of the material was next given with no observable ill effect. Next day A.H.G. 0.5 g. was injected intravenously, producing no untoward reaction apart from a transient sensation of tingling of the lips. A general anaesthetic was given thirty minutes later, and the stump of a carious molar tooth was removed by Mr. C. Annand Smith, and the socket was scraped. There was very little bleeding at operation, and this stopped within a few minutes, the socket becoming filled with firm clot. At seven hours after the extraction there had been no bleeding, and a further dose of A.H.G. (0.8 g.) was injected. The socket healed completely within ten days without haemorrhage.

Laboratory findings.—Before treatment the patient's clotting-time was 12–15 minutes and prothrombin-consumption index 70–120%. The blood-A.H.G. level was less than 1%. After the first injection the A.H.G. level rose to 35%. Seventeen hours after the second injection it had fallen to 5%, but the clotting-time and prothrombin consumption remained normal. By next day, forty-three hours after the last injection, the clotting-time and prothrombin consumption had reverted to the untreated levels.

Case 2 (Reg. no. 188647).—A man, aged 38, had the typical history of haemophilia. Three brothers are also affected. He had been in hospital many times with haematuria, haemarthroses, and melena, requiring many transfusions. One tooth had been removed previously, after which he had bled for fourteen days but did not require transfusion.

Trial.—An intradermal skin test with bovine A.H.G. gave no reaction. Next day A.H.G. 0.4 g. was given intravenously, and thirty minutes later a general anaesthetic was given and a carious premolar tooth was removed by Mr. C. Annand Smith, and the socket was scraped. There was little bleeding at the time of extraction, and the socket was dry and filled by a clot within about thirty minutes. A second dose of A.H.G. (0.5 g.) was given eight hours after the extraction, and a third (0.5 g.) twenty-six hours after the second. During each injection the patient experienced "specks and flashes of light" in the eyes but no other sensations and no constitutional disturbance. There was no bleeding until four days after the last injection, when there was slight oozing around the clot, which stopped spontaneously in a few minutes. Two days later the clot became detached and the socket was found to have healed beneath it.

Laboratory findings.—Before admission this patient had been investigated by Dr. J. V. Dacie, of the Postgraduate

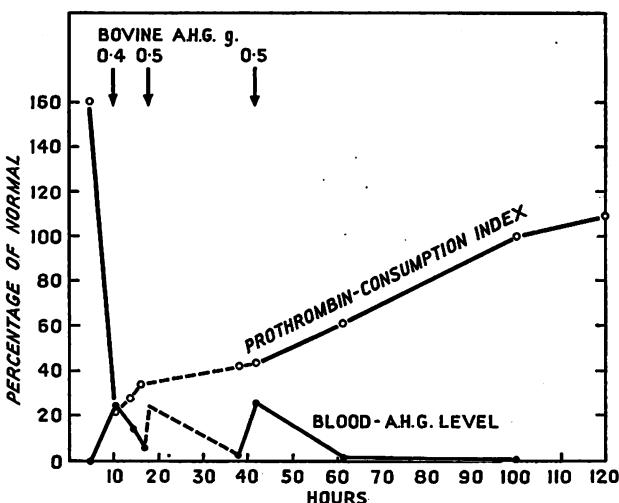


Fig. 1.—Changes in A.H.G. level and in prothrombin-consumption index, expressed as percentage of normal, during treatment of case 2 with bovine A.H.G. Interrupted line indicates probable changes after second injection of A.H.G., no readings having been made in this period.

Medical School, London. Some of the laboratory investigations made during the trial are summarised in fig. 1. Before treatment the clotting-time was 26–35 minutes, and the prothrombin-consumption index 160%. After the injections the clotting-time was maintained within the normal range until twenty hours after the last injection. The blood-A.H.G. level was maintained for only a relatively short time after the injections, having fallen to 5% of normal within seven hours, and to 2% after twenty hours. The prothrombin consumption fell to 21% after the first injection, but after the third it unexpectedly rose slightly instead of falling, although the blood-A.H.G. level had risen.

Case 3 (Reg. no. 189223).—A haemophiliac, aged 34, with four affected brothers and one affected nephew, had been admitted to hospital many times with haemarthroses and required transfusions on losing his primary teeth. At the age of 23 he had sixteen teeth removed in one operation and bled for six weeks, requiring the transfusion of some 40 pints of blood. At the age of 26 he had a transient left hemiplegia, and later one epileptic attack. Since this time he has been treated with 'Epanutin' and phenobarbitone. On admission for the trial he was most anxious to have all his remaining sixteen teeth removed, since many of them were grossly carious and causing trouble. With some reluctance it was agreed to comply with his wishes.

Trial.—An intradermal skin test made with bovine A.H.G. was negative. Next day the volunteer was given A.H.G. 0.4 g., and fifteen minutes later the sixteen teeth were removed under general anaesthesia by Mr. J. M. Helsby. Bleeding was not excessive at operation, but throughout the day there was persistent oozing from all tooth sockets despite two further injections of A.H.G. totalling 0.8 g. In the evening dental splints lined with alginate soaked in 'Styptiven' (Russell's-viper venom) were fitted, and the bleeding stopped. During the next three days there was no bleeding and three injections of A.H.G. were given totalling 1.3 g. At each injection the patient experienced "light-flashes" in front of his eyes. Treatment with A.H.G. was then stopped because severe thrombocytopenia was discovered at this time. On the fourth day after extraction the dental plates were removed, and the sockets were found to be dry and to be filled with firm clots. Throughout the following two days there was no bleeding. On the sixth day after extraction (three days after the last injection) slight oozing started first from one and then from several sockets. This was readily controlled by light pressure and Russell's-viper venom. It recurred, however, from time to time for a further seven days but was always controllable, and transfusion was not considered necessary, though the Hb level fell to about 50%. The sockets healed within fourteen days but in the next three weeks developed several blood-filled overgrowths of granulation tissue which required excision, the operation being covered

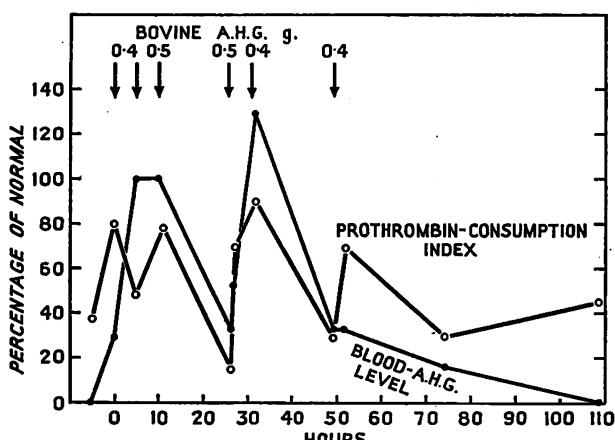


Fig. 2.—Changes in A.H.G. level and in prothrombin index expressed as percentage of normal, during treatment with bovine A.H.G.

by the transfusion of 3 pints of fresh blood and $7\frac{1}{2}$ pints of fresh plasma. These superficial blood-cysts may possibly have been related to the effects of epanutin.

Laboratory findings.—This patient had been previously investigated by Dr. E. K. Blackburn, of the Royal Infirmary, Sheffield. Some of the findings obtained during the trial are summarised in fig. 2. Before treatment was started, the clotting-time was 13 minutes and the prothrombin-consumption index 37%. The clotting-time decreased to normal after the first injection and remained within normal limits for five days. The results of the prothrombin-consumption tests were both unexpected and disturbing (fig. 2), since after each injection of A.H.G. the index rose above its pre-injection level. This rise was inexplicable until it was discovered, after the fifth injection, that the patient's blood contained no platelets. During the night which followed this injection the platelets increased to 33,000 per c.mm., and after the sixth and final injection they decreased again almost to zero. Since the decrease in the platelet-count appeared to be directly related to the injection of A.H.G., treatment with this material was then stopped. After the last injection the platelet-count increased by an average of 22,000 per c.mm. a day until it reached the normal range. During the period of thrombocytopenia there were no hemorrhagic manifestations of the purpuric type, and the bleeding-time determined by needle punctures in the ear lobe was normal. Another feature of this case was the fact that the blood-A.H.G. level was kept higher than in either of the two other patients.

Other Investigations

Antibodies

In each patient tests for the presence of antibodies were made at three and six weeks after the dental extractions. Incubation of the patient's plasma with bovine A.H.G. caused no loss of the activity of A.H.G., suggesting that specific antibodies to A.H.G. had not developed to any significant extent. Intradermal skin tests gave very slight positive reactions in cases 1 and 2 and negative reactions in case 3. Precipitin reactions, done by Dr. A. C. Allison, gave weakly positive reactions between the patients' sera and A.H.G. dilutions in all three cases.

Platelet Agglutinins

Bovine A.H.G. agglutinated human platelets but had no effect either on human red cells or on rabbit platelets. Platelets were agglutinated by concentrations as low as 0.125 mg. of protein preparation per ml. of blood; hence the injection of 0.5 g. of A.H.G. would allow an agglutinating concentration to be reached in vivo. The platelet agglutinin was also present in the ox plasma. When re-examined some weeks after their injections the platelet counts of cases 1 and 2 were normal.

Effect of Oral A.H.G.

Ten days after dental extraction case 2 ate 2 g. A.H.G. in powder form mixed with cereal. Clotting-times and

blood-A.H.G. levels estimated at intervals during the following twenty-four hours indicated that no active material had been absorbed into the blood-stream.

Discussion

The principal reason for using an animal source of A.H.G. was the realisation that supplies of human blood must be inadequate for the effective treatment of haemophilia. A haemophilic adult probably requires the administration of an amount of A.H.G. contained in 5 pints of blood to achieve temporary haemostatic normality, and studies of the survival of both human and bovine A.H.G. in haemophilic blood indicate that this dose must be repeated daily to maintain the effect. Even if this treatment is used only in cases of actual haemorrhage, or to cover a minor operation, very large amounts of blood would be required. Failure to attain the therapeutic level will lead to the use of still more blood, because continuous bleeding will cause further loss of A.H.G. Case 3, after a previous dental extraction, had received some 40 pints of blood but bled for six weeks. Incidents such as these put a great strain on an already overloaded transfusion service.

The ultimate goal of treatment with A.H.G. is continuous replacement, as in the treatment of pernicious anaemia with vitamin B₁₂, and of diabetes with insulin. Only in this way can the patient be maintained in a normal state and the danger of internal haemorrhage and haemarthroses avoided. But such maintenance therapy would be impracticable if only human A.H.G. were available, since it would need a special panel of about 500,000 donors to treat the 500 haemophiliacs estimated to exist in this country. It would be quite practical if the A.H.G. could be derived from ox blood, which is about sixteen times as active as human blood and is available in ample amounts.

This preliminary clinical trial of a preparation of bovine A.H.G. is sufficiently promising to warrant further active investigation. Its administration to three haemophiliacs produced the expected effect on clotting, which was in each case restored to a physiologically effective level for several hours after each injection. In cases 1 and 2 there was virtually no bleeding after dental extraction, a result which previous experience demonstrates must be highly significant. In case 3 the removal of sixteen teeth at the patient's own wish was a severe test, and there was fairly brisk bleeding for the first few hours after extraction. In this case, however, there was the later recognised complication of thrombocytopenia; and the fact that no transfusion was necessitated by the postoperative haemorrhage indicates that even the curtailed course of A.H.G. therapy must have had a considerable beneficial effect.

The general objection to the use of animal material is its antigenicity. Injections of ox-plasma protein will probably induce the formation of antibodies and lead to the danger of allergic reactions on further injections. Our own material seems to have produced slight sensitisation, since only doubtfully positive skin tests and precipitin reactions have been obtained during the weeks following the therapeutic trial. The bovine A.H.G. used by us therefore seems not to be a powerful antigen—a point which is being investigated by experiments on animals. If better purification is achieved, the antigenicity may be reduced further. The nature of the antihaemophilic factor is unknown; it might be a substance which, like insulin, is relatively non-antigenic.

The specific objection to the preparation used in this trial is its power to agglutinate human platelets in vitro and the occurrence of profound thrombocytopenia in the one patient in whom platelet counts were made after its use. It is not known if a similar effect was produced in the two other patients, because there being

no reason to suspect thrombocytopenia, platelet-counts were not made after the injections. But an increase in the prothrombin-consumption index after injection in case 2 suggests that the platelet-count may have been reduced in that case also. Although the temporary thrombocytopenia in case 3 produced no apparent ill effects and caused no purpura it was felt to be a sufficiently serious complication to postpone further human trials with bovine A.H.G. until more information on the nature of this effect is obtained. Inter-species platelet agglutinins have been described by Musshett et al. (1953), and these could be separated from other agglutinins by fractionation of the plasma. It may prove possible to separate the antihæmophilic effect from the platelet-agglutinating activity. If this is so, more extensive trials of the material will be made.

Summary and Conclusions

The effective treatment of hæmophilia by replacement of the deficient factor requires large amounts of blood not easily obtainable from human sources.

Bovine blood has about sixteen times the antihæmophilic activity of human blood, and enough would be available for the continuous treatment of the whole hæmophilic population of this country.

A preparation of bovine antihæmophilic globulin has been produced, of which 1 g. has an activity equivalent to about 20 pints of normal human blood, assayed by the thromboplastin-generation test.

Three hæmophilic patients received intravenous injections of this material, with the expected rise in the antihæmophilic activity of their blood.

In two cases so treated dental extraction produced no abnormal bleeding. In the third case the removal of sixteen teeth caused bleeding for several hours but did not necessitate transfusion.

No ill effects were observed in the first two cases. In the third case the injections produced thrombocytopenia but no purpura.

The bovine material used agglutinated human platelets, and attempts will be made to eliminate or reduce this action before proceeding with further trials in man.

The material has shown some slight antigenic properties, which it is hoped may be reduced as purification methods are improved.

We wish to thank Dr. A. H. T. Robb-Smith for his encouragement and valuable advice; the three volunteers for their courageous co-operation; Dr. P. C. Mallam for admitting the three volunteers to his wards, his acceptance of clinical responsibility, and the help given by his staff; Messrs. Metropolitan Vickers for advice on sterilisation by ultraviolet light and for lending us the necessary equipment; Dr. B. R. Frisby, of the Oxford Regional Public Health Laboratory, for the sterility tests; and Mr. C. Annand Smith and Mr. J. M. Helsby for the dental extractions. We gratefully acknowledge the technical assistance of Mrs. J. Eveling and Miss G. Richards.

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ANGINA OF EFFORT

USE OF HEPARIN FOR ITS CONTROL

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RECENT work has suggested a relation between the amounts of certain classes of lipoprotein molecule in the plasma and a tendency to atheroma (Gofman et al. 1950, 1951, Jones et al. 1950). In particular, an increase of lipoprotein molecules in the Sf 10-30 range has been associated with the development of atherosclerosis in both animals and man (Lindgren et al. 1951). The possible relation of these abnormal lipoprotein patterns to myocardial infarction and anginal pain is of considerable practical interest.

Graham et al. (1951) claimed that in cholesterol-fed rabbits the quantity of large-molecule lipoproteins in circulation was reduced by a single injection of sodium heparin intravenously. Daily injections of heparin to half of a group of rabbits on an atheroma-producing high-cholesterol diet had a protective action. Of the group receiving heparin, only 3 out of 20 showed atherosclerosis, whereas of those not so treated 15 out of 20 developed gross atherosclerosis.

Lyon et al. (1951) reported a higher rate of myocardial infarction and of angina of effort when the Sf 10-20 concentration was highest (Svedberg unit range of rate of migration in the ultracentrifuge). They added that in coronary disease low-fat low-cholesterol diets reduced the Sf 10-20 level and considerably reduced the occurrence of new myocardial infarction. Also, in 30 out of 32 patients with angina of effort pain was relieved for 3-10 days by a single injection of heparin 20-100 mg.

This was confirmed by Donzelott and Kaufmann (1952), and Basud and Stewart (1950) concluded that heparin lowered the plasma-cholesterol most when the initial figure was high. Ethyl bicoumarate ('Tromexan') as an alternative anti-coagulant had no effect on the blood-cholesterol level. In a series of cases in which the plasma-cholesterol range was 200-268 mg. per 100 ml., the total cholesterol fell by 20-80 mg. when heparin was given.

Graham et al. (1951) described a clearance of lipid particles in human plasma in vivo by heparin. They treated atherosclerotic patients by twice-weekly injection of heparin 50-100 mg. intravenously or intramuscularly, and of their 59 patients who had angina of effort (45 had had a definite coronary thrombosis) 55 obtained great benefit and needed far less nitroglycerin.

A Clinical Investigation

We felt that the possible value of heparin for the relief of anginal pain deserved further investigation and that this could well be undertaken by a group of general practitioners. Most practitioners have several patients with angina of effort whose behaviour, trinitrin needs, and so on, are well known to them. In view of the statement that great relief of pain followed a single injection of heparin, we thought that with twice-weekly intramuscular injections of 100 mg. for one month any benefit gained should be apparent. As an additional check the following sequence of courses was given so as to see whether there was any detectable difference when heparin was administered and when it was omitted. (Procaine was included because intramuscular injection of heparin is painful.)

1. Twice-weekly intramuscular injection of 100 mg. of heparin, with 0.5 ml. of 1% procaine, for four weeks; followed immediately by
2. Twice-weekly injection of 1 ml. physiological saline solution, with 0.5 ml. of 1% procaine, for three weeks; followed immediately by
3. Twice-weekly injection as in the first period, for five weeks.

SUMMARY OF FINDINGS

Case	Sex	Age (yr.)	Duration	Previous infarct	E.C.G.	X-ray screening	Serum-cholesterol before and after	B.P. before	B.P. after	Assessment of improvement
1	M	67	2 yr.	1951	Deep Qs	N.A.D.	174/ 219+	155/ 85	140/ 95	2
2	F	51	6 mos.	Yes	Qs inv. CR7	L.V.2 +	227/ 235 +	215/ 120	170/ 100	2
3	M	65	4 yr.	1949	210/ 235 +	155/ 100	140/ 70	5
4	M	64	5 yr.	1948	N.A.D.	N.A.D.	210/ 235 +	155/ 100	140/ 70	2
5	F	72	6 mos.	No	L.A.D.	N.A.D.	220/ 243 +	200/ 110	190/ 90	3
6	M	58	6 mos.	1952	Q1	N.A.D.	236/ 300 +	180/ 110	140/ 90	4
7	M	61	10 yr.	?	Qs	N.A.D.	235/ 200 -	200/ 140	160/ 95	3
8	M	58	2 mos.	1952	Qs +	N.A.D.	210/ 231 +	170/ 90	168/ 75	1
9	M	40	9 mos.	No	N.A.D.	L.V.1 +	260/ 282 +	128/ 78	138/ 80	3
10	M	54	3 yr.	No	N.A.D.	N.A.D.	200/ 192 -	190/ 90	140/ 80	2
11	F	57	2 yr.	No	Slur QS	L.V.1 +	255/ 224 -	190/ 100	240/ 110	4
12	M	43	3 yr.	1950	Old	N.A.D.	270/ 205 -	158/ 85	125/ 80	1
13	M	65	3 mos.	No	N.A.D.	N.A.D.	190/ 267 +	165/ 100	135/ 80	1
14	M	56	10 yr.	No	N.A.D.	N.A.D.	167	125/	5
15	M	65	7 yr.	1948	Qs	L.V.1 +	370/ 217 -	170/ 100	168/ 100	2
16	M	59	8 yr.	1952	No	N.A.D.	268	148/ 88	140/ 70	1
17	M	62	3 yr.	No	N.A.D.	N.A.D.	192/ 275 +	130/ 90	130/ 80	2
18	M	53	2 yr.	No	N.A.D.	L.V.1 +	160/ 156 -	155/ 80	150/ 85	4
19	M	73	9 mos.	No	L.A.D.	L.V.1 +	..	160/ 235	214/ 120	3
20	F	60	7 yr.	No	L.A.D.	L.V.1 +	261/ 290 +	195/ 100	218/ 110	3
21	M	39	2 mos.	No	L.A.D.	N.A.D.	210/ 215 +	140/ 105	150/ 88	5
22	M	57	1 yr.	No	N.A.D.	N.A.D.	200/ 215 +	140/ 105	150/ 88	4

L.V.1 +, &c., refers to enlargement on a scale of 1 for minimal and 4 for maximal enlargement of the left ventricle observed on radioscopv.

N.A.D. = nil abnormal detected.

The changes of treatment were of course made without the patient's knowledge.

Before treatment began a careful history was taken, with full clinical examination, X-ray cardioscopy and barium swallow, electrocardiogram, and estimations of serum-cholesterol and haemoglobin. Particular attention was paid in the history to the trinitrin requirements, the amount of exercise normally taken, the severity of the pain, and the threshold of onset. As far as possible the cases chosen for treatment were stable in their use of trinitrin. Total-cholesterol estimations before and after treatment were made, in view of the statement of Ancel Keys (1951) that these give a more useful indication of the likelihood of atherosclerosis and coronary disease than do estimations of particular fractions. The general practitioners kept records of their patients' comments at different stages, and at the end of the test the patients' condition was again fully investigated.

In the accompanying table, which summarises the findings, the figures in the last column are to be interpreted as follows :

1. Great improvement, both in degree of pain and ease of production with increased exercise tolerance (4 cases).
2. Improvement, but qualified by a greater degree of care on the patient's part, or by concurrent loss of weight (6 cases).
3. Doubtful improvement (5 cases).
4. No change (4 cases).
5. Worse. I stopped treatment after three injections as he had unpleasant reactions; I stopped after five weeks because he felt he was being made worse; and a 3rd developed an infarct during treatment. It will be realised of course that heparin was not being given as a continuous anticoagulant.

Only 1 man, out of the 10 cases improving, noticed any difference when the saline injections were substituted. This is directly contrary to the experience of Graham et al. (1951) who found in 9 cases that the pain rapidly returned when heparin was stopped.

No consistent effect on the total-cholesterol levels was evident. Indeed in half the cases the level rose during the course; nor was there any strict correlation between serum-cholesterol change and clinical improvement. Radioscopy with swallowed barium demonstrated no hiatus hernias in this series. (We are indebted to Dr. J. Rabinowitch, radiologist to the Bushey and District Hospital, for his radiological help.)

Conclusions

1. Heparin in the dosage used had no consistent demonstrable effect on the electrocardiogram, on the serum-cholesterol (total) or on the blood-pressure.

2. The apparent effect on the pain of half the patients suggests that the method deserves trial where pain is frequent and easily produced. No more can be claimed than this.

The following general practitioners took part in this investigation based on a hospital where some of them are members of the staff :

Dr. K. J. AVELING, Bushey	Dr. LEES LOW, Bushey
Dr. J. BENDAS, Edgware	Dr. A. LETCHNER, Harrow Weald
Dr. A. CREE, Edgware	Dr. N. C. MOND, Kingsbury
Dr. G. N. GROSE, Edgware	Dr. J. B. RUSSELL, Kenton
Dr. D. G. JARMAN, Bushey	Dr. D. G. WILSON, Bushey Heath

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CHOLECYSTECTOMY

A METHOD FOR THE DIFFICULT GALL-BLADDER

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FOR the patient, traumatic stricture or damage to the bile-ducts is a tragic and perhaps fatal accident; to the surgeon a deep and humiliating disappointment; and to the one who attempts reconstruction a formidable and oft recurring trial of strength and endurance leading to failure or death to a considerable number of patients. Consequently any procedure that will protect the ducts from damage merits consideration and trial. I describe here a method which has been tried in a limited number of cases for some years and has proved safe and rational even in difficult and troublesome situations.

As Maingot (1948) says, "When access proves difficult or the parts concerned in the operation have not been clearly visualized, excision of the gall-bladder is always a hazardous undertaking." One of the main hazards in the difficult gall-bladder is the dissection of the structures at the neck. Here, owing to the inflammation, the structures cannot be readily exposed, especially above and to the left of the infundibulum and neck. In these circumstances accidents may happen and bleeding be excessive, requiring the blind application of forceps in a field flooded with blood. This type of case is often

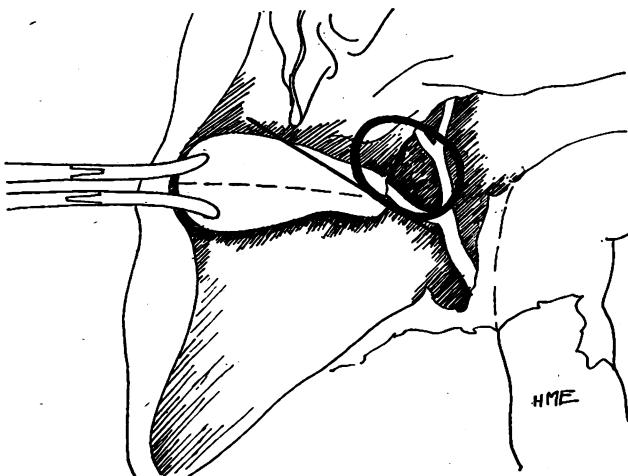


Fig. 1.—Forceps placed on fundus in preparation to opening gall-bladder down broken line. Heavy oblique line is "imaginary line" mentioned in text. Heavy oval line encloses "dangerous area."

complicated by a previous duodenal or colonic fistula, the gall-bladder being contracted and fibrosed, and its wall thickened, with a tendency to be as tough as cartilage. Here it is often decided to do a drainage operation for the present, to be followed by removal later.

Because benign strictures virtually always follow surgical trauma, prevention of them is all-important. Flickinger and Masson (1946) observe that cholecystostomy and choledochostomy appear to be of minor importance as agents responsible for damage to the bile-ducts.

The reason for describing this operation is the increasing incidence of damage done to the bile-ducts. Waugh et al.

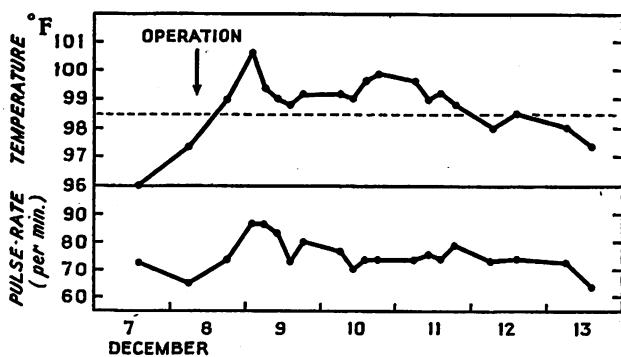


Fig. 2.—Typical postoperative temperature and pulse-rate.

(1952) at the Mayo Clinic reported 83 cases repaired in 1951—a 46% increase over the total for 1950.

In the present operation no attempt is made to dissect out the cystic artery or the cystic duct. The branches of the artery are stitched over as they ramify in the remaining gall-bladder wall. The cystic duct is not tied; its mucosa is fulgurated at its opening into the gall-bladder. Biliary fistula has not developed in any of the 23 cases done by this method. If no dissection is done above and to the left of the imaginary line shown in fig. 1, and all operating is done to the right and below this line, no possible damage can be inflicted on the ducts or vessels. To do this, one is obliged to leave *in situ* the cystic duct and part of the gall-bladder wall—i.e., that portion of the neck, infundibulum, and body lying above and to the left against the liver bed. This acts as a shield to the vulnerable structures. Apparently this can be done with safety, provided that the mucosa is destroyed with phenol or with the electric cautery.

This operation should not be confused with that practised and recommended by Pribram (1939), Love (1947), and Thorek (1936), who do the usual dissection of the neck, displaying the cystic duct and artery, and ligating and cutting the duct and artery as in retrograde cholecystectomy. They then leave in that portion of the gall-bladder wall attached to the liver, and fulgurate or coagulate its mucosa to avoid postoperative abdominal drainage which they consider harmful. I feel that, if the ducts and artery can be safely dissected out, conventional cholecystectomy should be done.

To date I have done 23 cases by this method, an average of about 2 cases every three years. On reviewing the records of the last 100 gall-bladders operated on by me at the Royal Jubilee Hospital, in Victoria, I find that 9 were done with the electric cautery and 2 with phenol cauterisation of the mucosa. These 23 cases have all done well, and there have been no complications, fistulae,

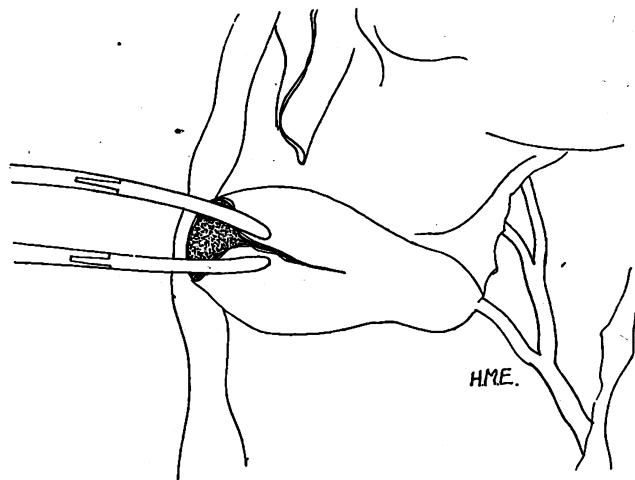


Fig. 3.—Forceps applied down wall, and gall-bladder opened further.

abscesses, or late sequelæ. Fig. 2 shows typical post-operative reactions of temperature and pulse-rate.

Possibly I do this operation more frequently of later years because I have confidence in its safety. It is done in any case where serious difficulties are anticipated in dissecting out the structures at the neck of the gall-bladder.

In planning this operation due regard has been paid to the possible presence of abnormalities. Flint (1923), reviewing the anatomy of the bile-ducts and vessels in 200 cases, found only 69 that agreed with the so-called

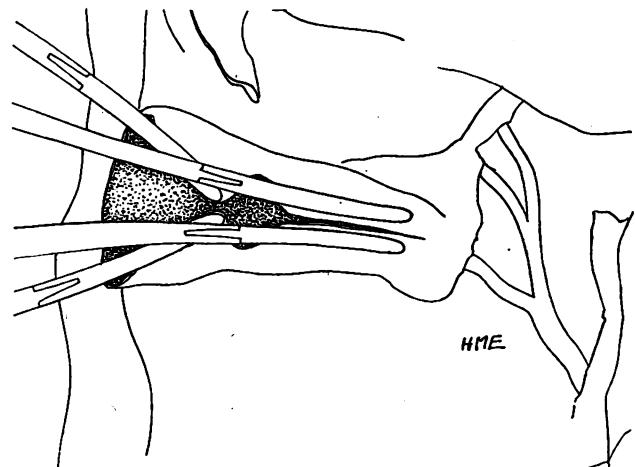


Fig. 4.—Gall-bladder being opened toward neck between forceps.

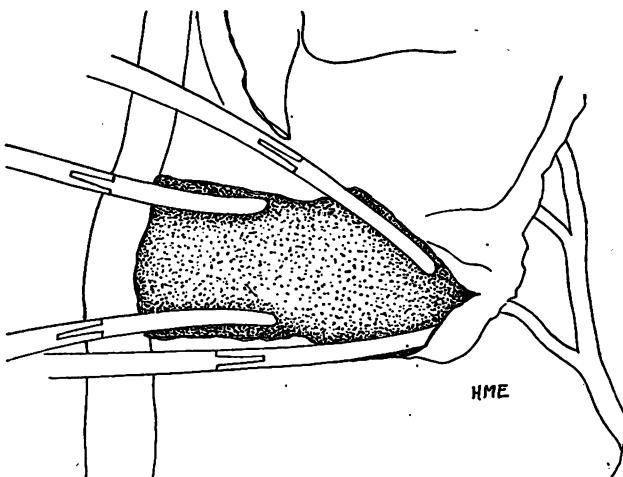


Fig. 5.—Interior of gall-bladder fully exposed in preparation for excision of wall.

normal anatomy of the textbooks. Only one common abnormality is involved, and it is no particular problem and will be discussed later.

THE OPERATION

When it is decided to do this operation instead of the usual cholecystectomy, the fundus of the gall-bladder is grasped with a pair of artery forceps (fig. 1), and an opening is made into its cavity, the bile is aspirated, and any stones are removed. Two pairs of artery forceps are applied down the wall on its free side (fig. 3), and a further incision is made between them with scissors. This cutting between forceps is continued until the region of the cystic duct is reached, any further stones being removed (fig. 4). The duct is next identified from within the cavity of the gall-bladder and is probed for stones and, if necessary, slit up over a narrow grooved director, the surgeon always cutting below and to the right. By carefully proceeding down the cystic duct

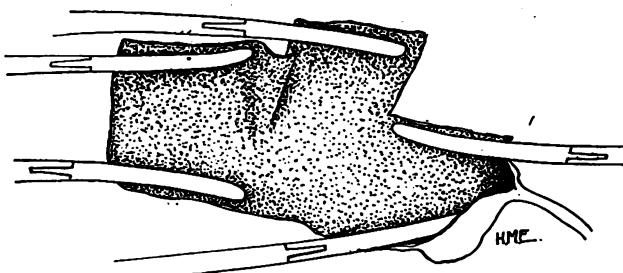


Fig. 6.—Starting excision of redundant wall.

the common duct can be opened if this is thought to be advisable. One should not hurry at this stage of the operation. When the common duct is reached, the incision passes downwards along its course, any necessary manipulations for clearing the duct are undertaken, and a catheter or T tube is inserted and fixed in the usual manner.

We now have the gall-bladder laid open and held by a series of forceps around its edge (fig. 5). Starting at the region of the neck, curved forceps are applied as in figs. 6-8, care being taken not to attempt a too generous removal of the wall. Forceps are only applied to that portion which can be exposed readily from within and from without. After the application of these forceps excision of the excess wall is begun and continued until all the excess wall is removed. Usually the portion remaining is from half to three-quarters of

the upper left wall, which is normally attached to the liver bed.

Figure-of-eight double-O chromic catgut sutures are next inserted round the edge of the remaining gall-bladder wall, the forceps being removed as the sutures are tightened (fig. 9). This controls all bleeding. Only the mucosa remains to be dealt with.

If phenol is used it is applied with a tightly rolled applicator to prevent flooding, and the whole area is gone over several times, great care being taken in the region of the cystic duct. Alcohol and saline solution are applied after the cauterisation with phenol.

With the electric cauterity a needle-pointed electrode is used, and all the mucosa is treated with a low current, care being taken not to be too thorough or vigorous and not to cauterise the interior of the cystic duct to within 5 mm. of the common duct. The mucosa should be superficially charred at completion. At no time should the needle be forced into the tissues to coagulate deeply. Any residual bleeding points around the edge are next touched with the needle. Personally I prefer the electric cauterity, but I can see no difference in the results of the two methods. Phenol was used originally for convenience. The electric cauterity is more controllable. With phenol there is always the potential danger that

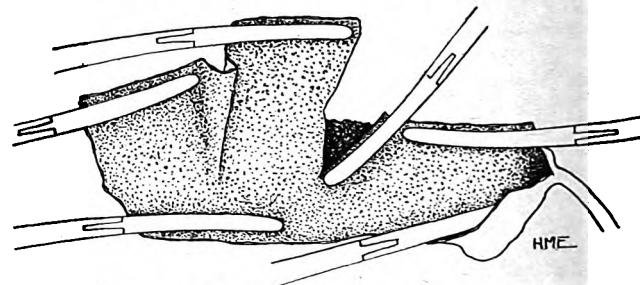


Fig. 7.—Further excision of wall.

some of it may accumulate in the cystic duct and eventually make its way into the common duct. When the cauterisation of the mucosa has been completed, a 1-inch soft rubber drain is inserted and held in position with one triple-O chromic catgut stitch placed in a convenient portion of the cut edge of the gall-bladder wall. A small catheter is placed down to the subhepatic space for the instillation of a suitable antibiotic after the skin is closed; this is not an essential part of the operation, and naturally was not used in the earlier cases. Little difference can be seen by its use, but it is comforting. The wound is closed in the usual manner, the drain coming out through the incision or through a separate stab wound as desired.

The aftercare is more or less routine except that the rubber drain is left undisturbed for about seven days and then is withdrawn 2 inches a day, being out on the tenth or the eleventh day. Some bile-stained mucoid material usually drains out. The patient may be ambulant early or late as the individual case indicates.

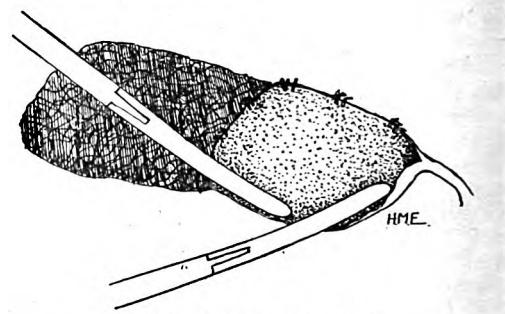


Fig. 8.—All redundant wall excised.

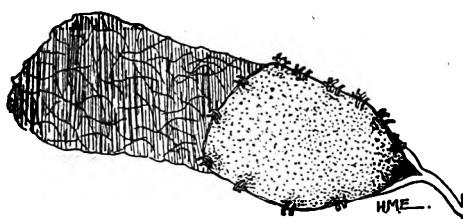


Fig. 9.—Sutures inserted around cut edge. Mucosa to be fulgurated.

POSSIBLE DANGERS

The possible dangers are as follows :

(1) Attempting to remove too much of the upper part of the wall of the gall-bladder in an effort to make this operation resemble the standard cholecystectomy, consequently entering the danger area, and imperilling the ducts and vessels. A generous portion of the wall should be left as a protective shield.

(2) By the too liberal use of phenol or by using too powerful a current when coagulating the mucosa and so damaging adjacent structures. These are only possibilities to be considered.

(3) Secondary haemorrhage due to sloughing along the edge of the gall-bladder wall and involving branches of the cystic artery. In this series this has not happened, but I have always felt this to be a distinct possibility.

(4) Damage to an abnormal cystic artery with haemorrhage in those cases where the cystic artery arises from the hepatic artery low down or from the gastroduodenal artery and enters the gall-bladder from its under surface—i.e., in the region of Hartmann's pouch. This should not give any trouble, because it will be clamped with the forceps applied to the wall before it is cut away.

(5) Persistent mucous fistula. Careful attention to cauterising the mucosa will prevent this.

(6) Persistent biliary fistula. Theoretically one would expect this to develop at times, but in this series it has not. Perhaps the cauterisation of the duct effectively seals it off.

None of the above complications has been observed in the 23 cases. On the contrary, all the cases have been singularly free from any trouble. Still, I think these and other possible dangers should always be in one's mind when using this method.

SUMMARY AND CONCLUSIONS

A safe method for the removal of a difficult gall-bladder is presented. It is of use in those cases in which, at the time of operation, the gall-bladder is considered too dangerous to remove because of inflammation around the neck, requiring hazardous dissection with attendant haemorrhage and possible damage to the biliary ducts and vessels.

In seventeen years 23 patients were operated on by this method with no untoward immediate or late postoperative sequelæ.

The method can be used together with exploration of the common duct.

The operation is not to be confused with the cauterisation method advocated by Pribram (1939) and others. Its principle is entirely different : all the surgical manoeuvres are confined to an area clearly visible at all times, and no attempt is made to dissect out the vessels and duct at the neck. On the contrary, one tries to keep as far away as possible from these structures. By working from within the cavity of the gall-bladder they are at all times protected by that portion of the wall left in situ.

The operation is not difficult and will probably appeal but little to some surgeons, but it may be of use to those who suddenly find themselves confronted with a situation which appears to be beyond their skill to solve at one stage.

I believe that damage will not be inflicted on the ducts or vessels when using this method, provided that

a portion of the gall-bladder wall is left as a protection and that no dissection is done in the vicinity of these structures.

I am indebted to Dr. H. M. Edmison, of Victoria, B.C., for the diagrams.

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KERNICTERUS FOLLOWING EXCHANGE TRANSFUSION

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A TRIALS committee of the Medical Research Council is at present considering the indications for, and the results of, treatment of haemolytic disease of the newborn. A preliminary report (Mollison and Walker 1952) shows that the use of exchange transfusion has greatly reduced the incidence of kernicterus : of 62 infants treated in this way 4 developed kernicterus, 3 of them being premature babies. A similar improvement has occurred in the U.S.A. with the use of exchange transfusions : "It seems entirely probable that kernicterus can be practically eliminated as a complication of erythroblastosis foetalis" (Allen et al. 1950).

Experience in Dundee in 1952-53 has, however, not been so encouraging. During these two years there were 30 infants with haemolytic disease of the newborn : 10 were considered to need no treatment, 16 had exchange transfusions, 1 died during exchange transfusion, and 3 had simple transfusions. Kernicterus developed in 5 infants, of whom 4 had had exchange transfusions, 3 of these 4 being premature babies.

2 cases of kernicterus following exchange transfusion also occurred in 1950-51. Both infants were mature, the birth-weights being 6 lb. 5 oz. (cord-blood Hb 12.6 g. per 100 ml.) and 7 lb. 13 oz. (cord-blood Hb 11.2 g. per 100 ml.). Both received exchange transfusions shortly after birth, packed cells being used. The 1st child was seen at the age of 1 year and 9 months and showed severe choreo-athetosis ; the 2nd died on the third day, and kernicterus was found at necropsy. These 2 cases are mentioned because the infants were mature, and because packed cells were used for the replacement transfusions ; they will not be considered further here.

Case-records

Case 1.—A boy weighing 5 lb. 1 oz. was born after normal pregnancy and labour at home. The mother's blood was not examined before the birth. This pregnancy was the mother's sixth. The fifth baby became jaundiced shortly after birth but was not treated ; the others were apparently unaffected. When jaundice developed in case 1 a few hours after birth, he was transferred to hospital, where the direct Coombs test was found to be positive, the blood group-A Rh-positive, and the capillary blood Hb 19.6 g. per 100 ml.

Exchange transfusion with group-A Rh-negative blood, seven days old, was given twenty hours after birth, 350 ml. of blood being exchanged. Later the same day the capillary blood Hb was only 9.6 g. per 100 ml. ; so a simple transfusion of 80 ml. of group-A Rh-negative blood was given. The jaundice, which was then considerable, increased steadily during the next two days. On the third day the capillary Hb was 16.8 g. per 100 ml. On the fourth day the infant developed head retraction, hypertonicity of limbs, inability to suck, and a cerebral cry. These signs gradually improved during the next few weeks, but at the age of sixteen months the limbs were hypertonic and the baby could not hold up his head or sit up.

He was alert and did not appear to be frankly mentally defective, but he was abnormally restless. There was no sign of deafness.

Case 2.—A boy weighing 4 lb. 10 oz. was born of a normal pregnancy by spontaneous breech delivery with difficulty, but there were no clinical signs of asphyxia. The mother's blood was group-AB Rh-negative and contained antibodies. This was her third pregnancy, and the second baby had been affected and treated by exchange transfusion. The direct Coombs test on the cord blood was positive, the baby's blood being group-A Rh-positive and his liver and spleen slightly enlarged. His cord-blood Hb was 10 g. per 100 ml.

Exchange transfusion with group-A Rh-negative blood, nine days old, was given one and a quarter hours after birth, 309 ml. of blood being removed and 332 ml. injected. The transfusion was well tolerated, and the capillary-blood Hb twelve hours later was 18.2 g. per 100 ml. During the second and third days the jaundice deepened, but there were no symptoms and the Hb was 16.8 g. per 100 ml. Early on the fourth day there was a sudden onset of cyanosis, head retraction, and inability to suck. The infant appeared collapsed and, though there was temporary improvement with resuscitation, terminal haemorrhagic phenomena developed six hours after the onset, and the baby died. Necropsy showed yellow staining of the nuclei in the medulla and of the periventricular white matter

Case 3.—A girl weighing 5 lb. was born of a normal pregnancy and labour, but the mother's blood was group-AB Rh-negative and contained antibodies. Her only previous pregnancy had produced an unaffected infant. The direct Coombs test on the cord blood was positive, the baby's blood being group-A Rh-positive and the cord-blood Hb 15.4 g. per 100 ml.

Exchange transfusion was given one and a half hours after birth with group-O Rh-negative blood, fourteen days old, 336 ml. being removed and 390 ml. injected. The baby collapsed at the end of the transfusion but recovered quickly with resuscitation, including the removal of 20 ml. of blood. Next day the jaundice deepened, and the capillary-blood Hb was 11.2 g. per 100 ml. On the third day there was a sudden onset of extreme rigidity of the limbs, spine, and neck, a cerebral cry, and failure to suck. Shortly afterwards rhythmic and athetoid movements of the upper limbs occurred. During the ensuing week the involuntary movements subsided, the muscle stiffness diminished, and feeding by bottle was resumed. At the age of three weeks no abnormal signs were present, but the capillary-blood Hb was 7.2 g. per 100 ml.; so a simple transfusion of 100 ml. of group-O Rh-negative blood was given. At the age of two months there were no abnormal physical findings.

Case 4.—A boy weighing 6 lb. 4 oz. was born of normal pregnancy and labour. The mother's blood was group-A Rh-negative and contained antibodies. This was her ninth child, the eighth child having died at the age of four days from severe icterus gravis. One of twins resulting from the fourth pregnancy also had icterus gravis. The direct Coombs test on the cord blood was positive, the baby's blood being group-A Rh-positive and the cord-blood Hb 14.7 g. per 100 ml.

Exchange transfusion was given one and a quarter hours after birth with group-A Rh-negative blood two days old, 440 ml. being removed and 480 ml. injected. During the next three days there were no symptoms, but jaundice slowly deepened, and on the third day the serum-bilirubin level was 17 mg. per 100 ml. On the fourth day, with capillary Hb 20.6 g. per 100 ml. and serum-bilirubin level 25 mg. per 100 ml., the baby developed head retraction and inability to suck, followed by hypertonicity of limbs and athetoid movements. The involuntary movements ceased after a further twenty-four hours, but head retraction persisted for three days. On the fourth day after the appearance of abnormal neurological signs bottle-feeding was resumed, and the baby went home at the age of twelve days, with capillary Hb 20.6 g. per 100 ml.

Readmission.—He was readmitted to hospital at the age of seven weeks because of increasing pallor and frequent epistaxes. Investigations showed that the serum-bilirubin level was 1.75 mg. per 100 ml., prothrombin-time normal, thymol turbidity 2 units, cephalin flocculation negative, alkaline phosphatase 55 King-Armstrong units %, and plasma-protein level 5.2 g. per 100 ml. (albumin 3.5 g. per 100 ml., globulin 1.7 g. per 100 ml.). No abnormal neurological signs were present, and the baby was transferred to another hospital, nearer his home, but he died. The necropsy

findings are not yet available; the brain was not sectioned before fixation.

Discussion

In cases 1-4 the onset of abnormal cerebral signs was preceded by steadily increasing jaundice, but only in case 4 were repeated estimations made of the serum-bilirubin level, and in this case, at the time of symptoms, the level was 25 mg. per 100 ml. The diagnosis was confirmed at necropsy in case 2, but in cases 1, 3, and 4 it rested on the clinical findings. It is generally agreed, however, that the clinical features are usually adequate for diagnosis, though the increased liability of these infants to intracranial haemorrhage must be borne in mind.

Indications for Exchange Transfusion.—We accept the following criteria of the need for exchange transfusion: (1) an affected baby weighing at birth 5 $\frac{1}{2}$ lb. or less; (2) an affected baby weighing at birth more than 5 $\frac{1}{2}$ lb. but with cord-blood Hb less than 14.8 g. per 100 ml.; and (3) an affected baby weighing at birth more than 5 $\frac{1}{2}$ lb. and having cord-blood Hb more than 14.8 g. per 100 ml., but with a bad family history—i.e., a previously severely affected sibling. These criteria correspond fairly well to those suggested as desirable by Mollison and Walker (1952). However, the amount of cord Hb may not truly indicate the severity or rapidity of the haemolytic process, and recent work by Walker and Turnbull (1953) suggests that a high level may be a reflection, in part, of intra-uterine anoxia, and the risk of cerebral damage may be greater in such cases.

Length of Storage of Blood.—It is well known that, with prolonged storage, potassium and phosphate pass from the red cells to the plasma, and that after fourteen days' storage the plasma-potassium levels may rise considerably (up to 70 mg. per 100 ml.). Since the newborn baby may already have a high plasma-potassium level (up to 30 mg. per 100 ml.) toxic levels may be reached during exchange transfusion. In case 3 the transfused blood was fourteen days old, and the infant developed cardiac insufficiency at the end of the transfusion. Since this baby had not shown much anaemia at birth (cord Hb 15.4 g. per 100 ml.), hyperkalæmia may have developed. This is not known to affect the incidence of kernicterus, but the possibility of its occurrence does call for care in transfusion. If there is no alternative to using stored blood over seven days old, the amount of calcium gluconate injected should be increased and the rate of transfusion slowed.

Amount of Blood Exchanged.—It is usually considered that an amount corresponding to 70 ml. per lb. of body-weight is adequate. In cases 1-4 the average amount was 75 ml. per lb. Only in case 4 were packed cells used; in the other cases whole blood was transfused. American workers have said that the use of packed cells is not only unnecessary but also contra-indicated (Hsia et al. 1952a), because the transfused cells may undergo more rapid hemolysis and raise the serum-bilirubin level unduly. Further, it is pointed out that the object of the exchange is to remove circulating antibodies and blood pigment in addition to supplying red cells, and that whole blood is the best medium for this.

Serum-bilirubin Level.—This has been estimated regularly only in case 4. Hsia et al. (1952b) have shown that a direct correlation exists between the height of the serum-bilirubin level and the development of kernicterus; with levels over 31 mg. per 100 ml. 50% of cases became affected, and with levels of 16-30 mg. per 100 ml. 18% were affected. The routine estimation of serum-bilirubin levels on small ill babies is unfortunately a difficult procedure. A micro-technique such as has been developed by Hsia et al. (1952c) in Boston would help greatly, but is not suitable for routine laboratory use. Another difficulty is to fix an arbitrary level of serum-bilirubin above which exchange transfusion is indicated.

Blood-sugar.—Although Gerrard (1952) has suggested that hypoglycæmia may contribute to the production of kernicterus, the normal standards for blood-sugar levels in newborn infants are not sufficiently defined to warrant interference with much hope of improvement. However, the question remains open.

Etiology of Kernicterus.—The following theory regarding the pathogenesis of kernicterus is perhaps most acceptable at present:

(1) *Increased serum-bilirubin level:* Küster and Krings (1950) have shown, in the case of the young rabbit, that bilirubin, when present in sufficient concentration and for a sufficient length of time, is toxic to nerve tissue. A similar mechanism may operate in man, and Claireaux et al. (1953) believe that the pigment involved in kernicterus is indirect-reacting bilirubin.

(2) *Increased vascular permeability in haemolytic babies and non-haemolytic premature babies:* in this connection Morison (1952) writes of haemolytic babies "this immaturity, and a real but not properly understood structural and functional inferiority of the tissues and organs of the foetus are not sufficiently appreciated." Perhaps, then, a haemolytic baby should be considered premature when its birth-weight is less than $6\frac{1}{2}$, or 7 lb. instead of the accepted $5\frac{1}{2}$ lb.

Treatment.—If the principal factor is bilirubin, treatment should logically be directed towards lowering the serum-bilirubin level by repeated exchange transfusions. This has been done in America (Hsia et al. 1952a), the aim being to keep the level below 20 mg. per 100 ml., and the results appear to have been satisfactory. However, it must be remembered that exchange transfusion carries a risk, and that the success of repeated exchanges depends a great deal on the operator. Perhaps, too, a rapid rise in serum-bilirubin level is as likely to cause kernicterus as is a moderate persisting level. Abelson (1953) reports 2 cases in which exchange transfusion was given at the onset of abnormal neurological signs, with apparent recovery and freedom from residual disability. In one case the exchange was the first, and in the other the second. If this could be confirmed, treatment would be simplified, but from the discussion reported (Hsia et al. 1952a) it appears that confirmation is lacking. It seems probable that, until we know more about the aetiology of kernicterus, a small proportion of cases of haemolytic disease will continue to develop kernicterus despite all therapeutic efforts, but that, in the meantime, keeping the serum-bilirubin as low as possible by repeated exchange transfusion offers the best hope of reducing the incidence.

Summary

4 cases of kernicterus have occurred in 16 infants treated by exchange transfusion for haemolytic disease of the newborn. 3 of the cases were in premature infants.

2 additional cases, both in mature infants, are briefly reported.

Possible factors bearing on the production of kernicterus are discussed.

The use of repeated exchange transfusions to keep the serum-bilirubin levels low is mentioned.

My thanks are due to Prof. J. L. Henderson for his constant help and encouragement in the preparation of this paper; to Dr. J. Thomson for permission to publish case 4; and to Dr. J. D. Andrew for giving the exchange transfusion in case 4.

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INTRASPLENIC PRESSURE AS INDEX OF PORTAL VENOUS PRESSURE

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The spleen is largely composed of red pulp, which communicates freely with the intrasplenic portal venous radicles (fig. 1). It therefore seemed possible that the pulp pressure might be related to the portal venous pressure. The introduction of a safe method of percutaneous trans-splenic portal venography (Dreyer and Budtz-Olsen 1952, Bahnsen et al. 1953, Walker et al. 1953) for the investigation of portal hypertension provided an opportunity of measuring the intrasplenic pressure through the needle used for injection of the contrast medium. Intrasplenic pressure has been measured by this technique and its validity as an index of portal venous pressure assessed. Results have been correlated with the portal venous pressure measured by occluding the hepatic vein (Paton et al. 1953) and directly at operation.

Methods

Intrasplenic pressure was measured in 28 patients with splenomegaly and suspected disease of either the liver or the portal vein, all of whom had a normal plasma-prothrombin time and blood-platelet count. They were placed recumbent with the left hand behind the head. A site was chosen in either the 8th or the 9th intercostal space in the mid-axillary line, and local anaesthesia was induced with 2% procaine solution down to and including the capsule of the spleen. A fine lumbar-puncture needle 7 cm. long, of outer diameter 0.7 mm., was inserted in a cephalad direction at an angle of 45° to the transverse plane. If the spleen was greatly enlarged below the costal margin, the needle was inserted subcostally directly into its outer surface. Resistance was met when the spleen was reached, and thereafter the patient was asked to breathe quietly. After penetrating 2 cm. into the spleen the stylet was removed, when blood could be seen dripping slowly from the needle. This was found to be a most valuable indication that the needle was in the correct position. The swing of the needle with respiration was

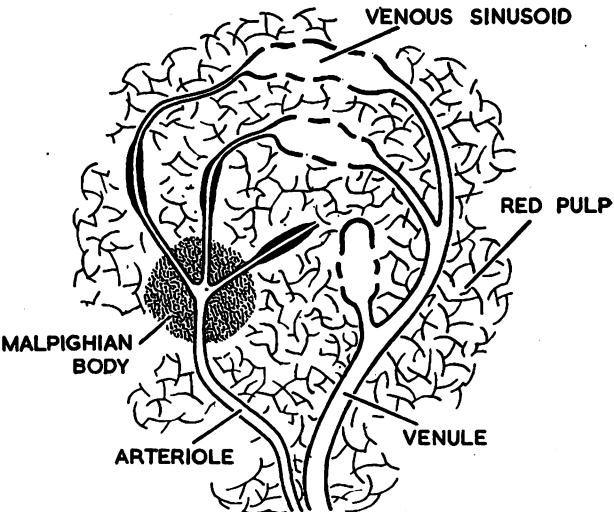


Fig. 1.—Diagram of circulation in spleen (modified after McNee 1931), showing free communication between red pulp and tributaries of portal vein in the spleen.

not in any way restricted. The needle was connected with a strain gauge by a length of 'Polythene' tubing, and the pressure was recorded with the patient breathing quietly. The zero level was taken at a point 5 cm. below the sternal angle with the patient supine. In every instance the position of the needle in the spleen was confirmed by subsequent injection of contrast material for trans-splenic portal venography. The needle remained in the spleen for only 30 seconds, the time taken for the two procedures.

In 12 patients, after the initial pressure had been recorded, the needle was advanced a further 5 mm.; in this way pressures were obtained from two or three different positions in the spleen.

Intrasplenic pressure was measured directly at operation in 7 patients undergoing gastrectomy and compared with pressures obtained at the same time from a main portal venous tributary. These patients had spleens

TABLE I—AGREEMENT OF PRESSURES TAKEN FROM DIFFERENT PARTS OF SAME SPLEEN

Case no.	Pressure in different parts of spleen (mm. Hg)			Range of variation (mm. Hg)
	1	2	3	
1	5	5	4	1
2	6	6	6	0
3	4	6	8	4
4	9	10	9	1
5	10	10	10	0
6	15	10	12	5
7	12	14	14	2
8	17	12	14	5
9	15	15	19	4
10	19	21	..	2
11	24	21	..	3
12	25	20	20	5

of normal size and no evidence of portal venous hypertension.

In 22 patients the pressure obtained by occluding an hepatic vein was measured at a later date by catheterisation of the hepatic vein. This pressure is a measure of the intrasinusoidal pressure and therefore of the portal venous pressure (Paton et al. 1953).

Results

Safety

There were no complications and in particular no clinical evidence of intraperitoneal bleeding, but it must be emphasised that a fine needle was used and deep respiration was avoided. Puncture of the spleen at laparotomy enabled inspection of the puncture site, and the blood-loss never exceeded a few ml. Review of the published reports has revealed only transient side-effects of percutaneous trans-splenic venography, and no death has been reported (Atkinson et al. 1954).

Variation of Pressure in Same Spleen

The pressure tracing obtained was steady without pulsations. The respiratory variation with quiet breathing did not exceed 2 mm. Hg.

It is possible that the needle may occasionally enter a large artery instead of the red pulp and give a falsely high pressure. This happened only once in 75 readings and was confirmed by prominent pulsations on the tracing. This difficulty is prevented if in every instance two readings are taken in the spleen by advancing the needle a further 5 mm. after the first recording.

The intrasplenic pressure varied little from place to place in the same spleen (table I).

Results in Patients without Portal Hypertension

The intrasplenic pressure was measured in 14 patients without portal hypertension. 7 with normal spleens were studied at the time of laparotomy and 7 with splenomegaly during portal venography (table II). The pressure varied between 3 and 17 mm. Hg, and this has been taken as the range of normal.

TABLE II—SUMMARY OF RESULTS

Condition	No. of patients	Mean intrasplenic pressure (mm. Hg)	Range (mm. Hg)
Portal cirrhosis ..	11	25.5	17-35
Biliary cirrhosis ..	5	22.6	17-28
Extrahepatic obstruction of portal vein ..	5	24.4	20-29
Other patients :			
Normal spleen ..	7	10.3	10.0
Large spleen ..	7	9.7	3-17

The pressure did not differ significantly between the 7 patients with spleens of normal size and the 7 with splenomegaly (table II). The size of the spleen therefore does not influence intrasplenic pressure.

Results in Portal Hypertension

The 11 patients with portal cirrhosis all showed an intrasplenic pressure greater than the upper limit of that found in the group without portal hypertension (table II). The mean value was $2\frac{1}{2}$ times that seen in the latter group.

The intrasplenic pressure was surprisingly high in the 5 patients with biliary cirrhosis. These patients, however, also showed a high portal venous pressure when it was measured by catheterisation of the hepatic vein.

Each of the 5 patients with extrahepatic obstruction of the portal vein had a high intrasplenic pressure.

Correlation of Intrasplenic Pressure with Estimated Portal Venous Pressure

In the 24 patients studied there was a statistically significant linear correlation between the intrasplenic pressure and the estimated portal venous pressure whether measured by occlusion of an hepatic vein or directly at operation (fig. 2). If the intrasplenic pressure is measured, it is possible to predict the portal venous pressure within 8 mm. Hg with a 95% degree of accuracy. The intrasplenic pressure exceeds the estimated portal venous pressure by 2-6 mm. Hg, the higher the pressure the greater the difference.

Extrahepatic Portal Venous Obstruction

In these patients the obstruction to the portal vein is extrahepatic, and the intrahepatic portal venous pressure is not raised. The pressure obtained by occluding an hepatic vein is therefore normal, and this finding,

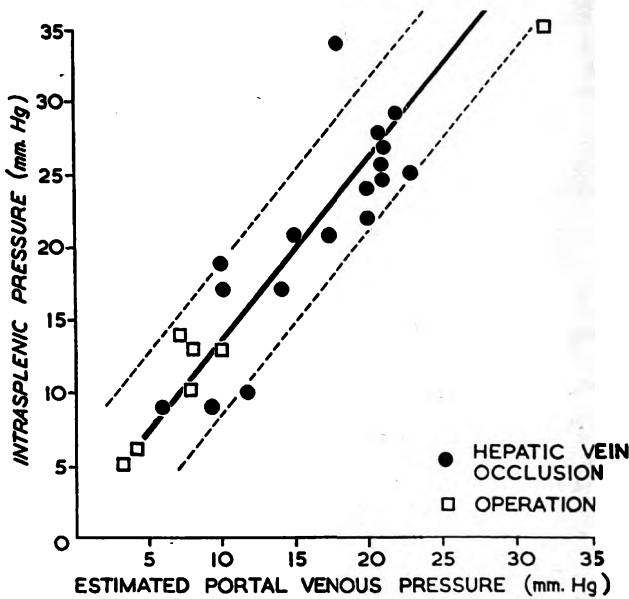


Fig. 2—Correlation of intrasplenic pressure with estimated portal venous pressure : solid circles, by occlusion of an hepatic vein; squares, at operation. Interrupted lines represent limits of 95% confidence.

in conjunction with a raised intrasplenic pressure, strongly suggests extrahepatic portal venous obstruction (fig. 3).

Case-report

A boy, aged 17, presented with gastro-intestinal bleeding. Four years previously he had had acute appendicitis complicated by pyelonephritis and liver abscesses. Splenomegaly was now the only abnormal clinical finding. Liver-function tests showed no evidence of hepatocellular damage, and aspiration hepatic biopsy revealed normal histology. Varices were not seen radiologically after a barium swallow. The intrasplenic pressure was raised (29 mm. Hg), but the pressure obtained by occluding an hepatic vein was normal (12 mm. Hg). These findings suggested that the portal vein was occluded as a result of the old infection, and this was confirmed by trans-splenic portal venography, which showed

OCCCLUDED HEPATIC VEIN PRESSURE

NORMAL

INTRASPLENIC PRESSURE

HIGH

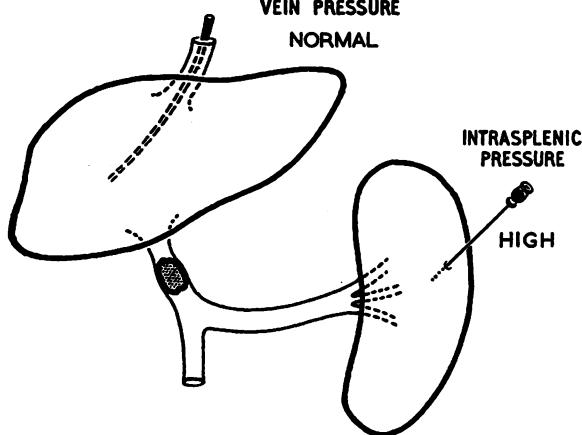


Fig. 3.—Extrahepatic obstruction of portal vein.

compression of the portal vein within the liver, presumably by scar tissue.

Similar findings were observed in 4 other patients with extrahepatic portal venous obstruction which in every instance was confirmed by portal venography (table III).

Discussion

The tip of a needle introduced into the spleen will probably lie in the splenic pulp, which forms the great mass of the organ. Anatomically the pulp is in free communication with the splenic venules; therefore it is not surprising that intrasplenic pressure bears a close relation to the portal venous pressure measured directly or by occluding an hepatic vein. The intrasplenic pressure is slightly higher than the portal venous pressure, as would be expected from the direction of flow in the portal system.

A rise in intra-abdominal pressure will increase the portal venous pressure and will be reflected in both intrasplenic pressure and the pressure obtained by occluding an hepatic vein. Patients with tense ascites were not included in this series; high pressures on occlusion of an hepatic vein, however, are found in such patients, and a rise in the intrasplenic pressure would be expected. Contraction of the muscles of the abdominal wall will raise the intra-abdominal pressure, the portal venous pressure, and the intrasplenic pressure by not more than 2 mm. Hg.

Intrasplenic puncture is as safe as, and much simpler than, other current methods of determining the pressure in the portal venous system—e.g., catheterisation of an hepatic vein, puncture of oesophageal varices during oesophagoscopy (Allison 1951), and directly by puncture of a portal venous radicle at operation. It is simpler and can be done more frequently than transsplenic portal venography.

The technique has many practical clinical applications. It may be used to confirm the diagnosis and to assess

TABLE III.—ASSOCIATION BETWEEN PRESSURE OBTAINED BY OCCLUDING HEPATIC VEIN AND INTRASPLENIC PRESSURE IN EXTRAHEPATIC OBSTRUCTION OF PORTAL VEIN

Diagnosis	Age (yr.)	Sex	Pressure obtained by occluding hepatic vein (mm. Hg) (normal range 2-12)	Intrasplenic pressure (mm. Hg) (normal range 3-17)
Obstruction of portal vein by scar tissue ..	17	M	12	29
Portal cirrhosis and thrombosis of portal vein ..	49	F	7	25
Portal cirrhosis and thrombosis of portal vein ..	56	F	11	24
Portal cirrhosis and thrombosis of portal vein ..	59	M	10	20
Biliary cirrhosis and thrombosis of portal vein ..	41	F	7	24

the severity of portal hypertension in the patient with liver disease. It is useful in following fluctuations in the portal venous pressure during the course of cirrhosis of the liver. Measurements of intrasplenic pressure provide a convenient base-line before operations are undertaken to relieve portal venous hypertension, and may be repeated postoperatively as an indication of the efficacy of the operation. A rise in intrasplenic pressure after the operation of portacaval anastomosis, for instance, would strongly suggest closure of the venous shunt.

The intrasplenic pressure can conveniently be measured in the medical ward without simultaneous trans-splenic venography, and may be useful in elucidating the cause of undiagnosed splenomegaly. It may prove of value in the investigation of the cause of gastro-intestinal bleeding in association with splenomegaly. It should not be done until the bleeding has ceased.

Used in conjunction with catheterisation of an hepatic vein the method is useful for the diagnosis of obstruction of the portal vein.

Summary

Percutaneous splenic puncture with a fine needle is a simple and safe method of estimating the portal venous pressure. The intrasplenic pressure varies little throughout the spleen and is uninfluenced by the size of the spleen. It bears a linear relationship to the portal venous pressure estimated by other methods.

In 14 patients without portal hypertension the intrasplenic pressure was 3-17 mm. Hg, with a mean of 10 mm. Hg. In 11 patients with portal cirrhosis the mean intrasplenic pressure was 25.5 mm. Hg, in 5 patients with biliary cirrhosis 22.6 mm. Hg, and in 5 patients with extrahepatic portal vein obstruction 24.4 mm. Hg.

The value of this technique in the diagnosis and management of portal hypertension is discussed.

We are indebted to Mr. M. R. Ewing, F.R.C.S., for his co-operation; Dr. N. F. Coghill, Dr. E. D. H. Cowen, Dr. P. Gibson, Dr. J. D. Paulett, and Dr. J. D. Whiteside for kindly referring patients; Mr. J. I. MacNaughton and Mr. B. Rowe for technical assistance; and the Lund Fund of the Diabetic Association for an expenses grant.

ADDENDUM

Since this paper was written, we have observed that in one patient intrasplenic pressure fell from 35 to 18 mm. Hg after successful construction of a portacaval anastomosis, and in one other patient repair of a stricture of the common bile-duct resulted in a fall in intrasplenic pressure from 28 to 12 mm. Hg one year later.

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Preliminary Communication

HOMOLOGOUS SERUM JAUNDICE

AFTER TRANSFUSION OF WHOLE BLOOD, DRIED SMALL-POOL PLASMA, DRIED IRRADIATED PLASMA, AND KAOLIN-TREATED FILTERED LIQUID PLASMA*

For more than a decade homologous serum jaundice has been recognised as a delayed complication of transfusion of blood and plasma. The highest incidence has been observed after the use of large-pool plasma or serum—i.e., plasma or serum prepared from pools containing the plasma of 300 or more donations of blood. In 1946 Spurling et al.¹ in a survey of 1054 patients who had received such plasma, found that 77 (7.3%) had developed homologous serum jaundice between one and five months after transfusion, whereas no cases were found among 891 recipients of whole blood. Brightman and Korns,² in the United States, observed the complication in 29 (4.5%) of 649 patients given dried plasma (size of pool not specified); 4 of the 29 patients died of hepatic necrosis.

Because of the high incidence of homologous serum jaundice after the transfusion of large-pool plasma, the Medical Research Council decided, in June, 1945, to discontinue the production of large-pool plasma and instead to prepare plasma from small pools in an effort to restrict the dissemination of the infective agent. The latter type of plasma is known as small-pool plasma and is derived from not more than 10 donations of blood.

In 1949 Lehane et al.³ reported the results of a comparative survey of the use of dried large-pool plasma, dried small-pool plasma, and whole blood. These are summarised in table I.

TABLE I—RESULTS REPORTED BY LEHANE ET AL.

Transfusion fluid	No. of patients on whom incidence of jaundice is based	No. developing homologous serum jaundice attributed to transfusion	Deaths attributed to homologous serum jaundice
Whole blood . . .	2772	22 (0.8%)	0
Dried small-pool plasma with or without blood	814	12 (1.47%)	1
Dried large-pool plasma with or without blood	820	100 (12.2%)	6

This survey showed that restriction of the size of plasma pool greatly reduced the incidence of homologous serum

jaundice, and that the risk of this complication after dried small-pool plasma was little greater than that attaching to whole blood.

The observations of Olliphant and Hollaender⁴ in 1946 and Wolf et al.⁵ in 1947 had suggested that irradiation with ultraviolet light would inactivate the infective agent. Blanchard et al.,⁶ using a known icterogenic pool of serum, reported in 1948 that, of a group of 15 volunteers, 3 developed hepatitis with jaundice, 1 hepatitis without jaundice, and 3 had presumptive hepatitis. Of 11 volunteers who received plasma from

TABLE II—INCIDENCE OF JAUNDICE AFTER TRANSFUSION OF BLOOD, OF SMALL-POOL PLASMA, AND OF IRRADIATED LARGE-POOL PLASMA

Transfusion fluid	No. of patients on whom incidence of jaundice is based	No. developing homologous serum jaundice of doubtful aetiology	No. developing homologous serum jaundice attributed to transfusion	Deaths attributed to homologous serum jaundice
Blood	2538	4	4 (0.16%)	0
Dried small-pool plasma with or without blood	867	0	1 (0.12%)	0
Dried irradiated large-pool plasma with or without blood . .	984	5	39 (3.96%)	1

the same pool which had been irradiated, none showed any evidence of hepatitis. In the light of these results, "Minimum Requirements" of the U.S. National Institutes of Health, issued early in 1949, made the ultraviolet irradiation of plasma obligatory.[†] In 1950 reports of homologous serum jaundice after the transfusion of irradiated plasma appeared in the United States (James et al.,⁷ Rosenthal et al.,⁸ Barnett et al.⁹) but insufficient data were given to allow any assessment to be made of the incidence of this complication.

Since irradiation with ultraviolet light under suitable conditions appeared to eliminate or at least reduce the risk of homologous serum jaundice, it was important to discover whether irradiated plasma in fact carried a smaller risk than small-pool plasma. The Ministry of Health and Medical Research Council therefore decided that plasma should be irradiated under carefully controlled conditions and that surveys should be made in the areas of three regional hospital boards (Cardiff, Liverpool, and Manchester) with the object of comparing the incidence of homologous serum jaundice after dried irradiated plasma with that (a) after dried unirradiated small-pool plasma, prepared concurrently by the usual methods in use since 1945, and (b) after whole blood alone. In these surveys each member of the population at risk was followed-up in a manner similar to that described by Spurling et al.¹ and Lehane et al.³ The surveys were carried out during the period January, 1952, to June, 1953.

The plasma was irradiated in an apparatus designed on the Habel-Sockrider principle (Habel and Sockrider¹⁰) using a flow-rate of 5 litres per hour with an ultraviolet emission

* The surveys reported here were organised and carried out on behalf of the Ministry of Health, Medical Research Council, and the Department of Health for Scotland by an ad-hoc group consisting of: Dr. R. J. DRUMMOND and Mrs. B. F. WILLIAMS, Regional Transfusion Centre, Cardiff; Dr. D. LEHANE and Miss K. DAVIES, Regional Transfusion Centre, Liverpool; Dr. F. STRATTON and Mrs. K. J. COOPER, Regional Transfusion Centre, Manchester; Dr. J. WALLACE and Miss K. J. CLARE, Glasgow and West of Scotland Blood Transfusion Service, Glasgow; Sir ALAN DRURY, F.R.S., Institute of Animal Physiology, Babraham; Dr. W. d'A. MAYCOCK, Lister Institute, Elstree, Herts (consultant adviser to Ministry of Health); Mr. L. VALLET, Lister Institute, London, S.W.1; and Dr. J. T. BOYD, Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

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3. Lehane, D., Kwanten, C. M. S., Upward, M. G., Thompson, D. R. *Brit. med. J.* 1949, ii, 572.

4. Olliphant, J. W., Hollaender, A. *Publ. Hlth Rep., Wash.* 1946, 61, 598.
5. Wolf, A. M., Mason, J., Fitzpatrick, W. J., Schwartz, S. O., Levinson, S. O. *J. Amer. med. Ass.* 1947, 135, 476.
6. Blanchard, M. B., Stokes, J., Hampil, B., Wade, G. R., Spizizen, J. *Ibid.* 1948, 138, 341.
7. James, G., Korns, R. F., Wright, A. J. *Ibid.* 1950, 144, 228.
8. Rosenthal, N., Bassin, F. A., Michael, S. R. *Ibid.* p. 244.
9. Barnett, R. N., Fox, R. A., Snavely, J. G. *Ibid.* p. 226.
10. Habel, K., Sockrider, B. T. *J. Immunol.* 1947, 56, 273.

of 5.5 watts at 2537 Å. Voltage supply to the ultraviolet lamps, rate of flow, and other physical conditions were held constant during each "run." 15-litre pools from approximately 60-80 donors were first prepared from the 10-donor pools, and these larger pools were filtered and run through the irradiator in continuous sequence. The plasma from 600-800-donor pools was irradiated in this way during one "run." These operating conditions caused no significant changes in protein detectable by electrophoretic analysis.

The combined results of these three surveys are summarised in table II.

A fourth survey, arranged by the Department of Health for Scotland on the advice of the Advisory Committee on Medical Research and with the co-operation of the Scottish National Blood Transfusion Association, was organised in the same way as the English surveys and made in the Glasgow area during the period June, 1951, to August, 1953, to compare the incidence of homologous serum jaundice after kaolin-treated filtered liquid plasma (Maizels¹¹) with that after whole blood alone. The liquid plasma was kept at room-temperature for varying periods of time; it was never "younger" than three weeks, and some was over twelve months old when transfused. Storage of plasma at room-temperature has been advocated by Allen et al.^{12 13} as a means of inactivating the agent in plasma responsible for homologous serum jaundice. The maximum size of pools was derived from 140 donations of blood, seven 15-20-donor pools being clarified and filtered in continuous sequence. The results of this survey are summarised in table III.

TABLE III—INCIDENCE OF JAUNDICE AFTER TRANSFUSION OF BLOOD AND OF KAOLIN-TREATED PLASMA

Transfusion fluid	No. of patients on whom incidence of jaundice is based	No. developing jaundice of doubtful aetiology	No. developing homologous serum jaundice attributed to transfusion	Deaths attributed to homologous serum jaundice
Blood	1387	3	5 (0.36%)	0
Kaolin-treated filtered liquid plasma ...	1366	8	16 (1.17%)	0

GENERAL CONCLUSIONS

1. It is apparent that the exposure of plasma to ultraviolet light under the conditions used did not inactivate the causative agent of homologous serum jaundice.

2. The incidence of homologous serum jaundice after transfusion of the dried small-pool plasma is very low and does not differ significantly from that found after transfusion of whole-blood; both are less than that found by Lehane et al.³

3. The incidence of homologous serum jaundice observed after kaolin-treated filtered liquid plasma was slightly smaller than that reported after dried small-pool plasma by Lehane et al.³ but greater than that after dried small-pool plasma in the present English surveys. One of the cases of jaundice occurred after the transfusion of plasma ten months old, and another after plasma seven months old, which had been stored at room-temperature.

Full details of these surveys will be published elsewhere.

11. Maizels, M. *Lancet*, 1944, ii, 205.
12. Allen, J. G., Sykes, C., Enerson, D. M., Elghammer, R. M., Grossman, B. J., McKeon, C. L., Galluzzi, N. J. *J. Amer. med. Ass.* 1950, 144, 1068.
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Reviews of Books

Progress in Clinical Surgery

Editor: RODNEY SMITH, M.S., F.R.C.S., surgeon, St. George's Hospital, London: J. & A. Churchill. 1954. Pp. 414. 36s.

THE young surgeon seeking helpful instruction on those developments in clinical surgery which are too recent to be found in the textbooks is often faced with dogmatic but contradictory opinions which he must evaluate as best he can. Most of the original articles in medical periodicals are one-sided, and many postgraduate lectures are no less an expression of personal opinion. What the young surgeon needs is a balanced assessment of opposing views on controversial matters, with the arguments for and against fairly stated.

This symposium, by 20 well-established but not too senior surgeons, has been produced with the avowed purpose of helping "the postgraduate student working for his final F.R.C.S. examination and the younger surgeon with a recent hospital appointment," and it serves this purpose admirably. In comparatively short space most of what the postgraduate student requires to add to his textbook studies is condensed in highly readable form; and this is achieved without exclusion of the more specialised branches of surgery. There has inevitably been considerable selection of material but few will quarrel with the choice. The only omission calling for comment is that the otherwise excellent chapter on brain surgery contains no reference to tentorial impaction; but some will regret that the chapter on cancer of the mouth and pharynx has not the same impartiality as the rest of the work.

The book can be confidently recommended not only for the young surgeon but for more senior surgeons who find themselves unable to keep pace with the journals.

Plague

R. POLLITZER, M.D., formerly of the division of epidemiological and health statistical services, World Health Organisation, Geneva: W.H.O. Monograph Series no. 22. H.M. Stationery Office. 1954. Pp. 698. £3 5s.

WE have long been waiting for an authoritative and comprehensive textbook on plague, and here it is. Dr. Pollitzer was a co-author of a classical manual on plague published in 1936 and has spent his time since then continuing the struggle against plague in China. (An example of his scientific indifference to the wars and political upheavals going on around him was his arrest, when working with a League of Nations anti-epidemic team, for taking a photograph of entomological interest which unfortunately included a battery in action.) His new book is a re-edited compilation of studies published in the *Bulletin of the World Health Organisation* (1951-53) covering every aspect of plague, and it will undoubtedly be the standard textbook for some years to come.

Its ten chapters deal with the history and present distribution; the plague bacillus; immunology; pathology; laboratory diagnosis; hosts; insect vectors; clinical aspects; epidemiology; and control and prevention. It is fully up to date, in that it deals with the sulphonamides and antibiotics in treatment and with the new poisons and persistent insecticides in control. Most of the superb illustrations, particularly those in an annex on the identification of flea-vectors contributed by F. G. A. M. Smit of the Museum at Tring, have never previously been published.

Those of us who think of plague as a menace of bygone days, or as something which affects the other fellow and not ourselves, will be convinced by a glance at the world maps showing recent human infections in 1952 that this is a parochial view. Even when the control of human plague is successful, the epizootic threat remains, as the insidious spread of rodent plague across the United States has shown. As with yellow fever and tularemia, watchfulness cannot be relaxed even in non-epidemic countries while the fire smoulders in the woods, since at any time a burning ember may start a conflagration, though modern methods of control and treatment should

limit the outbreak more quickly and with less serious results.

This is exactly the kind of major international scientific work which W.H.O. should sponsor.

Practique de l'hibernothérapie en chirurgie et en médecine

H. LABORIT and P. HUGUENARD. Paris: Masson. 1954. Pp. 256. Fr. 1400.

PAPERS on artificial hibernation began to find their way into the medical press of this country only recently, though the elements of the technique and the use of individual drugs concerned in it have been slowly introduced into clinical practice during the last year or two. Its value cannot yet be assessed, but a controversy has already begun on its merits and potential dangers—even though the pharmacologists are at present unable to offer an account of all the actions of chlorpromazine, the agent chiefly used to produce it.

In this book Dr. Laborit and Dr. Huguenard, the surgeon and anaesthetist who first started the method and popularised the term "artificial hibernation," set out their ten years' experience; and numerous contributors, representing nearly every branch of medicine, add their opinions. Hibernation is recommended for conditions ranging from the treatment of premature babies to cerebral surgery, and from carbon-monoxide poisoning to malignant hypertension. Both theory and practice are dealt with in considerable detail. The complexity of the technique and the polypharmacy that it entails—as many as 15 drugs being used on occasion—will not appeal to many clinicians here, even though there is an apparently rational basis for all that is recommended. Nevertheless, hibernation undoubtedly has value for selected patients, and British workers who have tried it, using a limited number of agents, are mostly enthusiastic. The value of this volume would be greater if the results of hibernation had been compared with those produced by more orthodox methods of anaesthesia or treatment.

Hepatic Circulation and Portal Hypertension

CHARLES G. CHILD, M.D., professor of surgery, Tufts College Medical School, Philadelphia and London: W. B. Saunders. 1954. Pp. 444. 60s.

THE circulation through the mammalian liver is complicated by its dual blood-supply. This introduces many difficulties not only for the student of this circulation but for everyone concerned with hepatic disease. The great importance of the subject, however, has stimulated an enormous volume of research on many animal species, and by diverse techniques. It is perhaps hardly necessary to say that the results of such a varied approach have been far from uniform, and often contradictory. The development of the various surgical operations for the relief of portal hypertension, however, has made necessary a better understanding of the problems, and has stimulated Professor Child to collecting into one volume the main contributions to this subject during the past fifty years. A series of six short appendices describe some of the experiments performed by the author and his associates; a seventh deals with the case-histories of patients subjected to various types of shunt operation for portal hypertension.

Students of the liver have long needed a book of this kind, and most of them will wish to thank and congratulate Professor Child. The illustrations are a credit to all concerned.

Preservation and Transplantation of Normal Tissues

A Ciba Foundation Symposium. Editors for the Ciba Foundation: G. E. W. WOLSTENHOLME, O.B.E., M.A., M.B.; MARGARET P. CAMERON, M.A., A.B.L.S. London: J. & A. Churchill. 1954. Pp. 236. 25s.

FROM the clinical viewpoint tissue storage is the provision and storage of spare parts for replacement surgery, and with few exceptions it entails the storage of tissues obtained from other human beings. Since the use of stored tissues is restricted by the fact that some living tissues will not form permanent grafts after transplantation a survey of the problems must take into account the problems of transplantation immunity reactions, leading to death of the graft. Appropriately,

P. B. Medawar's opening contribution to this symposium refers particularly to skin homografts, and later F. K. Sanders describes the difference in behaviour between nerve homografts and nerve autografts. Endocrine homografts are dealt with by P. F. Jones and other contributors. A survey of general surgical problems of tissue transplantation by W. P. Longmire and his associates paves the way for detailed accounts of the surgical application of different tissues, both fresh and preserved, viable or non-viable. Two contributions describe the maintenance and operation of "tissue banks." Other articles of general interest deal with long-term storage of endocrine tissues and skin in a viable state, the preservation of blood, and biophysical aspects of freezing living cells. W. R. Earle describes the maintenance of long-term large-scale tissue cultures; Pomerat and Lewis, methods for the analysis of thermal stress; and P. J. Gaillard the transplantation of cultivated parathyroid tissue in man. This book does full justice to its title.

The Homosexual Outlook

A Subjective Approach. DONALD WEBSTER CORY. London: Peter Nevill. 1953. Pp. 326. 18s.

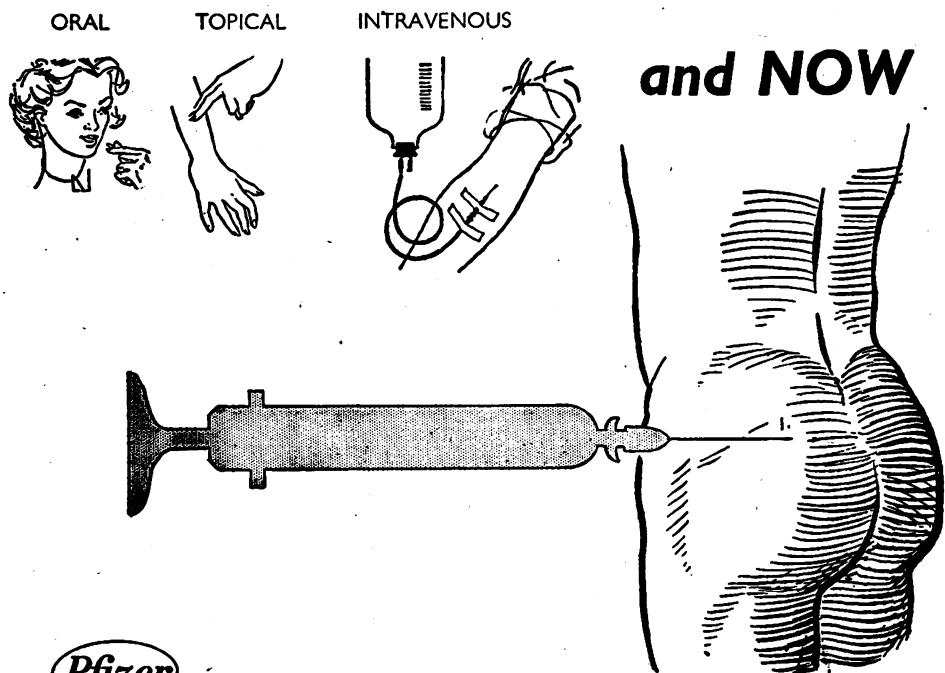
THE author of this book writes sincerely and responsibly about the effect upon his own life of a strong homosexual drive. He describes from direct observation the language and social habits of homosexuals in a large American city, and the personal and social conflicts they must encounter. Of the psychological aspects he gives a review influenced by his reading and his experience of psycho-analysis: he was treated by this method for a long time, and in consequence overcame his feelings of shame and remorse but not his homosexual impulses. He is convinced that psychological treatment cannot change a homosexual into a heterosexual, though it may enable him to marry happily while maintaining a homosexual attachment. Like most educated men and women who are homosexual, the author emphasises the advantages which he believes are conferred by homosexuality, and he names the famous men who are said to have been homosexual (his list includes Francis Bacon, Byron, and Shelley). His argument is, in the main, a plea for a minority—a minority who are, in his view, not so much in need of toleration or therapy as of acceptance and equal treatment, in the light of a reorientation towards sexual life in modern civilisation. He develops this argument with such candour and moral dignity that his book deserves close attention, even though its thesis is repugnant to many.

Pneumoconiosis Abstracts. Vol. 2 (London: Pitman. 1954. Pp. 517. 80s.).—This volume of abstracts, made and compiled by Dr. E. L. Middleton and reprinted from the *Bulletin of Hygiene*, brings us up to 1950. The abstracts are in general clear and precise. The collection is comprehensive and well arranged with a good index, and therefore forms a very valuable reference book; but it is a pity it costs so much.

Basis of Clinical Neurology (3rd ed. London: Baillière, Tindall, & Cox. 1953. Pp. 510. 54s.).—Prof. Samuel Brock's textbook, eight years older since the last edition, maintains its workmanlike tradition. Collaborators have revised sections, and contributed new material, on electro-encephalography, electromyography, electrodiagnostic methods, the visual pathways, cerebral angiography, sensory extinction, and double stimulation; and the whole book reflects the synthesising mind of its editor. As he says in his preface, neurology and psychiatry are drawing nearer to one another; and he believes that one day they will not only be inseparable but will speak the same language.

Medical Progress, 1954: A Review of Medical Progress during 1953 (London: J. & A. Churchill. 1954. Pp. 345. 36s.).—This book, edited by Dr. Morris Fishbein, consists of essays on trends of research in many subjects, including cardiology, surgery, rheumatic diseases, the newer drugs, infectious diseases, gynaecology, reablement, physical medicine, and many other specialties. The contributors, authorities in their fields, make careful and critical surveys of work published during the year, endeavouring to distinguish as far as possible between work making a permanent addition to our knowledge and that which is still experimental; and they provide a guide to rewarding reading in the long bibliographies which end the chapters.

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THE LANCET

LONDON: SATURDAY, JUNE 26, 1954

Cortical Localisation

THE extension of neurosurgery beyond the relatively narrow bounds of tumour removal has given strong impetus to investigation into cerebral activity and cortical localisation. The development of psychosurgery, scar excision, topectomy, gyrectomy, and even hemispherectomy,¹ together with electrical stimulation of the brain at operation, have made it possible to apply to human physiology techniques previously restricted to research on animals. Paradoxically (but in keeping with experience in other fields of research) more direct and detailed knowledge has lessened the absolutism of theories on cortical localisation.

Discussing motor representation in the cortex, FULTON² asserted that "the controversy would seem clearly to be one which can be resolved more readily by recourse to experiment than by philosophical reflection." But the information from recent experimental work on the human brain is exceedingly complex and has given rise to argument and counter-argument in abundance; in WALSHE's³ words, "our knowledge has achieved a high degree of differentiation but yet awaits integration." The trans-oceanic debates of FULTON and WALSHE have been echoed by GOODDY⁴ and JEFFERSON.⁵ The details of these controversies are not identical, but in both the main schism relates to the parcellation of the cerebral cortex—to the notion that the cortex is or is not an anatomico-physiological mosaic. There is a spectrum of theories on the subject, at one edge of which are the earlier views of PENFIELD and RASMUSSEN,⁶ whose famous gargoyles epitomise the absolutist concept. Their monumental industry, applied both to the interpretation of epileptic-seizure patterns and to the electrical exploration of five hundred brains, resulted in extremely detailed maps of cortical activity. Lately PENFIELD⁷ has modified his ideas and has declared "that the function of the precentral gyrus is to transmit and no doubt transmute the impulses which reach it from the central integrating system . . . and if a homunculus is drawn it is no more than an aid to memory." At the other end of the spectrum is the view expressed by GOODDY and MCKISSOCK⁴ that "there is not a standard brain with all functions set and localised for use. The brain stands ready for training." LASHLEY⁸ emphasised the integrative relation between the "specialised" centres and the rest of the brain, and cast doubt upon the validity of the cyto-architectonic approach to localisation. Further, KALINOWSKY,⁹ reviewing the results of selective cortical ablation, indirectly supports the idea of equipotentiality in asserting that at least in the

prefrontal areas the intensity of the mental change appears to be determined by the quantity of pathways destroyed.

This divergence of views expressed by careful and responsible workers is bewildering. Are they in some way reconcilable? A clue seems to emerge from closer consideration of the techniques employed by the different theorists. It is not really surprising that the cerebral map produced by the histologist differs from that produced by the electrical stimulator: an analogy may be found in the differences between geological and ethnological cartography of the earth's surface. Again, clinical assessment of the diseased brain permits yet another equally valid interpretation of localisation, based on functional deficit. Finally, the results of ablation and of hemispherectomy, viewed against a temporal background in which improvement and even redesign of functional patterns takes place, indicate that there must be some equipotentiality of cerebral tissues. FULTON's claim for the superiority of experiment to philosophy now seems rather less convincing: it is the interpretation of the integrated experimental results that is so important. In the first place the cyto-architectonic method is clearly valueless in localising function: it requires physiological corroboration. Furthermore, since the effects of strychninisation and of electrical stimulation in no way resemble normal cerebral activity, no firm deduction about localisation of normal function can be made from such techniques. In the face of this experimental confusion it is tempting to resort to clinical pragmatism, but one must beware of the fallacy of identifying the localisation of sign-producing lesions with the localisation of normal function. The apostles of BROCA would be confounded by the recent revelation that ablation of the third frontal gyrus in the dominant hemisphere fails to produce any aphasic symptoms.

Ablation and hemispherectomy may seem to offer means of gaining more precise information. If an area of brain tissue can be removed without disturbing a particular function, it is reasonable to suggest that this function is located elsewhere. The production of gross functional defect by removing a given area of the cortex is powerful prima-facie evidence that the area excised is related to the function lost. But this idea, however attractive, implies that the cerebral cortex is made up of independent nerve-cells, and neglects the complex interweaving of neurones and their dendrites. For if, as seems most probable, cortical function is mediated by interconnected neuronal circuits, ablation can produce its effects by interrupting a particular circuit at a relatively remote point without indicating exactly where function is initiated. Indeed the varying results of topectomy, and the preservation of some motor function after hemispherectomy, can best be explained in terms of variable neuronal patterns, possibly including bilateral connections. Such neuronal patterns could exhibit functional flexibility and allow for some degree of compensatory re-education. This concept in no way involves accepting the view that there is no localisation of function at all—"that all parts of the brain stand ready for training." There seems to be no training of new visual areas, and the residual motor function after hemispherectomy is only a crude parody of the fine movements controlled by an intact brain. Thus the weight of evidence,

1. Krynauw, R. A. *J. Neurol. Psychiat.* 1950, 13, 243.

2. Fulton, J. Functional Localisation in the Frontal Lobes and Cerebellum. London, 1949.

3. Walshe, F. M. R. *Brain*, 1943, 66, 104.

4. Gooddy, W., McKissock, W. *Lancet*, 1951, i, 481.

5. Jefferson, M. *Ibid.* p. 635.

6. Penfield, W., Rasmussen, T. The Cerdbral Cortex of Man. New York, 1950.

7. Penfield, W. *Brain*, 1954, 77, 1.

8. Lashley, K. S. *Arch. Neurol. Psychiat.* 1937, 38, 371; *J. comp. Neurol.* 1946, 85, 223.

9. Kalinowsky, L. B. *Arch. Neurol. Psychiat.* 1953, 69, 582.

which is against a point-by-point localisation of function, nevertheless supports the notion of specialisation of certain cortical areas. We have in fact returned to the doctrine expounded by WALSHE,³ who regards the "hand area" of the motor cortex as a macula of the field of hand movement. This idea is based on the earlier thesis of HUGHINGS JACKSON¹⁰ that the arm centre represents movements of all parts of the body, but particularly of the arm itself. Such a view would account for certain apparent contradictions in clinical interpretations of cortical localisation—particularly in relation to complex sensory aurae which appear to transgress the classical boundaries of sensory representation.¹¹ This concept is not simply of academic interest. The knowledge that less specialised areas can take over control in the event of injury to the functional maculae is an encouragement to neurosurgeon and neurologist in the treatment of patients who have suffered cortical damage of any type.

Serum Hepatitis

PROGRESS in controlling the spread of infection with hepatitis viruses continues to be slow; for we lack a suitable animal host, culture medium, or specific laboratory test. Nevertheless the use of two more tedious methods—tests in volunteers (in the U.S.A.) and carefully controlled field observations (in Great Britain and the U.S.A.)—have thrown some light on the maintenance and transmission of serum-hepatitis virus in man. Three recent papers¹²⁻¹⁴ have confirmed earlier suspicions, which had been strengthened by brief reports by the same workers, that there exists an undefined proportion of adults—possibly as many as 0·5% at some times in some places¹⁵—who, without ever having had symptoms or signs of hepatitis, carry in their blood an agent which will produce hepatitis when injected into others. The mechanism by which the virus is maintained has long been a puzzle; for the disease is transmitted nearly always—possibly always—by injection. An obvious possibility was transmission in utero; and the observations by STOKES and his colleagues^{12,16} on a single mother and child, as well as several recent observations of acute and often fatal hepatitis in infants,¹⁶⁻¹⁸ strongly support this hypothesis. How long virus persists after such infection is still undecided; but it has frequently been observed that in children and adolescents serum hepatitis, though no less severe than usual when it does occur, is relatively uncommon,^{19,20} whereas infective hepatitis is commonest in these age-groups. Among blood-donors carriers of virus have been shown to be

10. Selected Writings of John Hughlings Jackson, edited by James Taylor. London, 1931; vol. 1, p. 69.
11. Petit-Dutailly, D., Chavany, J. A., Pertuiset, B., Lobel, G. *Pr. méd.* 1953, 61, 429.
12. Stokes, J., Berk, J. E., Malemut, L. L., Drake, M. E., Barondess, J. A., Bashe, W. J., Wolman, I. J., Farquhar, J. D., Bevan, B., Drummond, R. J., Maycock, W. d'A., Capps, R. B., Bennett, A. M. *J. Amer. med. Ass.* 1954, 154, 1059.
13. Neefe, J. R., Norrie, R. F., Reinhold, J. G., Mitchell, C. B., Howell, D. S. *Ibid.* p. 1066.
14. Murray, R., Diefenbach, W. C. L., Ratner, F., Leone, N. C., Oliphant, J. W. *Ibid.* p. 1072.
15. World Health Organization, Expert Committee on Hepatitis. *World Health Organ. techn. Rep. Ser.* 1953, no. 62.
16. Stokes, J., Wolman, I. J., Blanchard, M. C., Farquhar, J. D., Drake, M. E. *Amer. J. Dis. Child.* 1951, 82, 213.
17. Bodian, M., Newns, G. H. *Arch. franc. Pédiat.* 1953, 10, 169.
18. Dible, J. H., Hunt, W. E., Pugh, V. W., Steingold, L., Wood, J. H. F. *J. Path. Bact.* 1954, 67, 195.
19. Oliphant, J. W., Gilliam, A. G., Larson, C. L. *Publ. Hlth Rep., Wash.* 1943, 58, 1233.
20. Brightman, I. J., Korns, R. F. *J. Amer. med. Ass.* 1947, 135, 268.

infective for several years,¹²⁻¹⁴ the longest proven period being five and a half years. All these carriers were clinically healthy, although liver damage was demonstrated in some by liver-function tests and biopsy. Of 14 donors¹³ found to be carriers, only 1 subsequently developed clinical hepatitis. Eight months after this patient recovered clinically, transfusion of his blood led to fatal hepatitis in another patient. A few previous experiments had failed to demonstrate persistent carriage after the clinical disease, but this catastrophe supports the contention that a past history of jaundice precludes donation of blood, except in an emergency. How best to prevent such accidents is still uncertain: NEEFE et al.¹³ suggest that donors should be submitted to two or three liver-function tests; but they admit that some carriers give normal results, and some patients with diseases other than hepatitis give abnormal results. In Britain such a plan has been considered several times, but deemed impracticable.

In the late war, in addition to blood for transfusion, there was a need for large quantities of a stable substance for transfusion, easy to transport and store in any part of the world. Out of this arose the method of freeze-drying plasma from pools derived from 50 to 1000 or more donations of blood. By the end of the war it had become apparent that this method seriously increased the chances of disseminating the virus. In the U.S.A. the problem was attacked by seeking physical or chemical methods of treating whole blood or plasma, to inactivate virus. The hepatitis viruses had already been proved extremely resistant to heat at the highest temperatures that would not involve change in the constituents of the serum or plasma, and to the usual preservatives such as phenol and tricresol.¹⁵ Each treated substance had to be tested on small groups of volunteers. Progress was slow, and the difficulties of reaching conclusions and relating these to large-scale production was shown by the work with ultraviolet light (U.V.L.).^{21,22} In Great Britain the first step was to reduce the size of plasma pools to one where the risk would be relatively slight; each pool was restricted to 8-10 donations, yielding four or five 400-ml. bottles of plasma. The wisdom of this measure was evident from a survey of its application in the period October, 1945, to March, 1948.²³ When, however, the early successful results from the use of U.V.L. treatment were reported from the U.S.A.,²¹ it was thought advisable to see whether this provided any further protection; and a preliminary account of a comparative trial of U.V.L.-treated large-pool plasma (600-800 donations), small-pool dried plasma, and whole blood is given on p. 1328 of this issue. Use of small-pool plasma has been clearly vindicated. What is even more gratifying is the drop in incidence of serum hepatitis among those who received whole blood or small-pool plasma in 1952-53, compared with the 1945-48 series²³; parts of the two series were in the same area. This incidence is also very much less than that reported in recent years from the U.S.A. after transfusion of blood or plasma. Any of several different factors may underlie this reduction, but none can be established.

21. Blanchard, M. B., Stokes, J., Hampil, B., Wade, G. R., Spizizen, J. *Ibid.* 1948, 138, 341.
22. James, G., Korns, R. F., Wright, A. J. *Ibid.* 1950, 144, 223.
23. Lehane, D., Kwanten, C. M. S., Upward, M. G., Thompson, D. R. *Brit. med. J.* 1949, ii, 572.

A further method of dealing with plasma has been suggested by ALLEN et al.,^{24 25} in Chicago, who point out that all the present methods of storage tend to preserve any virus present, and that viruses in general tend to die more rapidly in the liquid state at room temperature (21°–30°C). They also dispute the common assumption that proteins in the plasma undergo early and serious deterioration, and they claim that plasma which has been stored for six to nine months at room-temperature is satisfactory for preventing or treating shock or hypoproteinæmia. ALLEN and his colleagues used pooled plasma from 25–32 donors, and found that 4% of their pools were contaminated (presumably with bacteria or moulds). Bacterial contamination would seem to be one of the main hazards of such material. Additional refinements of filtration and treatment with U.V.L. (neither of which was applied by ALLEN) have been suggested as useful adjuvants; but these measures seem to be just as laborious as preparing small-pool plasma. The Chicago workers claim that they have greatly reduced the risk of hepatitis from plasma by storage for six months at room temperature, and this agrees with the results from a questionnaire completed by 124 blood banks which had used the method; but the Chicago workers' own results in 1942–53 are not so convincing. From the article that we publish this week it seems that in this country such material is unlikely to carry less risk than small pools (dried) as normally prepared here. Furthermore, MURRAY²⁶ has recorded hepatitis with jaundice in 1 of 5 volunteers who received only 1 ml. of a known infected pool which had been left for six months at room temperature.

Though there is still no certainly effective method of treatment which is harmless to blood or man, one can feel relatively safe in Great Britain when administering fresh whole blood, or plasma prepared from pools of 8–10 donations. These carry about the same risk—a risk that is very small indeed.

Certification

SINCE well over half the patients admitted to our mental hospitals now enter voluntarily, the stigma of mental illness is evidently fading. This wide acceptance of voluntary treatment shows, too, that the stigma attaches not so much to treatment in a mental hospital as to legal and compulsory detention in a mental hospital—to judicial certification, in fact. This point was brought out by witnesses from the Ministry of Health and the Board of Control who recently gave evidence to the Royal Commission on the Law relating to Mental Illness and Mental Deficiency.²⁷ It is possible, though not perhaps

24. Allen, J. G., Inouye, H. S., Sykes, C. *Ann. Surg.* 1953, 138, 476.
25. Allen, J. G., Emerson, D. M., Barron, E. S. G., Sykes, C. *J. Amer. med. Ass.* 1954, 154, 103.

26. Murray, R. *Ibid.* 1954, 155, 13.

27. Minutes of Evidence, first day. H.M. Stationery Office, 1954. Pp. 69. 3s.

The members of the commission are Lord PERCY OF NEWCASTLE (chairman), Mrs. H.A. ADRIAN, J.P., Mr. C. BARTLETT, R.M.N., Mrs. E. M. BRADDOCK, M.P., Sir RUSSELL BRAIN, F.R.C.P., Sir CECIL OAKES, J.P., Dr. T. P. REES, Dr. D. H. H. THOMAS, Dr. J. GREENWOOD WILSON, and Miss H. M. HEDLEY (secretary). The Ministry of Health and the Board of Control were represented by Mr. I. F. ARMER, deputy secretary of the Ministry and chairman of the board, Mr. H. R. GREEN, legal senior commissioner of the board, and Dr. W. S. MACLAY, medical senior officer of the board, and a principal medical officer of the Ministry.

probable, that as enlightenment spreads, and mental illness in general is regarded with more equanimity, the stigma attaching to certification, too, will fade. But at present, at all events, the public think of the patient under certificate as "really mad," whereas they assume that a voluntary or temporary patient is suffering merely from some mild aberration or nervous breakdown. Again, certification of a member of a family may harm the employment prospects of other members—and of course the prospects of the mentally sick man himself, when he recovers. Since recovery often takes place in a matter of months, certification must often appear to patients as an unwarranted and damning piece of aggression by society. No other sick person is penalised in quite the same way. One method of changing the public attitude to certification would be by gradual education; but a quicker way, favoured by the Ministry and the board, would be to admit all patients to hospital without a judicial certificate, and only later to certify those whose dangerous or self-punitive impulses had not been modified by treatment. At present even a voluntary patient must apply in writing to be admitted to a mental hospital, though if he needed treatment in a general hospital his family doctor would arrange it for him. His admission, moreover, is notified to the Board of Control, which makes the whole undertaking seem more formidable than it is. Whatever virtue or value there was at the outset in such notification, the witnesses were agreed that it has now evaporated, and that voluntary patients ought to be able to use their mental hospitals with as little formality as they do a general hospital.

When a patient is unable to say whether he is, or is not, willing to accept mental-hospital treatment, the law already provides that he may be admitted without certification as a temporary patient.

The application is made by the spouse or other near relative, and is supported by the recommendation of two doctors, and these documents constitute authority for the detention of the patient up to six months, provided he does not in the meanwhile recover the power to express his willingness or unwillingness to remain. If towards the end of the six months it seems probable that he will not recover before the time runs out, but that he may do so soon afterwards, the period may be extended by two further periods of three months; and if then he still needs treatment, and is unable or unwilling to agree to remain as a voluntary patient he must either be certified or discharged.

This is a tried and valuable way of postponing certification for a patient who has lost his volition; but of course such patients are few, and their situation is very different from that of the patient who objects strongly to being detained in hospital. When it is obvious to everybody except the patient himself that it would be a good thing for him to have treatment in hospital, should it be possible, Mr. ARMER asked at the hearing, to force him—without a judicial order—to have it? And he answered, for the Ministry and the board, that, on balance, they thought it ought to be possible—that indeed it is highly desirable, both for him and his relatives, that he should be able to have treatment for a temporary period (say six to twelve months) without being certified. It could be done, Mr. ARMER suggested, by arranging for the unwilling patient to be taken to hospital by the duly authorised officer, under section 20 of the Mental

Treatment Act, or a modified form of it, and kept there for three to seven days. His detention beyond this time would depend on medical recommendation, which instead of operating for fourteen days as it does with the present reception order would last for up to six months. It could perhaps then be extended for a further six months, thus delaying judicial certification for twelve months in all. Whether a person should be deprived of his liberty for twelve months merely on medical recommendation needs careful thought of course; but the Ministry and the board are convinced that on the whole it would be more to his advantage, and that of his relatives, than is immediate certification.

Such delayed certification, as Mr. WOODLEY reminds us in the correspondence columns, is already being tried in Northern Ireland, apparently with good success.

As a means of admission to a mental hospital, judicial certification has been abolished there, all patients being

admitted as either voluntary or temporary patients. The application for admission of a temporary patient must be made to the medical superintendent by a relative, or—if no relative is available—by a welfare officer, and must be supported by a recommendation from one doctor, who must give reasons why he thinks the treatment necessary. The patient is admitted on these documents, and the initial period of temporary treatment may last twelve months. It may be extended, however, on application to the Northern Ireland Ministry of Health and Local Government, for two further periods of six months, and in exceptional circumstances a further extension is possible—over two years, in all. If, however, the patient is then thought to be unlikely to recover, and further mental hospital care is needed, a judicial order must be obtained.

It seems entirely reasonable that a patient should not be certified until he has had a period of skilled treatment, and that it should only take place when he has been for some considerable time in a mental hospital under psychiatric observation. As Mrs. BRADDOCK put it, "certification for a mental complaint should be the last resort, not the first."

Annotations

H.M. OVERSEA CIVIL SERVICE

TODAY many countries are moving steadily towards self-government. They do so with the good will and help of the Colonial Office and the Colonial Service. And it is a sign of this good will that all are anxious to ensure that such skilled help should continue to be available to these young governments.

Today all those who govern have to lean heavily on the expert, and the people who are called to govern these rapidly developing countries face enormous technical problems, with very few doctors, engineers, scientists, or administrators of their own; and, as the leaders in these territories themselves recognise, their need for British experts will remain for some time to come. The undertaking lately offered by Nigerian delegates shows¹ that these new countries are aware of their responsibility towards the men and women whose help they seek. But the Secretary of State for the Colonies feels that he too shares the obligation to safeguard the legitimate interests of these officers who were appointed under his name. To meet this changing situation he has, in a white-paper, described his plans for the *Reorganisation of the Colonial Service*.²

Since 1930 the members of this service have been employed and paid by the government of the territory where they worked, but they have been under the "general direction and patronage" of the Secretary of State for the Colonies. If the territory where they are working becomes self-governing, these officers, the white-paper suggests, are entitled to expect that the terms of service offered them shall not be less favourable than their present ones; that their pensions and other benefits shall be safeguarded; that they shall be eligible for transfer and promotion to posts in other territories; and that if their employment is ended because of constitutional changes they shall be given adequate notice and alternative employment or compensation. The Government in the United Kingdom is prepared to secure them these rights by formal agreement with any country which attains self-government, and as a first step the Government is compiling a list of all the officers entitled to these rights, and giving them the new name of Her Majesty's Oversea Civil Service. Those eligible for admission to the new service will include members of the Colonial Service (including the Colonial Medical

Service). In future any offer of appointment made by, or on behalf of, the Secretary of State will include a clear statement whether it carries with it membership of the new service or whether the officer's contract is solely with the territorial government. The Government hopes that "this new form of service will ensure that qualified men and women may be attracted to come forward in future as in the past, in a spirit of confidence, enthusiasm and partnership, to help the oversea governments and peoples along the path of social, economic and political progress."

GENETIC PREDISPOSITION TO DISSEMINATED SCLEROSIS

WHEN the genetic predisposition to an illness is weak its existence can be tested in two ways. Careful twin studies may reveal greater concordance of identical twin pairs, compared with fraternal twin pairs; or large-scale family studies may show that the disease prevails in the near relations of the index cases at a rate definitely higher than in the general population.

No major twin studies have yet been made for disseminated sclerosis. Thums¹ in 1949 found 1 of 20 identical twins also affected. This indicates that genetic predisposition, if present at all, must be weak. Four family studies have each given essentially similar results, though the workers have differed in the interpretation of their findings. Curtius and Speer² were the first to publish figures suggesting that near relations are unduly liable to be affected. Subsequently Pratt³ found 6 of 609 siblings and 7 of 1441 parents affected. Müller⁴ in Sweden last year and Allison and Millar⁵ this year have reported much larger series. Müller studied the families of 750 index cases and found 5 of 1493 parents, 22 of 2815 siblings, and 4 of 692 children affected. After correction for age he calculated that these figures represented incidences of 0.3, 1.0, and 2.3. Allison and Millar studied every case they could find in Northern Ireland—700 in all (476 "probable," 145 "possible," and 79 "early")—and in 2939 siblings they found 34 affected (about 1%). They also found that the highest incidence in the general population for any area or age-group (County Fermanagh, aged 40–59) was only 0.18%.

1. Thums, K. Cited by Pratt (footnote 3).

2. Curtius, F., Speer, H. *Z. ges. Neurol. Psychiat.* 1937, 160, 226.

3. Pratt, R. T. C. *Ann. Eugen., Lond.* 1951, 16, 45.

4. Müller, R. *Arch. Neurol. Psychiat.* 1953, 70, 731.

5. Allison, R. S., Millar, J. H. D. *Ulster med. J.* 1954, 23, suppl. 2.

1. *Lancet*, June 12, 1954, p. 1249.

2. Colonial no. 306. H.M. Stationery Office, 1954. Pp. 7. 4d.

Thus it is generally agreed that the proportion of siblings affected is about 1%—though the risk of a sibling developing the disease is probably rather higher than this when allowance is made for age and for the degree to which the probability of ascertainment is independent of the number of affected individuals in the family. The risk to parents and children is probably of the same order. But these figures mean little except in comparison with the risk to a random member of the general population, and this risk is less well established. Müller alone of these workers felt that the incidence he found in near relations might not differ significantly from that in the general population; but he was not aware at the time of the findings in Northern Ireland. While this general risk no doubt varies from country to country, it seems unlikely to exceed 0·2%. Therefore the risk to near relations is probably at least five times greater than that to others.

There are several possible explanations of these findings besides the obvious one that genetic factors predispose (though rather weakly) to disseminated sclerosis. One is common environment; but this is unlikely to extend over three generations. A more probable explanation is that the familial cases may have been, not disseminated sclerosis, but some form of genetically determined spinocerebellar ataxia. The workers concerned were all aware of this possibility (Allison and Millar show that the figures for the "probable" cases do not differ from those for the whole group), and they agree that differential diagnosis may be difficult.

ACCIDENT-PRONENESS IN MINERS

A not wholly unattractive picture of the accident-prone was drawn for us in 1943 by Flanders Dunbar.¹ She found them unusually healthy, seldom off work, lively-minded, happy-go-lucky, agin the government, and inarticulate about their feelings. Since she wrote about them, however, some doubt has been thrown on their existence. They are, in any case, difficult for statisticians to lay hands on, for after an accident anyone—accident-prone or not, and whether from choice or necessity—may change his job. However, as we have noted,² some clinicians are inclined to think that temperamental qualities do affect liability to error, and so to accident. Mr. J. W. Whitfield³ in an investigation which should mollify the most exacting of statisticians, has studied disabling accidents in one colliery between July 1, 1944, and Dec. 31, 1946, and has drawn some conclusions based on an actuarial risk, calculated for each man according to the number of shifts worked, the place of work, and the type of work done. Discrepancies between calculated risk and actual accident experience were analysed, and accident-proneness demonstrated: that is, there were measurable individual differences in accident susceptibility.

Men who had worked in the mine for only a short time were excluded from the study. That left 1384 miners who, during the period covered, suffered 1265 accidents severe enough to keep most of them from earning full wages at their normal work for more than three days. Some accidents, presumably, are unavoidable: if a thunderbolt strikes one, or the earth abruptly swallows one up, no amount of resource and sagacity, no expertness in motor response, is likely to preserve one from damage. Such catastrophes apart, however, accidents can be considered, in Whitfield's phrase, as "failure to make an adequate response to a hazardous situation." We may fail either because we do not appreciate the hazard in time and decide what response to make, or because we do not make the appropriate response quickly enough. Such failures in appreciation

and in performance can be demonstrated by appropriate tests, and the accident-prone men in Whitfield's study gave poor scores in one or other of the two groups of tests. The type of accident-proneness differed with age. The younger accident-prone miners were heavier and of better physique than their contemporaries, and their motor control and coördination were good; but they scored very poorly on tests of perceptual, memory, and cognitive processes. The older accident-prone men, on the other hand, scored average or above average in the perceptual and cognitive tests, but were much poorer in motor control and coördination. Perhaps the younger accident-prone leave this industry before they reach middle age: or perhaps they learn to keep out of trouble.

In the older men, accident-proneness may have been slowly developing as motor ability declined; and perhaps perceptual and cognitive ability were declining too. A man who is deficient in motor ability commonly compensates for this by anticipation, but as age advances he may become less able to do this. Whitfield suggests that if further studies confirm his findings, the "older type" of accident-proneness might be watched for and detected early. Methods could then be devised to protect those in whom it was developing. Accidents are undesirable, in the interests not only of the men but of the industry: the older men are of great value, and the loss of their skill, even temporarily, is serious. The younger accident-prone present a different, and more difficult, problem. Whitfield found some evidence that their temperamental development might have been unfavourably affected by adverse factors in childhood and upbringing, but, as he rightly says, "this is not susceptible to direct action by the industry." The proper way of tackling them, he concludes, is by training: for though it may be impossible to teach caution to those who are temperamentally careless and happy-go-lucky, yet they can be taught to use specific working methods appropriate to their lack of foresight. It will be something, he thinks, if safety officers recognise that good motor coördination alone is not enough.

HEEL LESIONS IN RHEUMATOID ARTHRITIS

It is well known that in rheumatoid arthritis the distribution of the joint lesions spreads centripetally as the disease progresses, but in the early stages only the hands and feet may be affected. For early diagnosis, therefore, attention is particularly directed to the hands, which show characteristic changes; in the feet early lesions are perhaps less easily recognised, and the changes produced in the tarsus by rheumatoid disease less well known.

Bywaters¹ has described heel pain as an early or even a presenting symptom in rheumatoid arthritis, and has reported a small series of cases in which he investigated the underlying lesions. He found two different heel lesions, occurring with about equal frequency, and usually together, in 2-3% of unselected cases. The first, a sub-Achilles bursitis, involves the bursa which lies between the tendon near its insertion and the fibrocartilage of the posterior surface of the calcaneum. It is manifested clinically by swelling, pain on walking, and tenderness, and radiographically by rarefaction and erosion of the subjacent bone. The second lesion consists solely in erosion of the plantar surface of the calcaneum, involving the plantar spur and the area behind it. In both lesions the histological appearances of rheumatoid granulation-tissue are found, including the cell formations typical of the rheumatoid nodule. Healed lesions examined at necropsy showed obliteration of the sub-Achilles space and loss of normal fibrocartilage from the bone surface at the site of erosion.

1. *War Medicine*, 1943, 4, 1. See also *Lancet*, 1952, i, 1296.

2. *Lancet*, 1953, i, 730.

3. *Brit. J. Industr. Med.* 1954, 11, 126.

1. Bywaters, E. G. L. *Ann. rheum. Dis.* 1954, 13, 42.

The type of heel pain to which these lesions give rise includes the "achillodynbia" described many years ago, and hitherto regarded as a complication of chronic infection—usually gonorrhoeal. Bywaters believes that rheumatoid arthritis may be the commonest cause of these lesions, and that this diagnosis should be especially kept in mind when heel pain is among the presenting symptoms.

RECEPTION HOME

"There are several doctrines about reception homes: the approach psychometric; the approach analytical; and the approach nihilistic, the last displayed by those who claim to have opened such homes and closed them again. Perhaps more precious than any is our own pose of being plain honest-to-goodness social workers. That child, we say, is best served by the reception home who never goes into it."

In Case Conference, a new journal for social workers and administrators, Mr. Kenneth Brill,¹ from whom we quote above, describes the achievements of a reception centre during its first year of life, and with pleasant irony tells something of the strength and weakness of social work in this setting. The aim of the staff is to get the children who come into the centre either safely back to their mothers or else into a settled home life with someone who will take the mother's place; and their results speak for themselves: of 47 children under the age of fifteen who came into the centre during the year ending March, 1953, 35 have since been restored to their families, 6 are in foster-homes, and 6 are still in group care.

The children come into the centre for the usual reasons—on a "place of safety" order, because of temporary difficulty at home (such as admission of the mother to a mental hospital or sanatorium), because the family has been evicted, or because they have been committed to care by a court, for delinquent behaviour. The first thing they notice is that they have not come to a permanent haven: they see other children coming and going, and they probably derive a feeling of safety from the fact that they are all in the same boat—temporarily away from a home to which they hope to return. This helps them to accept the situation and look forward to a coherent plan for the future; and they are quite aware of what is going on, it seems.

A boy of ten, committed by the juvenile court for larceny, and rejected by his mother, got tired of waiting in the home, and accosted the boarding-out officer with the inquiry, "When are you going to make a plan for me?"

A child who has led a roving life with an evicted parent is sometimes at a loss to see why he should change his arrangements. They have, as far as he can see, worked fairly well, and they have, at all events, generally supplied him with an independent spirit. An eleven-year-old, sounded on the question of a foster-home, replied maturely: "I don't want to live with any stinking auntie, whatever the Government wants."

The results achieved by this reception centre form part of the experience of the Devon Children's Committee, which set it up. The county as a whole can claim that of 233 children under fifteen who came into care in the year ending March, 1953, only 20 remained in institutions a year later. Children for whom the committee foresee the end of their stay in care (classed as short-stay children) are now nearly all sent into foster-homes from the start; and, in particular, admission of short-stay children to a residential nursery has almost ceased. There were 132 short-stay children among the 233, and all are now back in their own homes. Moreover, nearly half the long-stay children, whether committed

by the courts or not, went home within two years, and two-thirds of the remainder are now in foster-homes.

This first year's experience, Mr. Brill says, contains an administrative lesson. Nowadays children's committees are urged to invest in plenty of qualified child-care officers; and those who do so will be surprised at the dividend. The chief gain—which is both spiritual and financial—is that only a tiny fraction of the children received ever need to be in residential care: residential nurseries and family homes can be closed down. "Invest," he says, "in bricks or mortar or in properly trained social workers, but not in both at once."

The reception home has proved to be a terminus for several lines of social work; and, since some twelve statutory agencies² have an interest in protecting children from neglect and ill-treatment (quite apart from the children's officer, her field worker, the staff of the reception home, almoners, police, probation officers, private people such as doctors and clergy, and all the voluntary agencies), Mr. Brill advises those who are opening such homes to have a room large enough to take twenty or more social workers at a time at a case-conference. Fortunately few families attract the interest of more than six or eight agencies; but representatives of all these must be present at the case-conference, or else—as he illustrates from an authentic case—the one forgotten agency will take independent action astonishing to the rest. The difficulty, he says, is in forecasting which agencies to invite. Nevertheless the justification of such gatherings lies in the experience of children now back with their families or beginning a new life in foster-homes.

SURVIVAL OF DRIED CULTURES

BACTERIA survive for long periods in the dried state, and drying under controlled conditions is now a standard method for maintaining stock cultures for teaching or reference purposes. The techniques used may be simple or complex, but all involve the destruction of 90–99% of the organisms being dried. In September, 1953, the British Commonwealth Collections of Micro-organisms organised a discussion of drying methods to which workers from different parts of the Commonwealth were asked to contribute their experiences. Papers circulated before the meeting are included in the report of the discussion,³ which ranged from the problems of the designer of apparatus to the technical methods for checking the viability of the dried cultures.

The discussion showed that the fundamental principles underlying the method are still only imperfectly understood and that many of the procedures are empirical. The most important single factor affecting viability of the dried product seems to be the material in which the micro-organisms are suspended, and of glucose, the addition of which was first suggested by Fry and Greaves,⁴ is the most successful of the additives. Record and Taylor⁵ have recently shown that bacteria themselves, presumably by autolysis, can contribute some protective factor, so the survival-rates of heavy suspensions are greater than those of lighter suspensions, but the difference is not as great as the glucose effect. Ultimately it may be possible to correlate survival-rates with residual moisture content, but technical difficulties of determining residual moisture have so far prevented this. Apparatus described at the discussion may bring moisture determination within the range of routine procedures.

2. Home Office Circular no. 157, 1950.

3. British Commonwealth of Nations Scientific Liaison Offices, B.C.S.O. (London): A discussion on the maintenance of cultures by freeze drying. H.M. Stationery Office. Code no. 88-1311. 5s.

4. Fry, R. M., Greaves, R. I. N. *J. Hyg., Camb.* 1951, 49, 220.

5. Record, B. R., Taylor, R. *J. gen. Microbiol.* 1953, 9, 475.

Special Articles

NEGLIGENCE

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WITHIN recent times the number of actions against hospitals has increased. For this increase there appear to be four main reasons: (a) the payment of doctors from public funds, (b) the national ownership of hospitals, (c) the effects of the Legal Aid and Advice Act, 1949, and (d) certain changes in the outlook of the doctors themselves.

In the days when the consultant staffs of voluntary hospitals were unpaid, the fact that their service was gratuitous made them as immune against charges of negligence, in fact though not in law, as the barrister is today. The practice of bringing actions against hospitals may be said to date from the beginning of public ownership of hospitals, when certain of the poor-law hospitals and institutions "appropriated" by the local authorities in 1930 took on the functions of general hospitals; and it advanced further when the ownership of hospitals was taken over by the State in 1948, since when neither the public nor their legal advisers have hesitated to bring actions against members of the medical staffs—knowing that behind them are virtually unlimited resources. (Also the fact is not unknown to the public that all prudent doctors are insured against actions through one of the medical defence societies.) Under the Legal Aid and Advice Act, 1949, any man with a reasonable cause for action can be given the means of seeking a remedy, and State funds are now available even for action against the State. And finally the medical profession no longer appears united, presenting an impenetrable front. Some doctors do not hesitate to take sides in the lay press, and the medical press is a happy hunting-ground for the journalist. The serious effects of conflicting evidence by expert witnesses will be referred to later.

NEGLIGENCE IN LAW

Negligence may be of two kinds, criminal and civil. Criminal is distinguished from civil negligence in that in the former the degree of negligence must be a criminal one; it must be a *wicked* negligence, or negligence which shows so little thought for the safety and life of others that it merits punishment, while in the latter damages are sought from the wrongdoer to recompense the sufferer. Whereas the degree of negligence which will support a claim for civil negligence may not be sufficient to constitute criminal negligence, the degree sufficient to amount to criminal negligence will be more than enough to support the civil kind. A charge of criminal negligence does not preclude the instituting of civil proceedings on the same facts.

In common law civil negligence is a tort, defined as a civil injury or wrong, the remedy for which is unliquidated damages—i.e., damages which are not ascertained previously but are left to the court to determine in its discretion. (There are of course other remedies for a tort, such as an injunction; but they are in addition to the damages, and do not apply to negligence.) It has been said that a tort is "a civil wrong for which the

remedy is a common law action for unliquidated damages, and which is not exclusively the breach of a contract or the breach of a trust or other merely equitable obligation,"¹ but the same facts might give rise to a tort and also to a breach of contract, for the doctor-patient relationship is usually one of contract. Nevertheless when there is a breakdown in this relationship owing to some malfeasance on the part of the doctor it is generally under the heading of tort that a claim is made.

Negligence, as a tort, is the breach of a legal duty to take care which results in damage, undesired by the defendant, to the plaintiff.² It consists, therefore, of three elements, and it is only if these three exist together that an action for negligence can arise. They are (a) a legal duty to take care, (b) a breach of that duty, and (c) damage arising from the breach.

(a) No problem arises with regard to the duty of care, because it is obvious that the doctor-patient relationship involves this duty.

(b) Speaking generally, a breach of duty is the omission to do something, or the doing of something which should not be done by a reasonable man, and in this context a reasonable man is generally taken to mean the ordinary man in the street. However, where members of a profession hold themselves out as exercising particular skill, this must be of the order which can reasonably be expected from members of such profession, having regard to the knowledge of the time. A doctor will be as liable if he renders treatment voluntarily to an unknown person in a street accident which he encounters merely when passing, and is negligent, as he would be if treating one of his regular patients, except that the circumstances in which he is compelled to work will, of course, be taken into account. Whether or not there has been a breach of the duty of care is a question of fact for the jury to decide, or for the judge should he be sitting without a jury.

There are no degrees of quality in civil negligence, and although such terms as "slight," "moderate," and "gross" may be used they have no bearing on whether or not negligence exists.

(c) The result of the breach must be damage to the sufferer. If there is no damage there can be no negligence. The object of an action for negligence, therefore, is to obtain damages for the plaintiff for a wrong suffered—not to punish the defendant. There are, however, other possible results of such an action and they will be discussed later.

In passing it should be mentioned that an action for negligence is one of the remedies for breach of a statutory duty. The damage suffered must be that which it was the purpose of the statute to avoid and not other damage resulting from the breach. It will be interesting to see whether there are any developments along this line in future, relative to the statutes, said to number about 180, which now have some bearing on the practice of medicine.

THE CONDUCT OF A CASE

The case may never reach the courts. The negligence may be admitted, the amount of damages may be agreed between the parties, and after settlement the matter may end without publicity, the whole business being conducted privately between the parties and their representatives. Even when a writ has been issued against the defendant, the matter may be settled by the parties before the action comes up for trial.

On the other hand, though the defendant may admit negligence, and may be willing to pay what he thinks is a reasonable amount as damages, the injured party may regard the amount as insufficient. The case is then taken to the court for an assessment of damages, and perhaps (if more than one person has suffered) for an apportionment.

1. Salmon, *Law of Torts*, 1953, p. 15.

2. Winfield, *Law of Tort*, 1950, p. 405.

If negligence is denied, the object of the action is to decide whether there was negligence. If the case is proved, damages will be assessed. The burden of proving negligence rests on the plaintiff, and he must prove not only that the defendant was negligent but also that this negligence caused the injury.

There are, however, cases where, though the plaintiff can prove that an accident has happened, he cannot prove how it happened, and consequently cannot show that it was due to the negligent act of the defendant. There are many acts which, performed in the normal way, lead to no untoward happening; and in which, should anything go wrong, it might be presumed that it was due to the fault of the person in charge of or performing the act. This has given rise to the rule of *res ipsa loquitur*. If the accident speaks for itself, the plaintiff does all that is required of him if he proves the event, and it then becomes the duty of the defendant to show that it was not due to negligence on his part. If, however, the defendant can show that the accident could have occurred either by his negligence or without negligence the burden of proof moves once more to the plaintiff to show that it was due to negligence.

A case is proved or disproved in the courts by means of evidence, which was defined nearly two hundred years ago as "that which demonstrates, makes clear or ascertains the truth of the very fact or point in issue, either on the one side or on the other."³ There are three types of evidence :

- (i) Oral evidence—i.e., the testimony of witnesses.
- (ii) Documentary evidence—i.e., the production of documents.
- (iii) Real evidence—i.e., the inspection of things.

(i) *Witnesses* may be of two kinds. Firstly, there is the ordinary witness of fact who makes a statement of fact and gives no opinion on it. Thus a man in the street may say that he saw a man fall from a roof, and when he picked him up he found that he was unconscious and had a large cut over the top of his head. Secondly, there is the expert witness who may give evidence of fact and follow this up with an opinion. If, for example, the man who fell from the roof was taken to a hospital, the medical officer may say that he saw the man on admission, that he was unconscious, and that he had a large cut over the head. Treatment was given and the patient put to bed in a ward where he died in half an hour. These are facts; but the doctor may say in addition that in his opinion death was due to compression of the brain due to haemorrhage, following injury to the head. He then becomes an expert witness. Alternatively the expert witness need not give evidence of facts before giving his opinion on them, but may give his opinion on facts which have been established by others. He may, for example, apply his special knowledge and experience to the facts already known to the court. Normally it is for the court to form opinions from facts given by witnesses but when the court cannot form an opinion because the subject is technical, or because special study or skill is required, then experts may be called.

(ii) The production of *documents* means the production before the court of any written or inscribed matter relative to the case. The term is used in its widest sense to mean anything permanently recorded, and includes hospital and doctors' notes of cases. Privilege, in the sense that they contain information of a confidential nature which was obtained in a professional capacity from patients, is not attached to these notes, the production of which can be ordered by the court. If, however, their production would tend to criminate the person producing them, then privilege may be claimed.

(iii) The term "*things*" means anything other than documents as defined above. Thus there may be produced in court the splint used in a particular case, or an anaesthetic machine may be brought as an exhibit to explain how it works. In the case of documents and things, witnesses usually come forward and testify about them either as to fact or in an expert way.

A plaintiff or defendant is under no obligation to engage a lawyer to advise him and to look after his interests, or to represent him in court; but in almost all cases litigants are represented, and today there is no reason why any person with a reasonable case—this term is used to eliminate frivolous and vexatious actions—should not have legal assistance, however poor he may be.

Where he is engaged, counsel's duty is to further the interests of his client by bringing before the notice of the court all the facts which, with fairness, will support his client's case. Counsel does this by presenting the evidence in favour of his client in what is known as examination-in-chief. After each witness has been so examined, opposing counsel does his best to upset or belittle this evidence by cross-examination. Cross-examination is never pleasant, and medical men, as do others, sometimes feel that they are being personally attacked and resent this. It should be mentioned here that barristers do not enjoy pulling to pieces a member of another learned profession; it is simply their duty to do so to further their client's interests.

After cross-examination the first counsel may re-examine his witness to obtain enlightenment on any question which has been brought out in cross-examination and which is not clear. It is hardly necessary to add that the evidence of a medical man is not privileged in respect of knowledge which he has acquired in a professional capacity, and that the court can compel the doctor to answer questions. Failure to do so will result in his being punished for contempt of court.

THE EFFECTS OF PUBLICITY

The disquiet in the medical profession at the recent trend in litigation is not entirely due to the increase in the number of cases which are being brought against the hospitals and doctors. It arises partly from the way in which cases are sometimes reported in the lay press. Thus the plaintiff's case on the first day may be reported in full, whereas on succeeding days the defence, and final decision, may be reduced to one paragraph. We make no suggestion of deliberate unfairness: it is merely that, after a day or so, other news makes headlines.

Press reports may have an impact on three sections of the community—the general public, the defendant doctor, and the medical profession generally. No small part of their effects is due to the conflict of opinion of expert witnesses engaged to support the plaintiff and the defendant; for those employed by each side are called because they will support the evidence which one or other side can bring forward. Suppose, for example, that each side has three expert witnesses. This means that on each side there are three medical men who may give diametrically opposite opinions to the other three and, this being so, the layman must assume that one side is right and the other wrong. It appears to him also that, given one set of circumstances, three doctors would have done one thing and three others the opposite. What is not apparent to the layman is that the defendant doctor may have been in the position of having to make one of these very decisions. Using all possible care and skill he selects one which may be right or wrong: it is a selection which is later supported by one set of witnesses, and the fact that it has proved unfortunate does not imply negligence. An expert witness may say that he would have done something different; but it is sometimes difficult to see how he can put himself—post mortem so to speak—in the position of the defendant doctor, who may well have less experience and knowledge than the witness but may nevertheless have shown all the care and skill within his competence.

These divergences of opinion between expert witnesses, each of whom may claim that his opinion on the given facts is the correct one, may have an unexpected effect

on the case ; for in order to reach a decision the judge and jury are thrown back on their own common sense. It is possible that some of the very heavy damages awarded recently would not have been given if the true prognosis had been more clearly understood. Moreover, reports of such actions can have a damaging effect on public confidence, for a patient in the future may suffer extra fear and trepidation when he is ill, or undergoing special manipulations.

It has been noted already that the object of an action for negligence is not the punishment of the defendant doctor. But in fact he may be severely punished, in that he suffers mentally, sometimes physically, and possibly financially. By reason of the trial his professional confidence may be shaken or lost ; the mental worry may lead to a physical breakdown, and he may suffer a loss of practice income.

The effect on the medical profession generally may be cumulative, for it may lead to a state of affairs where the doctor's first interest will be to make sure that he is fully protected against any possible charges. We may not come to the point of the surgeon taking his legal adviser into the operating-theatre with him, but the patient might conceivably be asked to sign an indemnity form against all liability before treatment is commenced.

DISCUSSION

The practice of medicine being one which demands that the mind of the practitioner should be free from fear and untrammelled by extraneous worry and care, it might be possible to postulate a set of principles, and see whether there are any means by which these could be fulfilled without prejudicing the rights of any other person should the practitioner fail in his duties. What the doctor requires are freedom of action to use methods of diagnosis and treatment which are in his judgment best for the particular case being dealt with ; freedom from fear of consequences of a genuine mistake or of an untoward and unforeseen reaction on the part of the patient, and freedom from fear of frivolous actions and vexatious litigation.

How can this freedom be ensured ? In regard to negligence, doctors are not members of a privileged profession. They must bear the responsibilities for their actions as do other members of the community, and this is not altered by the fact that they must show care and skill. What is causing concern today is not that doctors are liable for negligence—for no-one will deny that if a wrong exists it must be righted—but the way in which the existence or absence of negligence is decided.

A number of alternative means could be found for deciding claims for negligence. Thus the position might remain as at present, cases of negligence against hospitals and doctors being tried openly in the courts by a judge sitting with or without a jury. Or the case might be tried behind closed doors—though such a suggestion strikes at the roots of English justice and would be open to the objection that it creates a special procedure for medical negligence, as compared with negligence in general. Alternatively a degree of privacy which would appeal to the medical profession might be achieved if the publication of medical evidence in the lay press could be limited like the publication of details in divorce and certain other cases. The doctor giving evidence would then feel that the professional confidences which he had obtained were not being so widely broadcast, and the medical histories in the hospital notes would once more assume a confidential nature. Furthermore the confusing and contradictory opinions of expert witnesses would no longer harass the public and tend to destroy confidence in the medical profession.

From the legal point of view it would be impracticable to do away with the expert witness ; for he is necessary for the preparation of the case, and his examination and

cross-examination are essential for its efficient conduct in court. The expert witnesses might, however, be limited in number to one on each side, and one or more medical assessors might sit with the judge. These assessors, who would have to be doctors of undoubted ability and integrity, would assist the judge on points in the evidence which were not clear. They might also be given power to examine the plaintiff, and would thus have first-hand information which would assist in assessing the amount of damages to be awarded. The assessors might be drawn from a panel based on the assize circuits. Nautical assessors already assist in Admiralty cases, and thus form a precedent for the institution of such a panel in medical cases.

Another means of dealing with cases of negligence would be to entrust them to tribunals specially constituted for the purpose. The National Health Service Act, 1946, could be amended by an Act declaring that all actions for negligence in which damages will have to be met from public funds shall be heard by a tribunal and not in the ordinary courts. Such a tribunal could act in one of several different ways. It might act like the old "grand juries" (abolished some years ago), deciding merely whether the *prima facie* evidence of negligence was such that the case should be referred to the courts for trial. Or it might act as a court of law, hearing all evidence, deciding whether there was negligence, and assessing damages where appropriate. Such a tribunal might meet in private or be open to the public. If the latter it would differ in no essential respects from the courts.

Finally, it would not be impossible for the issue of negligence to be taken out of the case entirely and to make the liability strict. Patients attend hospital for help and treatment. They expect to obtain benefit from this, and if they do not obtain it they may feel aggrieved and think that they should receive recompence for this failure. The tribunal could be given power to award compensation—either as a lump sum or on a fixed scale—regardless of the cause of the failure and who was responsible.

CONCLUSIONS

When preparing this paper we consulted a number of people, including lawyers, both practising and academic. In our opinion drastic changes in the law are not indicated, and we believe that the use of medical assessors by the courts, the limitation of the numbers of expert witnesses, and a reasonable degree of restraint in the publication of medical evidence, would go far to improve the present position.

The laws of England are the results of the wisdom of centuries of judicial decisions, and in respect to negligence they are on a sound footing. What seems necessary today is not so much that the law of negligence should be changed, to suit the medical profession and the hospitals, as that medical students should be taught, and members of the medical profession have a sound understanding of, the law relating to negligence, and how negligence can be avoided.

One of the foremost ways by which a complaint of negligence may be avoided is to take the patient fully into confidence. A patient may enter hospital, and pass from one member of the staff to another, but still have little or no idea what the examinations and procedures are leading to. Nor is he always made to appreciate that some of the procedures are not devoid of risk, that the result may not be as anticipated, or that some unforeseen event may occur. If the significance of all that is taking place is explained to him and his consent obtained the risk of an action for negligence is greatly diminished. It may of course be argued that the explanation is not in the patient's interests—that if he is given too many details he will have cause to worry

and his condition will thus be made worse. But if the explanation is given in a reasonable way there can be no grounds for complaint; for "reasonable" is a word which is used frequently in connection with actions for negligence.

"Every person who enters a learned profession undertakes to bring to the exercise of it a reasonable degree of skill. He does not undertake, if he is an attorney, that at all events you shall gain your case; nor does a surgeon undertake that he will perform a cure; nor does he undertake to use the highest degree of skill. There may be persons who have higher education and greater advantage than he has; but he undertakes to bring a fair, reasonable and competent degree of skill." * This dictum must apply to all; there can be no exception in the case of members of the medical profession, who should bear in mind, in respect of negligence, *Punch's* advice to those about to marry.

USE OF ANTIMALARIAL DRUGS

Recommendations by Malaria Subcommittee of Colonial Medical Research Committee

In 1949 the Colonial Medical Research Committee drew up recommendations on the use of 'Paludrine' (proguanil) in suppression and treatment of malaria; these were tentative on the basis of knowledge available at the time and were stated to be subject to revision in the light of future experience and experiment. The additional experience since gained makes it advisable to revise the recommendations and also to indicate the suitable methods of use of the different antimalarials now available. The revision is specially necessary in view of the further evidence which has been obtained that (a) some drugs which are effective in suppression of malaria are unsuitable for use in the treatment of the overt attack owing to their slow schizontocidal action, and that (b) the unsuitable use of certain antimalarials for suppression or for treatment of the overt attack may result in the development of drug-resistant strains of the malaria parasites.

Actions and Uses of Antimalarial Drugs

No single drug at present available is effective against all phases of the cycle of development of the malaria parasite; the preparation to be used for a particular purpose will be that active against the appropriate phase. The purposes for which antimalarial drugs are used are:

1. For causal prophylaxis or suppression (destruction of the parasite in the pre-erythrocytic phase or in the asexual erythrocytic phase).
2. For treatment of the overt malarial attack (destruction of the asexual parasites in the blood-stream).
3. For radical cure of vivax and quartan malaria (destruction of the late exo-erythrocytic forms).
4. For prevention of transmission (destruction of the gametocytes in the peripheral circulation or interruption of sporogony in the mosquito).

CAUSAL PROPHYLAXIS OR SUPPRESSION

The onset of a clinical attack of malaria can be prevented either by a drug acting on the pre-erythrocytic forms of the parasite (causal prophylaxis) or by one acting on the asexual erythrocytic forms (suppression).

(1) *Causal prophylaxis*.—The 8-aminoquinolines (pamaquin, primaquine) show such action, but the margin between the prophylactic and the toxic dose is too narrow to permit of their use for this purpose. The only drugs which can achieve this effect with safety are the biguanides (proguanil) and the diaminopyrimidines (pyrimethamine): their action in this respect is definite

4. Per Tindall, C. J. In Lanphier and wife v Phipps (1838) 8 Car & Payne 474.

as far as falciparum infection is concerned. Since however they act also on the asexual erythrocytic forms of all species of human plasmodia their use as protective drugs is by no means confined to falciparum infections.

(2) *Suppression*.—Drugs used for suppression show the following characteristics, advantages, and limitations.

Quinine, formerly widely used for this purpose, has several disadvantages. For the effective suppression of falciparum malaria, it may have to be taken in doses as high as gr. 10 daily, and in New Guinea even this dosage has proved insufficient. Apart from the unpleasant side-effects which may arise from prolonged administration of this amount of quinine, its association with the precipitation of blackwater fever makes it unsuitable for use as a suppressant in areas where falciparum infections are prevalent.

Mepacrine is a very effective suppressant of all forms of malaria, but has certain disadvantages which detract from its usefulness. When taken over long periods it sometimes produces skin lesions, the most common of these being a lichenoid dermatitis. Yellow discolouration of the skin, a usual feature, is a further disadvantage.

Chloroquine and *amodiaquine* are probably even more powerful suppressants than mepacrine. Their action resembles that of the last-named drug, but they are on the whole less toxic and they do not tint the skin.

Proguanil and *pyrimethamine*, as well as being causal prophylactics in falciparum infections, are effective suppressants of all forms of malaria. They also have the advantage of preventing the completion of sporogony and of being considerably less costly than the 4-aminoquinolines. There is, however, a possibility that drug resistance may appear in areas where either of these compounds is in common use, particularly if they are employed indiscriminately as therapeutic agents, though proven examples of this are very rare. Cross-resistance has been shown to exist between proguanil and pyrimethamine, so that if resistance to either of them becomes apparent a switch-over to chloroquine, amodiaquine, or mepacrine is indicated; or, if none of these is available, to quinine.

TREATMENT OF THE OVERT ATTACK¹

(1) *In non-immune subjects*.—For this class of patient it is necessary to employ one of the more powerful schizontocidal drugs, such as chloroquine, amodiaquine, mepacrine, or quinine.

Quinine has the disadvantage of its association with the precipitation of blackwater fever, and is comparatively ineffective against certain strains of malaria parasites. It cannot be relied upon to effect radical cure of infections with some strains of *P. falciparum*.

Mepacrine has a rapid action in all forms of malaria, but minor toxic manifestations and occasional psychoses of a more serious nature are definite drawbacks. The yellow tinting of the skin sometimes produced is also undesirable.

Chloroquine and *amodiaquine* are probably the most effective agents for terminating the clinical attack, and toxic manifestations of a serious nature are rare with either drug.

Neither proguanil nor pyrimethamine are sufficiently rapid in action to warrant their use in the treatment of malaria in non-immune subjects.

(2) *In subjects partially immune*.²—For the dispensary treatment of partially immune populations of malarious countries, a single-dose treatment with chloroquine, proguanil, amodiaquine, or mepacrine has proved effective. Good results have also been reported with pyrimethamine given as a single dose. In view of the possibility of drug resistance arising with both proguanil and pyrimethamine it seems wiser to reserve these drugs exclusively for prophylaxis and suppression and to use for therapeutic purposes chloroquine, amodiaquine, mepacrine, or quinine. If quinine is used, 2–5 days' treatment is usually necessary.

(3) *For emergency treatment*.—In the treatment of pernicious forms of malaria, whether cerebral, algid, or gastro-intestinal, oral administration of drugs is seldom

1. As a general principle in areas where drug prophylaxis or suppression is in operation, a different drug should be used for treatment of the clinical attack.

2. i.e., The indigenous inhabitants of malarious regions.

practicable; and since prompt action is necessary to save the patient's life, antimalarial drugs must be given parenterally in such cases. Quinine dihydrochloride intravenously has been a standard and successful treatment for many years. Mepacrine methane sulphonate may be given intramuscularly as an alternative. Recent work indicates that chloroquine is equally successful when given intramuscularly or intravenously. The intramuscular injection of quinine, still widely practised in many countries, has the disadvantage that it causes necrosis and may produce abscess. Whatever is used, as soon as the patient is able to take drugs by the mouth, all further medication should be by this route.

RADICAL CURE

(1) *Vivax and quartan malaria*.—The only drugs which are effective against the late exo-erythrocytic forms of the parasite are the 8-aminoquinolines. Pamaquin has been used for this purpose for many years, but recently primaquine has been shown by American workers to be more effective and less toxic. If an overt attack is in progress standard treatment with a schizontocidal drug should precede or accompany the course of pamaquin or primaquine.³ This combined treatment is also applicable when falciparum malaria occurs in association with vivax or malariae infections. Treatment of chronic relapsing malariae (quartan) infections is the same as for vivax cases.

(2) *Ovale malaria*.—Many infections with *P. ovale* end in spontaneous recovery. Treatment with 8-aminoquinolines is not usually necessary.

(3) *Falciparum malaria*.—There is convincing evidence against the existence of late exo-erythrocytic forms of *P. falciparum*. Any relapses that may occur are due to the persistence of erythrocytic forms. Any of the more powerful schizontocides mentioned above will usually effect radical cure.

PREVENTION OF TRANSMISSION

The 8-aminoquinolines are the only drugs which are able to destroy the sexual forms of *P. falciparum* in the peripheral blood. Proguanil and pyrimethamine have no demonstrable action on the gametocytes in the blood, but both have the property of preventing them from undergoing full development in the mosquito, so that mosquitoes feeding on patients taking either of these drugs are unable to transmit the disease to others.

Suggested Dosage

Unless otherwise stated the dosage suggested is for adults. That for children should be calculated according to age and weight.

CAUSAL PROPHYLAXIS AND SUPPRESSION

(i) *Proguanil monohydrochloride*.⁴—Adults, 100 mg. daily. Children, 0–5 years, 25 mg. daily; 6–12 years, 50 mg. daily. Adults partially immune, 300 mg. once weekly. Or

(ii) *Pyrimethamine*.—Adults, 25 mg. weekly. Children, 0–5 years, 6·25 mg. weekly; 6–12 years, 12·5 mg. weekly. Or

(iii) *Chloroquine diphosphate or sulphate*.—Adults, 300 mg. base weekly. Or

(iv) *Amodiaquine dihydrochloride dihydrate*.—Adults, 400 mg. base weekly. Or

(v) *Mepacrine hydrochloride*.—Adults, 100 mg. daily. Adults partially immune, 300 mg. once weekly. Or

(vi) *Quinine sulphate or dihydrochloride*.—Adults, 650 mg. (gr. 10) daily. Recommended only when none of the drugs listed above is available.

No suppressive regimen will be effective unless followed with the utmost regularity.

3. Mepacrine should not be given concurrently with any of the 8-aminoquinoline drugs.

4. In parts of Africa the scale of dosage for proguanil given above has been found insufficient; in Nigeria, for example, the following scale has been recommended: Adults, 100–200 mg. daily. Children, 0–1 year, 50 mg. three to six times weekly; 1–3 years, 50 mg. daily; over 3 years, 100 mg. daily.

In the case of persons who have been resident in an endemic area for some time, or who have otherwise been exposed to malaria infection, a full therapeutic course should be taken before entering on a suppressive regimen, if there are grounds for suspecting active or latent falciparum malaria.

If mepacrine is the drug employed, administration should be commenced 14 days before entering an endemic area. Administration of the other drugs should be commenced immediately before entry.

If the drug used is not affording protection in the dosage recommended, when taken regularly, a change should be made to another suppressive.

The prophylactic regimen should be continued for one month after leaving an endemic area.

TREATMENT OF THE OVERT ATTACK

(1) For non-immune subjects :

- (i) *Chloroquine diphosphate or sulphate* 600 mg. base, followed in 6 hours by 300 mg. base, then 300 mg. base daily for 2 days. Or
- (ii) *Amodiaquine dihydrochloride dihydrate* 600 mg. base, followed by 400 mg. base daily for 2 days. Or
- (iii) *Mepacrine hydrochloride* 300 mg. t.d.s. on first day, 300 mg. b.d. on second day, then 100 mg. t.d.s. for 5 days. Or
- (iv) *Quinine sulphate or dihydrochloride* 650 mg. (gr. 10) t.d.s. for 7–10 days.

(2) For subjects partially immune :

- (i) *Chloroquine diphosphate or sulphate* 600 mg. base in single dose. Or
- (ii) *Amodiaquine dihydrochloride dihydrate* 600 mg. base in single dose. Or
- (iii) *Mepacrine hydrochloride* 300–500 mg. in single dose. Or
- (iv) *Quinine sulphate or dihydrochloride* 1000–1500 mg. (gr. 15–20) daily for 2–5 days.

(3) Emergency treatment :

- (i) *Quinine dihydrochloride* 650 mg. (gr. 10) in sterile normal saline injected intravenously and repeated in 6 hours if necessary. Not more than three injections should be given within 24 hours. Distilled water can be used as a solvent if the volume does not exceed 10–15 ml. It is imperative that quinine be injected slowly, at a rate not exceeding gr. 1 per minute. Or
- (ii) *Mepacrine methane sulphone* 375 mg. or *mepacrine hydrochloride* 300 mg. intramuscularly, repeated in 6 hours if necessary. Or
- (iii) *Chloroquine salts*.—The *hydrochloride* is given intramuscularly in dosage of 200–300 mg. of base (supplied in ampoules in aqueous solution), repeated in 6 hours if necessary; and intravenously, 400 mg. of base in 500 ml. normal saline by intravenous drip over a period of 1 hour. The *sulphate* supplied in 5 ml. ampoules (40 mg. base to 1 ml.) is given, in dosage of 200 mg. base intravenously, repeated after 8 hours if necessary.

RADICAL CURE OF VIVAX AND QUARTAN MALARIA

(i) *Pamaquin naphthoate* 8–10 mg. base t.d.s. for 10–14 days. Or

(ii) *Primaquine diphosphate* 15 mg. base daily for 14 days, or 7 mg. thrice daily for 14 days.

During an overt attack a course of treatment with a schizontocidal drug must also be given. This applies also when falciparum malaria is associated with either a vivax or a malariae infection. Some authorities include treatment with a schizontocidal drug even though no active symptoms are apparent.

Careful supervision is necessary over patients taking any of the 8-aminoquinoline drugs, because of the occasional unpredictable occurrence of acute intravascular haemolysis with or without haemoglobinuria.

NOTES

Each 261 mg. tablet of *amodiaquine dihydrochloride dihydrate salt* contains 200 mg. of base.

Each 250 mg. tablet of *chloroquine diphosphate* salt contains 150 mg. of base.
 Each 200 mg. tablet of *chloroquine sulphate* salt contains 150 mg. of base.
 Each 100 mg. tablet of *mepacrine hydrochloride* contains 79 mg. of base.
 Each 375 mg. ampoule of *mepacrine methane sulphonate* is equivalent to 300 mg. of *mepacrine hydrochloride*.
 Each 18 mg. tablet of *pamaquin naphthoate* or 10 mg. tablet of *pamaquin dihydrochloride* contains 8 mg. of base. For practical purposes 2 naphthoate = 1 base = 1 dihydrochloride.
 Each 13·2 mg. tablet of *primaquine diphosphate* contains 7·5 mg. base.
 Each 100 mg. tablet of *proguanil monohydrochloride* contains 87 mg. base.
Pyrimethamine is prescribed in the form of base, not as a salt.

Antimalarial Drugs and their Synonyms

Amodiaquine
 Cam-aq1, Camoquin, Flavoquine, Miaquin, SN 10751.
Chloroquine
 * Aralen, † Nivaquine B, Resochin, Tanakan, SN 7618, 3377 RP.
Mepacrine
 Acrquine, Arichin, Atabrine, Atebrin, Atebrine, Chemicochin, Chinacrin, Crinodora, Eriol, Haffkinine, Italchina, Malaricida, Methoquine, Metoquina, Palusana, Quinacrine.
Pamaquin
 Aminoquin, Beprochin, Fourneau-710, Gamefar, Pamaquine, Plasmochin, Plasmocide, Plasmoquine, Praequine, Quipenyl, Rhodoquine.
Proguanil
 Balusil, Bigumal, Chlorguanide, Chloriguane, Diguanyl, Guanatol, Paludrine, Palusil, Tiran, M 4888, SN 12837.
Primaquine *Purimethamine*
 SN 13272. B-W 50-63, Daraprim, Malocide.
 * Aralen is *chloroquine diphosphate*.
 † Nivaquine B, or Nivaquine, is *chloroquine sulphate*.

Reconstruction

AN EXPERIMENT IN FAMILY PRACTICE WITHIN THE NATIONAL HEALTH SERVICE *

F. CHARLOTTE NAISH
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DURING the past 6½ years I have been adding "extras" to my general practice in an attempt to make it truly a family practice.

The practice is mainly urban. 80% of the births are attended by me or my partner, either in the mother's home or in nursing-homes. An antenatal clinic is held at a separate time from the ordinary surgeries and the mothers are encouraged to attend monthly or at shorter intervals. During the past 2 years my partner has held a relaxation class once a week at which she gives instruction in antenatal and postnatal exercises; most of the primiparae and a few multiparae attend. Once a week we hold a clinic for mothers and babies only. A health visitor employed by the local authority attends to weigh the babies, and her advice is useful in sorting the cases for consultation. Before this the mother and baby (hospital cases as well as our own) are visited at home, and the baby is weighed with portable scales. It is usually sufficient to visit twice in the third week and then once weekly to the sixth week. Birth-control advice is offered at the postnatal examination, and, if it is wanted, the mother returns at an appointed time in the evening when she can leave the baby at home. She buys her own appliance, but no charge is made for the fitting and for the advice given.

For 4 years there has been a well-attended mothers' club, and a smaller, but equally enthusiastic, fathers' club. Here an attempt at health-education in its broadest sense is made and the talks and discussions have covered a wide range from infant care to juvenile delinquency. Here also the mothers are taught the early signs of illness, when to send for the doctor, how to nurse a sick child at home, how to prepare a child for admission to hospital, what a child-guidance clinic is for, and much else which improves the mother-child-doctor relationship. The fathers discuss many topics arising out of their

* From a lecture delivered at Oxford (Medical Consilia) on Oct. 15, 1953, and before the Caernarvonshire Paediatric Club on Oct. 22, 1953.

Year (July-July)	Population of practice	Children under 11 years	Births	Birth-rate per 1000 patients	Birth-rate for York	Admissions of children under 11 years to hospital						Deaths under 1 year	
						Casualty	Surgical	Tuberculosis	Tonsils and adenoids	Medical			Deaths under 1 year
1	2	Total	%							1	2	Total	
1948-49	3500	530	58	16·6	18·4	..	8	1	6	1	12	13	2·6 0
1949-50	3450	570	58	16·8	17·3	1	7	..	6	5	4	9	1·6 1
1950-51	3350	625	62	18·5	15·8	3	3	1	3	2	5	7	1·1 1
1951-52	3280	690	67	20·4	14·6	5	4	..	2	2	4	6	0·9 1
1952-53	3200	760	72	22·5	14·2	3	5	1	3	1	2	3	0·4 1

particular home problems and the wider issues of good citizenship. In doing so they get a better view of the mothers' difficulties and learn how they can enjoy giving help with the family problems.

It would seem obvious that such an attempt at family practice should give good results; but those results are hard to measure. How can one measure health? How can one measure the mental good-health of a family as a whole?

It occurred to me that there was at least one measurable index, and that was the non-admission to hospital of children with medical complaints which could be treated at home.

In the accompanying table, patients under "medical 1" were admitted as medical cases: those under "medical 2" were admitted as query-surgical cases and the diagnosis was proved incorrect.

Other notes on the table are:

1. Among the casualties admitted there was not one case of burns or scalds.
2. The tuberculosis cases consisted of two patients with mild general symptoms and positive Mantoux tests and a third with tuberculous meningitis, who recovered. (He reached hospital 5 days after the onset of malaise.)
3. The following are omitted from the table altogether:
 - (a) Three inevitable deaths (one leukaemia, one aplastic anaemia, and one sarcoma).
 - (b) Six cases of poliomyelitis (no deaths).
 - (c) All fever-hospital cases. All these were cases of scarlet fever, and admission to hospital was determined by the father's occupation, not by the wish of the mother or doctor. Where the father worked with food, home nursing was not allowed.
4. Of the infants who died, three were premature babies under 3 lb. in weight, two of these being twin births. All these were born in hospital. The fourth death was from whooping-cough in a twin of 7 weeks, birth-weight 5 lb.
5. The birth-rate has risen during the 5 years, and the number of children under 11 has risen apart from the increase by births. The practice population, on the other hand, has fallen, mainly because of re-housing on outlying estates and because of the N.H.S. "purge" of lists.
6. The number of children under 11 (this arbitrary limit has been chosen because I have been in York 11 years) is a poor estimate of infant deaths. No practice is ever static, and in a period as long as 12 months there is considerable movement of people. The average for the year has therefore been estimated; but the estimate (checked by two methods) is, I hope, fairly reliable.
7. For each year the expected number of infant deaths, calculated from the infant-mortality rate of the city, is between 1 and 2. So the actual deaths do not suggest that the reduced admissions to hospital have involved any added risk to the infants. Apart from the inevitable deaths mentioned above (3a) there have been no deaths among children more than a year old.

CONCLUSION

I think it would be fair to conclude that there have been some gains to the child patients. It would appear that their mothers are growing more capable of sending for the doctor in the early stages of illness, when the

condition can be treated at home, and also that they are managing to nurse them at home effectively.

To the doctor there appears to be a loss, at least as far as the first 5 years show. I have done more work than the N.H.S. demands, without increase of income. It may be that this work will pay a good dividend in healthy families in the future, but it seems unlikely that an unenthusiastic doctor would take it on without some financial inducement. As the duty of paying a doctor for preventive services rests at present on the local authorities, the Ministry of Health will naturally hesitate to offer such an inducement the cost of which will fall on the general medical services.

The Widdicombe File

XII. DOWN IN THE REGION

Underwater Hospital,
Underwater.

DEAR SIR DANIEL,

I am sending you, as you request, a summary of our findings in John Jones, aged 3. Biopsy shows that he has a Wilms tumour with extensive secondaries, and is beyond our aid. His end cannot be far off, and I only hope it gives his parents some comfort that he should die in a teaching hospital rather than with us. Mrs. Jones took him out of Underwater against our advice, and was rather unpleasant about the whole thing. She is convinced that you will know some new treatment that we have never heard about, and in her distraction I can forgive her anything; but she is only an example of an attitude of mind that is quite widespread down here. It is simply that when we cannot give a good prognosis and assure a rapid cure, the children are removed to London. Even if we offer them a second opinion they refuse it, for their one object is to get the child under a London consultant and be shot of us. Of course our diagnoses are sometimes wrong, and even more often we are completely foiled, but I find these are the cases we ourselves refer to you, and we are grateful for your help.

There is no mystery why parents do these things, and who can blame them if you and your hospital are famous and we are not. Lack of fame is not necessarily synonymous with ignorance or incompetence, but the public nevertheless believes that nothing later than Hippocrates has percolated down our way. Maybe there is an element of truth in it, but I am certain it is not the whole explanation, which is much more fundamental. Unfortunately we work in hospitals with a past, and we suffer a visitation of "the iniquity of the fathers upon the children unto the third and fourth generation of them that hate me."

* * *

Before the National Health Service started, the hospitals now administered by regional boards either were voluntary or belonged to the local authority. The former certainly had the voluntary spirit, and radiated the local pride which kept them going; but the staff were mostly general practitioners, and the ancillary services such as pathology and radiology not infrequently somewhat primitive. They could and did deal perfectly adequately with the routine stuff, but anything more difficult was sent to London. The local-authority hospitals lacked not only the voluntary spirit, but only too often the human touch as well. They had their origins in "The Workhouse"; and as a matter of fact the older inhabitants round here still refer to Underwater as "The Union." With the passage of time, the medical work grew and the workhouse shrank; so the name was changed from workhouse to hospital; but just as when the Rat-catcher became the Pest Officer, the change of title made no difference to the function. These so-called hospitals were managed by the public-assistance depart-

ment with its poor-law outlook; and though later on (in our case very much later on) the public-health department took over, they had neither the time nor the money to do much about it.

I first came to Underwater in 1939 with the E.M.S., and to one who had been nurtured in the gentle atmosphere of a teaching hospital it was horrifying. The buildings, with few exceptions, were bare and barrack-like, with the patients crowded in to overflowing. The nursing staff was insufficient and inefficient, and the male orderlies both callous and brutal. One sensed that the inmates were there to die and were expected to coöperate by not taking an unconscionable time about it. Can you wonder that its reputation stank for miles around, and that nobody would go there until he was unconscious or too weak to protest?

The E.M.S. changed all that, and the N.H.S. has improved things even more. The buildings were modernised and equipment flowed in. The original nursing staff departed in toto, without mourning or regret; and, though we are still desperately short of nurses, what we have are not bad. The medical staff, which in 1939 consisted of five general-duty officers, is now fourteen consultants, all properly qualified and trained, and ten residents. We have fewer patients to care for than in the bad old days. The pathological side of our service could and should be improved; for, though the quality is excellent, the quantity is too small. In London you have bacteriologists, biochemists, haematologists, histologists, and morbid anatomists, each with assistants and technicians, whereas at Underwater there is one pathologist and a few technicians who have to cope with all our work. This staff must be increased, and I hope that nobody will try and substitute an area central laboratory in its place. Such an institution is like a sausage-machine, with material going in at one end and results emerging at the other; and the results, like sausages, are often of dubious quality. We must be able to discuss our problems with the pathologist, so that both sides can know the extent of their limitations. This is particularly important in paediatrics, where biochemistry now looms so large; but Underwater is like Hamlet without the Prince of Denmark, for no biochemist walks our stage.

The deficiencies I have mentioned are fortunately not crippling, and in spite of them we are both competent and equipped to deal with most of the problems that confront us. We should have gained the confidence of our patients, and to a large extent we have; but memories of the past still lurk in too many minds. The public is not to blame, because nobody has ever told them of the changes that have been brought about in their hospitals. They can see the new chairs and the canteen in outpatients, but how are they to know the ability or training of Dr. A as compared with Dr. B? They cannot judge whether an X-ray film is good, bad, or indifferent—much less the value of the radiologist's report on it—and the whole working of the pathology department is entirely outside their ken. I think it would help if they were enlightened on these matters.

* * *

If then our need is publicity and propaganda, no opportunity is lost to see that we don't get it, and in fact the only time we are likely to get in the news is if somebody brings an action against us for negligence or some cataclysmic disaster befalls us. Our day-to-day work is unknown. Take television as an example. There have been two programmes depicting hospital life—both of them to my mind nauseating, but let that stand. The important thing is that they featured teaching hospitals, when one of them at least could have dealt with Underwater. On another occasion there was a film showing a coloured nurse undergoing her training at the Middlesex Hospital, afterwards returning home to

disseminate her knowledge. This was grossly unfair, because I am sure that most coloured nurses don't train at teaching hospitals, and if you met one in Central Africa she would more likely be familiar with Underwater than the Middlesex.

Another thing that would help us would be some visits from V.I.P.s. The press notices and photographs that go with them catch the public eye, and they rightly feel that a hospital worthy of such a visit can't be too bad. I do not forget that we ourselves must take a hand in the matter, and not expect everything to be done for us. My one experience in this line was quite encouraging, for I managed to get a small article and a photograph of one of our patients in a national daily. Quite a lot of local people saw it, and subsequently some of our ex-nurses and residents sent us reproductions that they had cut from their local newspapers in Australia, South Africa, Germany, and South America. I admit that this is only small stuff, and that for a major effort we shall require the help of the Ministry of Health; but, as they have nothing to be ashamed of, they shouldn't be too difficult to stimulate.

Do you think we could make this a co-operative effort? —because so far the teaching hospitals have been ivory towers, with little knowledge of what goes on around them. Our professional lives are widely affected by advice given and decisions made by the teaching hospitals, and we would accept this more readily if we thought you knew a little more about us.

Yours sincerely,
JAN STEWART.

Parliament

QUESTION TIME

Honourable Care of Aged

Sir WALDRON SMITHERS asked the Minister of Health if, in view of the high cost of maintenance of old patients in hospitals and of the shortage of nurses, he would consider the advisability of setting up a committee to inquire into the practicability of making an all-in payment to relatives or friends willing to take chronic cases into their homes.—Mr. IAIN MACLEOD replied: I do not think it would be feasible to introduce arrangements of the kind contemplated. Apart from the fact that sometimes it would not be in the interest of patients to be cared for at home, there is already provision whereby, in suitable cases, financial assistance could be sought from the National Assistance Board.

W.H.O.'s Budget

Replying to a question, Mr. MACLEOD said that the proposed increase in the World Health Organisation budget involved additional expenditure of about 1,800,000 dollars. The United Kingdom delegation was authorised to agree to an increase of about 1 million dollars but to oppose the further increase on the ground that it was attributable to projects which should be financed through the expanded programme of technical assistance.

Pay Beds

Replying to a question, Mr. JAMES STUART, Secretary of State for Scotland, said that about a quarter of the hospital beds for private patients in the Scottish Western Region were unoccupied, on the average, during the latest period for which figures were available. This represented about 100 beds scattered over 33 hospitals. He did not think that 100 beds vacant in 33 hospitals was a large number. There were always gaps whether for paying or non-paying patients between the discharge of one patient and the admission of another.

Dentists in the Forces

Replying to a question, Mr. E. N. C. BIRCH, parliamentary secretary to the Ministry of Defence, said that 512 qualified dentists were at present serving in the Armed Forces—97 were in the Royal Navy, 250 in the Army, and 165 in the Royal Air Force.

In England Now

A Running Commentary by Peripatetic Correspondents

I AM no good at gardening but I do enjoy trimming my privet hedge; for this humble occupation gives me a chance to turn philosopher. My hedge, with its uniform structure, its growth and decay, its activity and rest, its stability and change, is not unlike society. For instance, this cheeky twig, overtopping his fellows, reminds me of the human unit who shoots out his neck and tries to get the best of everything. Here is the woman who jumps the queue; the arrogant, flamboyant man who has got on; the nasty kid who is always shouting "Me first"; the aggressive, swaggering individual that no one can curb. Here to my hand are the bombast, the snob, the upstart, the cheat. Snip, snip, go my shears; and heads drop around me in my gigantic purge, giving the hedge a mathematical seemliness and my soul an artistic satisfaction.

"But," occasionally says my better self, "that may be a genius and should be preserved." Then I have an argument with myself, generally coming to the conclusion that genius is so rare that it is most unlikely to be found in any social structure or privet hedge of my acquaintance, and that my first diagnosis of swanky selfishness has more chance of being correct. In any case, a genius usually fills a gap, and is never quite the saucy twig I have in mind but rather the strong, resolute shoot which, in the old days, our forbears left here and there in our country hedgerows to greet us now as tall, well-spaced trees.

"But what about back pruning?" you may ask. Of course I haven't forgotten that. All too well I know the chunks of dead wood and the dead-alive branches that keep interfering with the clamant new growth, twisting and deforming active twigs into roundabout ways and leading to the deterioration of the hedge. Their social counterparts are the miserly curmudgeon of an old man; the enslaving, demanding old woman; the frustrated "youngsters" of 45 and more whose lives have been given up to mum and dad. Snip, snip, go my secateurs; for it is a tricky job dealing with the aged things that in their day contributed to the hedge which is now my delight; and I have abandoned the shears for more kindly treatment. Here one must ever be careful not to injure the solid living wood that gives to the hedge its substance and permanence—the wisdom and stability of its long heritage.

"But what a terribly uniform, uninteresting society you are going to make," you may say. Well, perhaps you're right. But I've got a jolly nice hedge.

* * *

"Where are the children?" asked my wife. "I left them in the department in the animal house. There are some new baby rabbits. I expect they will be back in a few minutes" I answered. But the minutes ticked on to something over an hour. "I wish you would go and see what they are doing, it's getting dark and they may be frightened."

Recognising the finality of the situation, I got up and went across to the department. The noise of my footsteps going up the stairs was an "indifferent stimulus" for the conditioned response of the guineapigs, and I opened the door of the animal house to a crescendo of squeaks. The children were not there.

Down the stairs again and I switched on the lights in the museum. Still no sign of them, but I could hear them. Quietly I looked into our long dissecting-room. There they were: George (11) and Catherine (10), the light on over a table, white sheet turned aside. "Don't be silly, George, the heart is not down there, it's up here." Catherine was always the quick one. "What's this, then?" asked George. From the distance it looked like the spleen. "I don't know. Do you think this is the liver? It's not like the liver Mummy gets from the butcher, it's hard." I walked over and sat down beside them and told them about the contents of the open abdominal and thoracic cavities.

Dislike for the "dead" does not appear to be an inherited characteristic. The female tremor of distaste and the hearty male laugh—symptoms of the adult taboo—are obviously an acquired reaction. Is it wholly

mimetic, simply a convention; or has it deeper roots as far back as our troglodytic ancestors who initiated the practice of burying their dead?

* * *

Sarah Milicent Brown lived in a small, terraced house, in a grim and sordid suburb of a northern city. She was cared for by an only daughter who was an albino, and who had been given, by some waspish twist of fate, the name of Blanche. This poor girl, who could not bear the light, moved about the darkened house like some pale spectre of the night. When I saw the old lady for the first time in 1953, she had already been bedridden for five years following a stroke which had left her paralysed.

She was in perpetual dread of draughts. The window of her bedroom was permanently closed and the heavy curtains drawn. The chimney was blocked by a mass of crumpled paper, and a small tongue of leather was attached to the key-hole to stifle the piping of the wind. Heat was supplied by a fuming oil-stove and light by a bracketed gas-jet, which spluttered fitfully in the choking atmosphere and did little more than trouble the gloom.

When I opened the door on my first visit, it took me some time to accustom myself to the dark, but as soon as I could see I went over to the curtains and drew them aside. For the first time in five years daylight flooded the bedroom. And then I threw open the window and took a long breath. Sarah Milicent Brown eyed me from her bed with a look of intense dislike and, in a voice surprisingly firm for an invalid, commanded me to shut the window at once. I was about to protest when Blanche, who had followed me silently into the room, slipped behind me and brought the window down with a bang as though the air outside had been thick with contagion. I realised I had committed a grievous offence, and it took me two years of patient visiting to regain the old lady's favour—two years and many more to follow with the curtains drawn and the window tightly sealed.

On the night of Nov. 5, 1953, the noise of fireworks in the street had made her fretful and sleepless, and Blanche had called me in to give her something to calm her down. I was groping around in my bag for my syringe when she leaned over and plucked at my sleeve and said :

"What kind of a night is it?" It was the first time I had known her to inquire about the world outside her room.

"Dark and foggy—you're better here in your bed." I thought she smiled—but in the dim and lurid light it was impossible to be certain.

"You may open the window, now, doctor."

I drew the curtains slowly and hesitated; but she nodded approval, so with difficulty, for it was stiff with disuse, I forced the window wide open. A thin November fog, acrid with the smell of gunpowder, trailed into the airless room. And when I turned round she was dead.

* * *

REACTIONS OF A MORBID ANATOMIST TO MAKING THE ACQUAINTANCE OF THE KAUFFMANN-WHITE SCHEME

I'm sure when White and Kauffmann wrote their Salmonella scheme

They little thought that they'd composed the poetaster's dream.

Who minds anaerogenesis or antigenic loss?

There's consolation in the sound of names like *Hvittingfoss*.

While *morehead* dreams of *poona*, with *havana* and *champaign*,
I drive uphill from *nottingham* with *thompson* in the rain.
We'll stop and have a *worthington* in *shipley* on the way
We'd have made it a *manhattan* had it been a *desundai*.

My mission will require me fly out to *kaapstad* soon
By *napoli* and *cairo* through an *equatorial* noon.

Mendoza, old *hidalgo*, will put on his *panama*

And join me in *nairobi*—then it isn't very *pharr*.

Aunts *adelaide* and *berla* will enjoy the *eastbourne* sun

An infant is quite happy with *banana*, *ball* and *bun*.

Let *hindmarsh* take *madelia* in his *austin* to *Dunoon*,

But give me *loma linda* and a *pensacola* moon!

Before the *Salmonella* lose their eponymous names

(*Way cross the wide missouri* and to *georgia* away!)

Ere *Arab* numerals replace the *Roman* ones, who blames

A london salmonellogist who *sanga* little lay?

Letters to the Editor

RAUWOLFIA IN HYPERTENSION

SIR.—The search for hypotensive drugs of low toxicity, and especially for those which are effective when given orally, has given rise to considerable interest in alkaloids from the root of *Rauwolfia serpentina*. Reserpine has been shown to have such a hypotensive action. The most recent communications, by Dr. Doyle and Professor Smirk, and Dr. Joiner and Dr. Kauntze (May 29), prompt me to send this note on results obtained in a small series of hypertensives.

Twelve patients suffering from chronic benign hypertension have been treated with reserpine ('Serpasil'). All were known to have had symptoms of high blood-pressure for five years or more. All presented secondary cardiovascular changes. In two there were retinal haemorrhages and exudate. The lowest blood-pressure recorded after a week's rest was 210/120 mm. Hg, the highest 250/160.

Each patient was kept in bed for the first week but allowed up for visits to the lavatory and bath. No restrictions were placed on diet. No drugs were given except for constipation or insomnia. The blood-pressures were recorded not less than four times daily, and if a daily variation of more than 20 mm. Hg systolic or 10 mm. Hg diastolic occurred during the last two days of the week, treatment was postponed until greater stability was established. Once it was started the patient was encouraged to lead a more active life, walking about the ward or in the grounds of the hospital.

At first the makers' recommended dose of 0.25 mg. four times daily was given, but it was soon apparent that no hypotensive effect was thereby achieved. Subsequently the amount was raised to 1 mg. four times daily, and, if ineffective, this quantity was doubled. In only one instance was as much as 16 mg. daily given. This dose had to be abandoned on account of dizziness and drowsiness unaccompanied by an appreciable fall of blood-pressure.

As to results, in two patients no effect on hypertension was produced by 16 and 8 mg. doses daily. In a further two a daily dose of 4 mg. resulted in a sustained reduction of systolic pressure by 30–40 mm. Hg and of diastolic pressure by 10 mm. Hg. The remaining eight patients required 8 mg. daily to achieve this or greater effect.

By far the most striking result is to be seen in the systolic pressure readings. A heart-rate of between 50 and 60 is usually noted within 3 days after treatment is started. There is no relationship between the slowness of the heart and the effect on blood-pressure.

Drowsiness and dizziness affected all patients on 8 mg. daily, but passed off in some after a few days. Of the twelve cases two developed pronounced tremor within 24 hours when the dose was raised from 4 to 8 mg. daily. This was of coarse type, accompanied by occasional twitching of the limbs, chattering of the teeth, and mental distress. On halving the dose the tremor disappeared. I have not encountered the pruritus described by Joiner and Kauntze.

It seems probable that reserpine will be of some value in the treatment of benign hypertension, but close supervision is needed. It is possible that lower doses in conjunction with other hypotensive drugs will be more effective. This is being studied. For the intelligent patient no substitute has as yet been found to equal hexamethonium bromide, self-administered parenterally.

London, W.1.

A. H. DOUTHWAITE.

ARTHOPLASTY v. ARTHRODESIS

SIR.—I am not at all sure what Mr. Norman Capener is getting at (June 19). Apart from his unhappy reference to insults and stigmata, which can safely be ignored, he admits even more strongly than I did the failure of many arthroplasties of the hip-joint, but without being willing to consider one obvious source of failure—namely, that the good idea of surgical reconstruction of a mobile and painless hip has often failed because of imperfect technique: “it was not that the operation was bad but that it was done badly” (June 12). His reply seems to be that the operation should not have been done at all.

We all know that ‘Vitallium’ cups have seized in the acetabulum, or been stuck on the neck of the femur—to our chagrin it has happened to all of us. We all know that free excisions of the femoral head, or even the femoral neck as well as the head, have been vainly replaced by prostheses which soon worked loose—and we should have known this from the beginning. If we know these things why do we not say them? Are we to be deterred, as has been suggested, by the fear of litigation? Are we not to write to *The Lancet* lest a solicitor reads our letters? If this is to be so we had better abandon all ideas of surgical progress and bask in safe mediocrity.

I for one will go on saying that hitherto the failures of arthroplasty of the hip-joint have very often been the consequence of failures of technique. If we pay more attention to the intelligent thought and precise technique of Fitzgerald in one type of operation, and of Crawford Adams in another, the next review of 500 cases after five years will be very different from the last.

It seems odd that I should find myself defending arthroplasty of the hip-joint, because the whole purpose of my letter of June 12 was to reiterate the belief I have held for many years that arthrodesis is best for mono-articular arthritis in all young patients up to the age of 60-odd years.

London, W.1.

REGINALD WATSON-JONES.

SIR.—I am unable to resist some comments on the statements by Sir Reginald Watson-Jones (June 12) that “there is no difficulty whatever in securing sound arthrodesis of the hip-joint . . .”, and that “if a surgeon wants to arthrodesise a hip-joint he can always do so.”

As one who believes ardently in arthrodesis of the hip-joint, I am in complete agreement with Sir Reginald regarding the excellence of hip fusion in unilateral disease. It is a great pity that patients cannot more easily be made less horrified at the first suggestion of “having the hip stiffened,” and it is a pity that the general public cannot know the disappointments hidden in the attractive-sounding operation of arthroplasty.

But to suggest that the painful hip can quite easily be got into the idyllic state of osseous union is certainly not the experience of most orthopaedic surgeons. If arthrodesis of the hip by standard methods were a trouble-free procedure recent exponents of arthroplasty would have had to face much more serious competition than has been the case. In osteo-arthritis (*malum coxae senilis*), where the bone is often densely sclerosed and where the leverage of the long shaft of the femur is immense, the hip is still the most difficult joint to fuse of any in the whole body. Stinchfield and Cavallaro¹ found that in 58 cases of osteo-arthritis 26% failed to achieve osseous union (and presumably therefore had to face a second operation). 10 cases of this series showed delayed union and required prolonged fixation, which means (my own calculation from their figures) that 43% did not proceed according to the plan that the surgeon had predicted when advising these patients to submit to the procedure. One can

fairly safely assume that this 43% must have lost permanently a considerable range of movement in their knees.

The fact is that the patient with a failed arthrodesis (by orthodox techniques) is in almost as pitiful a state as one with a failed arthroplasty. The only way a patient can cope with an arthrodesed hip is by virtue of a fully mobile knee. A stiff hip and a stiff knee is a calamity. So many surgeons have realised this that they have shown sound surgical judgment in deliberately choosing an imperfect arthroplasty, giving partial relief in a short time, rather than to risk the possibility of being landed with the long-drawn-out horror of a failed arthrodesis.

The technique of central dislocation of the hip which I advocate² guarantees full knee movement because the knee is fixed for only four weeks. But even by the central dislocation technique I have never evaded the frank admission that osseous union is possible in only about 75% of the older patients with osteo-arthritis. The almost uncanny feature of this operation, however, is that the ability to bear weight without pain is just as good when it is a fibrous ankylosis as when osseous. This is a statement which may appear exaggerated and irresponsible to surgeons accustomed to identifying fibrous ankylosis with failure. It would seem that fibrous ankylosis is painful after “orthodox” attempts at hip fusion because the hip is potentially unstable if osseous union fails and the fibrous union is thereby subjected to stretching forces. If osseous union fails after central dislocation, the hip still has greater stability than before operation, because a bone-block is present to sustain the weight of the body and the fibrous union cannot therefore be stretched.

By the central dislocation technique, as I use it in elderly patients with osteo-arthritis, the average stay in hospital is about eight weeks. At the end of this time they are able to look after themselves at home, do not require any form of physiotherapy whatsoever, and use a stick only during the first three or four months while regaining balance and confidence. This procedure of stabilising the hip and removing pain has many features in common with the displacement osteotomy of McMurray, but has important advantages in the shortness of the postoperative programme.

Department of Orthopaedic Surgery,
Royal Infirmary, Manchester. JOHN CHARNLEY.

IS HYPERTENSION A DISEASE?

SIR.—With reference to your leading article of June 12 I would like to make some observations and ask some questions based on my experience in general practice:

If disease means difficulty at being at ease, then hypertension is certainly a manifestation thereof.

If the western half of civilisation is hypertensive, then why not study the “abnormal” persons among us to get some idea of how to rearrange our existence to keep what is good and remain healthy?

Renal studies have shown a mechanism of producing hypertension. What about an equivalent, though apparently different, mechanism in other organs? For example, what diminution of blood-flow is to the kidney so could lack of exercise be to the extracellular electrolyte distribution; or could hypertension be an attempt to increase the hydrostatic element to compensate for disturbance of the electrolyte pattern brought about by dietary and/or endocrine imbalance?

If genetic inheritance is important then we cannot do a great deal about it unless we start selective breeding. (Or are we unwittingly selecting factors which carry with them diminished reserve to stress?) Why not consider “environmental” and/or “familial” inheritance as a pattern?

Awareness of hypertension seems to play a major part in the production of symptoms, but how many people have the symptoms of hypertension (if any) without an increased blood-pressure?

Can we study hypertension per se, or should we not study the pattern of abnormal reactions to stress in general? (For

1. Stinchfield, F. E., Cavallaro, W. V. *J. Bone Jt Surg.* 1950, 32A, 48.

2. Charnley, J. Compression Arthrodesis. Edinburgh, 1953.

instance, a hypertensive in one generation may have as an equivalent a thyrotoxic in the next; or an ulcer patient may have an accident-prone brother or a bankrupt uncle.)

The reason I put forward these jottings is that when, as now, we are floundering for a better understanding, this can often be achieved by reorientating what we already know.

Clapham, Lancashire.

J. A. FARRER.

EFFECT OF CONTROLLED HYPOTENSION ON CEREBRAL FUNCTION AND CIRCULATION

SIR.—Dr. Saunders (June 5) compares his $(A-V)O_2$ difference results during hypotension under anaesthesia with those in the non-anaesthetised subject. We feel his results should be compared with those in subjects under similar anaesthetic conditions without hypotension.

He states that the cerebral $(A-V)O_2$ difference represents the ratio of the cerebral metabolic demand to cerebral blood-flow. This is so, and the $(A-V)O_2$ difference varies inversely with the ability of the cerebral circulation to cope with the metabolic needs of the brain. Kety's figures¹ show the $(A-V)O_2$ difference to be 3.7 vols.% under anaesthesia. Thus Dr. Saunders's figure of 4.8 vols.% is an increase, and shows a decreased ability of the cerebral circulation to cope with the O_2 requirements of the brain.

Dr. Saunders uses Kety's figures for cerebral metabolic rate under light ether anaesthesia. These figures are based on the cerebral blood-flow obtained under light ether anaesthesia with normal blood-pressure. In Dr. Saunders's cases the blood-pressure is far from normal, and thus quite possibly the cerebral blood-flow may be changed—which is in fact suggested by the increased $(A-V)O_2$ difference.

This increased $(A-V)O_2$ difference may be sufficient to compensate for the decreased blood-flow through the brain and thus leave the oxygen uptake unchanged. Dr. Saunders is unjustified in assuming that the metabolic rate of the brain is the same under his hypotensive conditions as under normal anaesthesia, unless this is proved to be so by estimating the cerebral blood-flow under these conditions (i.e., estimating cerebral blood-flow under anaesthesia before and during the hypotension, thus ensuring that cerebral metabolism is unchanged).

We have done this.² Although we employ a 10° head-up tilt our level of hypotension is not so low as Dr. Saunders's—an average systolic pressure of 70 mm. Hg is obtained, and with this figure an average drop of 30% in cerebral blood-flow has been found by Kety's nitrous-oxide technique.¹

This drop in cerebral blood-flow does not appear to be dangerous since the $(A-V)O_2$ difference (average 5.5) increases sufficiently to give the same figure for cerebral metabolism under these conditions of hypotension as in the controls under normal anaesthesia.

Department of Anaesthesia,
University of Liverpool.

GOUGH HUGHES
H. RIDDLE.

SIR.—Dr. Enderby has done much to champion the valuable technique of controlled vascular hypotension, but his letter of June 19, referring to Dr. Saunders's paper, contains an assumption which may be dangerous if taken at its face value.

Dr. Saunders was careful to place the limits of safety of controlled hypotension at 55–60 mm. Hg systolic "when the patient is kept horizontal or nearly so," but Dr. Enderby has gone further and inferred the safety of cerebral arterial pressures appreciably lower than this. In my view, there is no satisfactory experimental evidence that these low levels are safe, and the hints we have suggest that they are not. Experimental work in

this field is extremely difficult, bedevilled as it is by varying cerebral oxygen consumptions in the conscious and anaesthetised states, but electro-encephalographic evidence in the conscious subject supports the view that 55 mm. Hg systolic is a critical level in healthy persons.¹

Griffiths has pointed out an added danger in the tendency to a fall of blood-sugar during administration of methionium.² With a respiratory quotient of 1.0 and absence of carbohydrate reserve, the brain is intolerant of hypoglycaemia, and unlikely to survive the combined insults of extreme hypotension and nutritional insufficiency at the same time.

Recently my own (unpublished) findings with total oxygen consumption show that an over-all oxygen debt is incurred at pressures below 55–60 mm. Hg, under light general anaesthesia, and the debt is discharged when the pressure is restored to higher levels. While the brain cannot incur an oxygen debt (it would rather die than do so), the presence of a debt at all indicates the existence of vascular insufficiency somewhere in the body.

Controlled hypotension is of great value in saving blood-loss and operative time; but we must insist that our limits of safety err on the high side, and as far as possible are based on experiment and not assumption, or disasters will follow and a useful technique fall needlessly into disrepute. A considerable portion of the brain can be destroyed without gross disturbance, but few of us would care to risk our higher faculties under profound hypotension, even in the interests of economy.

P. R. BROMAGE.

PATHOGENESIS OF RHEUMATIC FEVER

SIR.—Dr. Coutu, of Montreal (June 12), criticises conclusions reached by me in the Milroy lectures of 1954 (*Lancet*, March 13). He is correct in saying that I "question the relevance, for human beings, of experiments performed on rats." In fact, I go further and question the relevance to human beings of experiments performed on any animal. The prospects of relevance to human beings increase as the strength of the analogy between a given species of animal and man increases. On this basis, in my particular argument, the guineapig provides a stronger analogy than the rat.

Dr. Coutu is also correct when he says that I question the application of Professor Selye's views to rheumatic disease. Professor Selye showed that adrenocortical activity is readily stimulated in the rat by comparatively mild forms of "stress"—a phenomenon associated with involution of lymphatic tissue, ulceration of the gut, and hypofunction of the other endocrine glands. If such an easily detected phenomenon occurred in man, it is strange that it has not been described as a postoperative complication. Stress can precipitate an attack of rheumatic fever or rheumatoid arthritis, but it does not follow that a syndrome analogous to the rat adaptation syndrome is responsible.

Dr. Coutu is again correct in saying that I question not only the application of Professor Selye's views but his use of the term "antiphlogistic," which I consider meaningless and therefore confusing. I shall attempt to clarify the issue. In my hands, cortisone effectively depresses slowly developing allergic lesions of the tuberculin type, but is without effect on the size of inflammatory lesions resulting from the intradermal injection into guinea-pigs of various bacteria and/or of exotoxins. I conclude that the anti-allergic activity of cortisone in this particular creature cannot be attributed to a general anti-inflammatory action. A comparable experiment in man³ produced a similar result. It is likely, therefore, that the anti-allergic action of cortisone

1. Wechsler, R. L., Dripps, R. D., Kety, S. S. *Anesthesiology*, 1951, 12, 311.

2. Hughes, G., Riddle, H. In preparation.

1. Bromage, P. R. *Proc. R. Soc. Med.* 1953, 46, 919.

2. Griffiths, J. A. *Quart. J. Med.* 1953, 22, 405.

3. Lovell, R. R. H., Goodman, H. C., Hudson, B., Armitage, P., Pickering, G. W. *Clin. Sci.* 1953, 12, 41.

is so much greater than the anti-inflammatory action that if the latter exists its rôle in man and therapeutic significance is likely to be slight.

Dr. Coutu is confused by the term "antiphlogistic"; he provides a list of 22 references to support his contention that cortisone exerts an anti-inflammatory action. Of these, 9 are devoted to the anti-allergic action of cortisone and 7 to the effects not of cortisone but of corticotrophin. It is easy to select references to show that cortisone exerts remarkable effects which do not occur in my laboratory, but a mass of reports will not fill the rôle of a single convincing paper.

Dr. Coutu provides an excellent example of the difficulties in obtaining first-rate evidence. He worked on the effect of corticotrophin on the inflammatory response to mustard powder, and, in spite of the logical and practical objection that corticotrophin and cortisone are not the same thing, questions my work with cortisone. I spent some years working on the influence of corticotrophin on inflammatory responses. I found they were decreased, but only by certain batches of corticotrophin. Such responses bore no relation to the unitage and could not be duplicated with cortisone or with other available adrenal steroids. Moreover, the effects of corticotrophin in the guineapig were so transient that I could not distinguish between real and compensating effects. I could not therefore interpret my own results; neither can I interpret his.

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Mill Hill, London, N.W.7.

D. A. LONG.

SALICYLATES AND ADRENOCORTICAL STEROIDS

SIR.—In your issue of May 15, Dr. Smith and his colleagues and Dr. Bayliss and Dr. Steinbeck discuss the action of salicylates on the 17-hydroxycorticosteroids in man.

As regards the first of these papers, similar work with similar results was described by Hungarian authors in 1952,¹ and by Coste et al.² in France in 1953, using the biological method of Cope.³ The daily excretion of urinary cortisone-active material was unaltered during salicylate therapy.

On the other hand massive doses of salicylate commonly increased plasma 17-hydroxycorticosteroid levels in the patients of Ely et al.⁴ Finally, we have repeatedly suggested that the therapeutic effect of salicylate can hardly be explained in this way.^{1,5}

University Medical School,
Szeged, Hungary.

E. KELEMEN.

TRAVERSING WOUND OF THE HEAD

SIR.—Mr. B. H. Dawson's article of May 22, describing a traversing injury of the head with complete recovery, reminds me of a somewhat similar remarkable case.

In 1946, while serving with the Forces overseas, I was called out one afternoon to see a young soldier who had just shot himself through the head. I expected to find him dead, but instead he was lying on his bed with blood streaming from nostrils and mouth and able to talk coherently. He had been suffering from mental depression for several days and had resolved to commit suicide. He had fired one shot through the open mouth from a Smith-Wesson revolver while lying on his back with his head on a low pillow. After doing this, he was distressed to find that he could get up and walk around the room. He was pale. The pulse-rate was about 90, with poor volume. There was a small circular entry wound in the midline of the hard palate and a larger irregular exit wound in the left parietal region two inches from the midline

1. Kelemen, E. *J. clin. Endocrin.* 1952, 12, 1249. Kelemen, E., Majoros, M., Soltész, R., Tanos, B. *Disch. med. Wschr.* 1952, 77, 1317. Kelemen, E., Tanos, B., Soltész, R., Kovács, K. *Acta endocr. Copenhagen*, 1953, 13, 231.
2. Coste, F., Bourrel, M., Delbarre, F., Weissenbach, R. *Pr. méd.* 1953, 61, 979.
3. Cope, C. L. *Brit. med. J.* 1951, i, 271.
4. Ely, R. S., Done, A. K., Kelley, V. C. *Amer. J. Dis. Child.* 1953, 86, 656.
5. Kelemen, E., Majoros, M. *Lancet*, 1951, i, 962.

and about the same distance behind the coronal suture. There was little comminution of bone, and haemorrhage was mainly from the nose. He could see and hear normally. I took him several miles over imperfect roads by ambulance truck to hospital, where a careful wound toilet was carried out. The patient made an uninterrupted recovery, and several months later he was well enough to appear before a court-martial. There was no mental defect and no history of post-traumatic epilepsy. All the cranial nerves were functioning normally. It was remarkable that the left optic nerve escaped injury.

As a further illustration of the resistance of the brain hemispheres to trauma applied at right-angles to the skull, I might mention the ancient Chinese practice of passing metal needles through the head to provide an outlet for evil spirits.

Kirkuk, Iraq.

R. T. S. LOUTTIT.

CERTIFICATION FOR MENTAL DISORDERS

SIR.—Many of your readers are, like myself, deeply concerned with improving mental hospitals and the care of mental illness; and they chiefly want to know how they can do this with the means at their disposal. Yet, not only do many otherwise well-informed people still seem to regard certification as an essential and inevitable part of psychiatric care, but the great majority of psychiatrists seem to be unaware that certification has been virtually abolished in both Eire and Northern Ireland. To these I commend that masterpiece of humanitarianism, the Mental Health Act (Northern Ireland), 1948.

As a medical journal is hardly the best place for a lay writer to offer medical statistics, I will confine myself to the statement that in the British Isles—excluding Northern Ireland—we have today some 200,000 mental patients certified under an Act which is archaic and should be amended. That the Act is obsolete is evident from the establishment of the Royal Commission, to which it was recently my privilege to submit evidence on this score.

Surely, we—who were first in the field with anaesthetics, antiseptics, antibiotics, and other great advances—must advance also in the field of psychological medicine. For certain, the time has come for us to separate the "insanity" of the law from the "mental illness" of medicine. Let us, therefore, follow the lead given by Northern Ireland and Eire.

Edzell, Angus.

H. G. WOODLEY.

* * * This subject is discussed in a leading article—Ed. L.

FETAL HEPATITIS

SIR.—The following case may be of interest in view of your annotation of June 5.

A 3-week-old infant was brought to this hospital with deep jaundice of 2-3 days' duration. All the evidence pointed to the jaundice being obstructive in origin. The plasma-bilirubin was of the order of 30 mg. per 100 ml. and a 24-hour specimen of faeces was entirely free from stercobilin. The alkaline phosphatase, however, was 8.5 King-Armstrong units. The blood picture was entirely normal, and the Coombs test negative.

Thus bile-duct atresia was diagnosed, and the child was submitted to laparotomy. At operation, however, absolutely nothing abnormal was found. At this stage it was decided to regard the case as one of hepatitis due to umbilical sepsis and umbilical-vein pyæmia,¹ although there was no obvious evidence of either umbilical infection or umbilical pyphlebitis. Aureomycin was accordingly given, and the jaundice regressed rapidly after 3-4 days.

A complicating feature was the development of severe anaemia of aplastic type which reached its height when the recovery from the jaundice was almost complete. At this stage there was still no evidence of haemolysis or the presence of antibodies, and the anaemia was not considered to be due to the medication, which had been started after the anaemia was first detected. The child received a blood-transfusion,

1. Morison, J. E. *J. Path. Bact.* 1944, 56, 531.

and since then has not looked back. After the transfusion the thymol-turbidity level rose to 4 units; previously the level had been less than 1 unit.

This case has been regarded here as one of septic hepatitis, but viral infection of the liver may have been the cause of the illness.

St. Mary's Hospital for Women and Children,
London, E.13. D. MYMIN.

CHLORPROMAZINE IN STATUS ASTHMATICUS

SIR.—Status asthmaticus is not uncommon, and it may be fatal.¹ Treatment becomes very difficult when the patient does not respond to antispasmodic drugs—none of which is likely to prove of any value if subcutaneous adrenaline and intravenous aminophylline are ineffective. Sedatives, which relieve mental distress and may also lessen the asthma, may be tried; but a small dose is usually ineffective, and a larger dose may depress respiration to a degree dangerous in an anoxic patient.² We have ourselves seen a young woman die after two 3-grain doses of sodium amylobarbitone by mouth.

The pharmacology of chlorpromazine ('Largactil')³ suggested that it might be valuable. It is said to have a depressant action on the cerebral cortex but not on the respiratory centre. Electro-encephalographic tracings are comparable with those of normal sleep.⁴ Laryngeal and tracheobronchial reflexes mediated by the vagus nerve are depressed, and postoperative secretions are reduced.⁵ In animal experiments capillary permeability is reduced and oedema of mucous membranes is prevented. Chlorpromazine also lowers the metabolic rate.

We have tried chlorpromazine in four cases:

CASE 1.—Mrs. A, housewife, aged 50. Asthma began in 1948, and on Dec. 10, 1953, she was admitted for the fifth time. She was cold, pale, cyanosed and sweating profusely; pulse-rate 160, blood-pressure 160/90 mm. Hg. She was given oxygen and intravenous aminophylline 0.25 g., intramuscular phenobarbitone gr. 3, and oral ephedrine gr. 1; but four hours later (11.30 P.M.) her condition had deteriorated. She was put in an oxygen tent, and at midnight promethazine 100 mg. was given slowly intravenously. She became slightly drowsy and the "spasm" lessened a little. At 12.15 A.M. chlorpromazine 25 mg. was given intravenously. She now went to sleep, her colour became pink and the respirations much quieter; the extremities were warm and the sweating ceased. At 12.45 A.M. the blood-pressure fell to 100/80; at 1 A.M. it rose to 120/90, and, though she was still fast asleep, the expiratory wheezing had almost gone. The pulse remained at 160 throughout (tachycardia is often an effect of chlorpromazine). Next morning she was drowsy but cooperative and the attack had ceased.

CASE 2.—Mrs. B, aged 55, had her first attack of asthma in 1952, and had since been in hospital six times. She was first admitted to Whittington Hospital at 1 A.M. on Dec. 20, 1953, with status asthmaticus of three days' duration. She was cyanosed, with widespread bronchospasm; pulse-rate 120, blood-pressure 180/90. She was given intravenous aminophylline and intramuscular phenobarbitone, but three hours later she was much worse. She was therefore given a combined intravenous injection of chlorpromazine 12.5 mg., pethidine 25 mg., and promethazine 25 mg. She went to sleep and the spasm was relieved though not abolished. Next morning she was drowsy; there were a few rhonchi but no spasm.

CASE 3.—Mrs. C, aged 31, had had asthma for ten years, and in the past year had been off work for four months, with periods in hospital. On Jan. 4, 1954, at 10 P.M., she was readmitted, deeply cyanosed and in great distress; pulse-rate 140, blood-pressure 130/90. Intravenous aminophylline was without effect, so at 10.40 P.M. she was given chlorpromazine 50 mg. She became sleepy and less distressed

1. Earle, B. V. *Thorax*, 1953, 8, 195.

2. Houston, J. C., De Navasquez, S., Trounce, J. R. *Ibid.*, p. 207.

3. Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M., Koetschet, P. *Arch. Int. Pharmacodyn.* 1953, 92, 305.

4. Terzian, H. *Rassegna Neurol. veg.* 1953, 4-5, 211.

5. Foerster, S., Foerster, E., Maier, A., Blum, H. *Curr. Res. Anesth.*

1952, 9, 250.

and the colour improved; her pulse-rate rose to 160. At midnight she was sleepy but easily roused; pulse-rate 144, blood-pressure 100/80. As there was still some spasm she was given chlorpromazine 20 mg., promethazine 20 mg., and pethidine 20 mg., together intravenously. The breathing improved and the pulse-rate fell to 120; blood-pressure was 100/70. She slept through the night and by morning the asthma had ceased.

CASE 4.—Mrs. D, aged 51, an asthmatic of many years' standing, was admitted on Jan. 4, 1954, at 8 P.M. She was deeply cyanosed, in great respiratory distress and very restless; pulse-rate 100, blood-pressure 100/50. She was given intravenous aminophylline and intramuscular paraldehyde, and was put in an oxygen tent. She remained restless and dyspnoeic throughout the night, and at 7 A.M. was given phenobarbitone gr. 3 by intramuscular injection. When seen by us at noon she was semicomatose, restless, and cyanosed in spite of the oxygen tent. She was violent at times and had not been sufficiently cooperative to drink since admission. She was therefore given a combined intravenous injection of chlorpromazine 6 mg. and promethazine 6 mg. very slowly, being restrained for the purpose by three nurses; she fell asleep during the injection. The pulse-rate rose from 120 to 160 but fell again within twenty minutes to 124; the blood-pressure remained steady at 140/100. She slept quietly if not disturbed, and by 9 P.M. she was no longer cyanosed and the bronchospasm was much less though she was still confused and uncooperative. At 11 P.M., as the effect of the paraldehyde and phenobarbitone had worn off, she was given chlorpromazine 50 mg. and promethazine 25 mg. intravenously. She fell asleep and next morning she was rational and free of the asthma.

In these cases, though the promethazine and pethidine given were probably of some value, the greater part of the improvement appeared to be due to the chlorpromazine, which enabled the patient to sleep without depressing respiration. Relief of bronchospasm was not immediate, and may have been caused as much by the adequate sedation produced as by any direct antispasmodic action of the drug. After the injections sweating stopped, cyanosis was lessened or abolished, and the extremities became warmer. Although there was always tachycardia, the heart's action was not irregular and fall of blood-pressure was only slight and transient.

In our view parenteral administration of chlorpromazine should at present be restricted to the more severe cases; but we have given it by mouth in a few mild cases with some apparent benefit.

The first three cases were under the care of Dr. A. L. Jacobs and the fourth of Dr. M. G. C. Ashby, consultant physicians. We are grateful to them and to Dr. O. H. Belam, consultant anaesthetist, for their help and advice.

Whittington Hospital,
London, N.19.

K. C. ROBINSON
D. ZUCK.

BARBITURATE POISONING

SIR.—From time to time the question of how best to treat acute barbiturate poisoning is raised. Nabarro¹ has emphasised the importance of restoring consciousness promptly by administering amphetamine, in order to prevent bronchopneumonia. Others believe that expert use of the bronchoscope and assisted respiration are sufficient until the effect of the drug wears off. In the following case the patient had taken an unknown amount of sodium amylobarbitone ('Sodium amytal') and phenobarbitone.

A depressive patient, aged 59, was seen at 8.45 A.M. by his doctor. He was unconscious with shallow respirations, small fixed pupils, and absent corneal, limb, and abdominal reflexes. He was given 6 mg. of picrotoxin and was then admitted to the Lympstone and District Hospital under the care of Dr. R. J. McGill. In the next 3 hours he received a total of 60 mg. of picrotoxin, which resulted in generalised twitching and turning of the head, relieved by a small dose of thiopentone. Intravenous methylamphetamine was started, and at the end of 6½ hours he had been given 80 mg. The pupils

1. Nabarro, J. D. N. *Brit. med. J.* 1950, ii, 924.

became dilated and only the abdominal reflexes were absent. His blood-pressure was 136/80 mm. Hg and did not rise above 150/60 subsequently. He received 150 mg. of the drug in the next 4½ hours, after which he awoke and seemed to recognise his relatives. Dosage was continued with 330 mg. over another 4½ hours, at the end of which he was fully awake and able to eat without assistance. The total dose of methylamphetamine was 560 mg. over 15½ hours. For the next 24 hours he had decreasing visual hallucinations and was excitable though co-operative. Additional treatment during coma included oxygen by nasal catheter, rectal saline, and 1 million units of penicillin.

This patient was never on the verge of convulsions with methylamphetamine, as he was with picrotoxin; his blood-pressure remained normal. It seems safe to give large doses of methylamphetamine over a comparatively short time to patients in deep coma. Poe and Karp² describe a case in which a total of 520 mg. was given, but no times are stated.

Poole Hospital,
Nunthorpe, Middlesbrough.

C. F. HINGSTON.

DEMONSTRATIONS OF HYPNOTISM

SIR.—The Hypnotism Act of 1952 was initiated and passed to curb the dangerous and degrading spectacle of stage hypnosis and to stop the abuse of a recognised medical technique as entertainment for the public. Are we any further now that the Act is a fact? Today we read³ of a television demonstration of tooth-pulling by a dentist, using hypnosis. Yesterday we read⁴ of a layman who publicly demonstrated hypnosis on members of his audience and who was prosecuted under the Act and acquitted because he gave a "lecture" and no collection was made. We repeatedly read in the lay press articles by or about certain doctors and others practising hypnotism. This conduct should not be permitted and can only be controlled by a stronger Act or adequate action by a disciplinary body.

If hypnotherapy is to achieve its correct status and position in medicine, it must not be abused. We are not asked to witness the extraction of teeth under thiopentone or nitrous oxide on television, for it would not be tolerated by medical authority. Could we not expect the same consideration for a valuable therapy even now in the experimental stage?

London, W.1.

GORDON AMBROSE.

EXERCISE TESTS DURING TREATMENT OF HYPERTENSION

SIR.—In your issue of Oct. 3, Dr. Vagn Rønnov-Jessen reported 2 cases of hypertension in which, after the administration of hexamethonium, a fall in blood-pressure set in after physical exertion. He postulated that the change of blood-pressure following exertion was a guide to the level to which blood-pressure should be reduced by treatment.

We should like to report the results of similar tests on the effect of exercise on systolic and diastolic blood-pressure in normal and hypertensive individuals before and after the administration of tetraethyl ammonium bromide (T.E.A.B.). Our results partly confirm those of Dr. Jessen.

88 tests were performed on 73 people; 35 had a normal blood-pressure, 28 had essential hypertension, and 10+ had renal hypertension. Blood-pressure and pulse-rate were taken in the lying position until the resting level was reached. The patient then performed 20 deep knee-bends in one minute; immediately afterwards, the blood-pressure and pulse-rate were again recorded every minute for a period of at least 10 minutes. After a prolonged rest, 0.3 g. of T.E.A.B. was injected intravenously, and the above exercise test was then repeated.

We found that the systolic pressure of hypertensive and normotensive individuals rose after exercise. But the diastolic

pressure reacted differently in hypertensive and normotensive persons: in the normotensive it almost invariably decreased in the minutes immediately after exercise (out of a total of 41 observations, only 4 showed an increase); in essential hypertension it usually rose (a decrease was noted in only 5 out of 36 observations). The difference between the reaction of the two groups was significant by the "t" test.

Exercise after T.E.A.B. generally increased the diastolic pressure of hypertensive patients in the same way as before, the increase in the mean value being rather greater; in normotensive patients, however, the previous decrease was no longer observed.

These findings are opposed to the conclusion of Stevenson et al.¹ that the blood-pressure of patients with essential hypertension reacts differently from that of normotensive people because of psychic factors and not as a result of exercise.

The cardiac output per minute in both hypertensive and normotensive patients is known to increase as a result of exercise, so the different behaviour of diastolic pressure in the two groups can only be attributed to the fact that exercise produces a greater fall in the peripheral resistance of normal individuals.

Although exercise affected the diastolic pressure less after the administration of a ganglion-blocking agent, in 2 cases exercise was followed by a substantial drop in blood-pressure and a state of semi-collapse, which confirms Dr. Jessen's observations.

G. CZONICZER
T. ZSÓTER
Zs. SEBÖK.

THE AFRICAN MIND

SIR.—Your annotation of Jan. 30, under the title Comparative Psychiatry, discusses the psychiatric section of Dr. Carothers's monograph on The African Mind in Health and Disease. His observations are based on an earlier study,² which was devoted to a careful analysis of the cases admitted over a period of 5 years to the African mental hospital in Kenya, and which raises, as you suggest, many interesting points of comparison between types of mental disease found in European and African communities.

This section involves, however, only one chapter in Dr. Carothers's monograph—a chapter which will probably only attract the interest of specialists in this field. A chapter which will, I imagine, arrest the attention of a wider group of readers is that on psychology, in which the author develops his views on the African mind in health. These are also based upon a previously published study,³ but one which unfortunately falls far short of the earlier one in standard of scientific inquiry. The evidence, in fact, which Dr. Carothers presents in support of his view that African behaviour resembles that of a leucotomised European psychopath consists of 33 personal and subjective anecdotes purporting to depict "unreliable behaviour in Africans." For example, one of these (and not the most surprising) reads as follows:

"I put my shoes to be mended in my shopping basket the night before so that I shall remember to take them to the cobbler the next day; the house-boy takes them out, cleans them, and puts them elsewhere, though he might assume that they had been put in the basket for some purpose."

Readers—and particularly those with some experience of East African mores—will be able to think of many explanations for this alleged shortcoming, but the point I wish to stress is that this is not the kind of evidence upon which serious conclusions can be based.

In short, the contrast between the methods by which Dr. Carothers has arrived at his psychiatric and at his

2. Poe, M. F., Karp, M. *Curr. Res. Anesth.* 1948, 27, 176.

3. *News Chronicle*, May 25, 1954.

4. *Brit. med. J.* May 8, 1954, p. 1103.

1. Stevenson, I. P., Duncan, C. H., Flynn, J. T., Wolf, S. *Amer. J. med. Sci.* 1952, 224, 286.
2. Carothers, J. C. *J. ment. Sci.* 1948, 93, 548.
3. Carothers, J. C. *Ibid.* 1951, 97, 12.

psychological conclusions is so great that I think it would be regrettable if readers were to be led by the evident erudition of his monograph, or by the *imprimatur* given to it by W.H.O., to regard both parts as of equal scientific validity.

Kampala, Uganda.

J. MCFIE.

DIET AND CORONARY DISEASE

SIR.—Professor Duguid (May 1) distinguishes two forms of atherosclerosis but says: "in both processes the mechanism . . . is the same; solid matter is deposited on the intimal surface and in due course covered with endothelium and incorporated in the intima." Why not accept this as the essential pathogenesis, and regard narrowing as something additional?

A study of the pathology of mental disease (where the cardiovascular system is oftener at fault than the central nervous system) gives support to the mural thrombi origin of atheroma as put forward by Professor Duguid. In addition I have illustrated streptococci¹ attached to vessel walls; and atheroma localised to an area contiguous to a sphenoidal empyema,² presumably where phagocytes and red-cell clumping had adhered.

It is often possible to see in histological sections that local vessel dilatation is the result of an atheromatous process, and I generally find that extreme atheroma has fixed the vessel in a state of dilatation.⁴ Where, however, thrombosis is complete as in Professor Duguid's figs. 1 and 2, narrowing might be expected, as also where the adventitia becomes involved. In one case the internal carotid artery was reduced to a fibrous cord.⁵ (This patient died from thrombosis of the superior mesenteric artery.)

The effects of occlusion of the small coronary vessels are not, as Professor Duguid states, negligible. Acute cardiac failure or local heart-wall rupture⁶ occurs when anastomotic vessels cannot relieve an additional small occlusion or spasm.

Atheromatous ulcers release lipoid into the circulation,⁶ so a high blood-cholesterol level may be a sequel as well as a cause of atheroma.

Birmingham.

F. A. PICKWORTH.

SIR.—I cannot agree with Professor Duguid (June 5) that restricted fat consumption "could not have been the factor responsible for the discontinuity in the recorded death-rates beginning to appear as early as 1940."

The following figures⁷ show the supplies of "fat from all sources moving into consumption in the United Kingdom" as a percentage of the pre-war (1934–38) consumption:

1940	1941	1942	1943	1944	1945	1946
93	87	91	89	95	89	86
1947	1948	1949	1950	1951	1952	
82	85	93	101	97	94	

It will be seen that the most severe fat restriction occurred after the end of the war (not in the later war years as stated by Professor Duguid). My graph of coronary-disease death-rates (May 22) shows that the discontinuity first became evident in 1941 (not 1940), by which time the fat consumption had fallen to 87% of the pre-war level. Further it must be remembered that the fat-consumption figures are averages for the whole population and that the rationing of fats (which began early in 1940) would cut the consumption of those persons with the highest intake while those with the lowest consumption would be little affected. In my opinion all this fits in with the theory that restricted fat consumption could be the cause of the discontinuity in the recorded death-rates from coronary disease.

1. Pickworth, F. A. *Z. ges. Neurol. Psychiat.* 1932, 141, 420; fig. 3.
2. Pickworth, F. A. *Chronic Nasal Sinusitis*. London, 1935; fig. 16.
3. Pickworth, F. A. *Nursing Mirror*, Oct. 18, 1947, p. 45; fig. 2.
4. Pickworth, F. A. *New Outlook on Mental Diseases*. Bristol, 1952; plate II, p. 5.
5. *Ibid.*, plate II, o and r.
6. *Ibid.*, plate II, l.
7. *Ministry of Food Bulletin*, Sept. 19, 1953.

A possible reply to my argument is, Why is the discontinuity in the death-rates more or less confined to the war years, although the fat consumption fell still lower after the war and rationing was continued until this year? My answer to this is that I do not think the discontinuity is confined to the war years, but that it has continued long after the end of the war. Consideration of the trend of the death-rates from coronary disease is complicated by the steep upward trend probably largely due to changing fashions of certification and similar causes. This makes it difficult to determine the true extent of the war-time discontinuity, while there is also the further difficulty that the national statistics of deaths from all forms of heart-disease are notoriously difficult to interpret owing to what has been referred to as "a good deal of switching of diagnostic labels." Elsewhere⁸ I have tried to deal with some of these rather involved questions and have given a number of graphs of the death-rates from several different forms of heart-disease. Here I would say only that during the years 1931–49 the death-rates (by age-group) for degenerative heart-disease as a whole rose fairly steadily up to 1940, fell steeply until 1942 or 1943, and thereafter rose again, but at a slower rate than before 1940.

On the biological evidence for and against the fat theory, I am not competent to comment; but, if I understand it correctly, a possible interpretation is that a high consumption of fat may be a cause of coronary disease, and I feel that this interpretation is strengthened by the known trends of the death-rate and the consumption of fats since 1940.

Harrow, Middlesex.

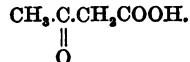
R. H. DAW.

CLINICAL TESTS FOR KETONURIA

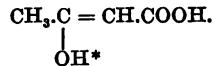
SIR.—Thank you for publishing the most enlightening paper by Dr. Nash and his colleagues (April 17). The nitroprusside-tablet test is of particular interest. I strongly deprecate the disgusting business of old-fashioned urine-testing, as still practised in such semi-public places as hospital clinics and doctors' consulting-rooms.⁹ It is very much to be hoped that tablet tests will soon become the generally accepted routine when testing urine for pH, reducing substances, ketone bodies, and bile pigments.

It is a pity that Dr. Nash and his colleagues do not tell us the exact composition of these nitroprusside tablets. It is also a pity that obscurity should have been allowed to creep into an otherwise remarkably lucid paper, over the chemistry underlying the tests described. It is not quite correct to state that some consider only acetone gives a purple coloration with nitroprusside, whereas others consider both acetone and aceto-acetic acid give it.

Actually, it is a very simple matter. Compounds with a ketonic grouping in a certain position give this reaction—e.g., acetone, which is dimethylketone ($\text{CH}_3\text{C}=\text{O}$). Aceto-acetic acid, however, exists in solution as an equilibrium mixture of two slightly different forms, known respectively as keto and enol tautomers. The keto form has the following configuration:



With a shift in the position of the double bond, caused by the migration of one hydrogen atom, the enol form is produced which has the following configuration in which, for clarity, I have asterisked the hydrogen atom which has migrated:



The keto form has a structure closely akin to that of acetone. This form—and this form only—reacts, like

8. *J. Inst. Actu.* (in the press).

9. Adams, A. V. *Med. World, Lond.* 1952, 76, 464.

acetone, with nitroprusside, as might be expected. However, by the law of mass action, in proportion as the keto form is used up in the reaction so will more be regenerated from the (non-reacting) enol form.

Likewise, the enol form has a hydroxyl group closely resembling that of such compounds as phenol and salicylic acid. It is the enol form—and this form only—that gives the Gerhardt reaction with ferric chloride, as do phenol and salicylic acid. It is precisely this that accounts for the interference with the Gerhardt test caused by the excretory derivatives of many commonly used drugs. Distinction from these is possible because aceto-acetic acid is readily hydrolysed on boiling, either to acetone and carbon dioxide or to acetic acid, according to the pH of the solution.

Heathfield, Sussex.

ADRIAN V. ADAMS.

SIR.—With reference to the article by Dr. Nash and his colleagues and subsequent letters (May 1 and 15), I should like to draw attention to a simple test for distinguishing between true and false positive Gerhardt reactions.¹

1-drop of concentrated nitric acid is added to 1 inch (about 4 ml.) of urine in a test-tube, and the mixture is boiled for one minute. After cooling thoroughly, $\frac{1}{2}$ inch (about 2 ml.) 10% ferric-chloride solution is added.

Aceto-acetic acid is completely destroyed by this procedure, and the reaction will now be negative. Drugs will still give a positive reaction.

Department of Physiology,
University of Cape Town.

H. ZWARENSTEIN.

ACUTE APPENDICITIS IN LATE PREGNANCY

SIR.—In his interesting article last week Mr. Parker rightly stresses the difficulty of deciding whether the source of tenderness is uterine or extra-uterine. No single sign is likely to clinch the diagnosis in an abdominal emergency during pregnancy, but the sign described by me² may be found useful in this connection:

With the patient lying straight on her back, the examining fingers find the area of maximum tenderness to pressure on the abdominal wall. While the fingers remain in contact with that area without altering the intensity of pressure they are exerting to elicit pain, the patient is made to turn over on to the opposite side so that the plane of the anterior abdominal wall is approximately vertical. The pain produced by the pressure of the fingers will be less or will have entirely disappeared if the lesion is uterine and has fallen away from the examining fingers—“shifting tenderness” (concealed accidental haemorrhage, Case 3, or degenerated uterine fibromyoma, Case 4); pain sensation will be unaltered if the lesion is extra-uterine—“fixed tenderness” (due to appendicitis, Cases 1 and 2, renal or gall-bladder disease, ovarian cyst with twisted pedicle, diverticulitis).³

Bournemouth.

N. ALDERS.

B.C.G. VACCINATION

SIR.—After reading that in the U.S.S.R. children are vaccinated repeatedly from birth till leaving school,⁴ I would like to describe my experience of ordinary intradermal injections of 1 ml. and of multiple puncture by Professor Heaf's six needles.

By the end of 1952 I had done 2500 ordinary vaccinations with only 1 case of adenitis and half a dozen with ulcers 12–15 mm. in diameter. However, as even the mildest of vesicular reactions takes some considerable time to heal and in many cases ulcers 6–8 mm. in diameter last for months and may cause parents to withhold permission for vaccination, I thought I would try multiple puncture.

Early in 1953 I applied this method to 40 children—the technique was to put a drop of B.C.G. ordinary intradermal strength (0.25 mg. per ml.) on the arm and release the spring of the M.R. apparatus half a dozen times. On

subsequent test 35 gave a positive Mantoux reaction, although the local reaction on the deltoid area consisted simply of numerous tiny papules 1·5 mm. in diameter and height. The reaction was not so strongly positive as after intradermal injection. Hence doubt arose as to the value of this method and as to whether the conversion would persist for any length of time. Now after fifteen months all except 2 of the 22 children re-tested have given positive reactions varying from very slight to quite definite.

I had requested permission to use B.C.G. 20 mg. per ml., or dried B.C.G. which I could dilute to the required concentration; but the authorities would not countenance this experiment.

It seems to me that if this simple, safe, and rapid procedure can produce allergy lasting two years it will appeal to a much wider public and prove unobjectionable to parents.

Stornoway, Lewis.

R. STEVENSON DOIG.

AN AMERICAN IN BRITAIN

SIR.—I was greatly discouraged and depressed that a journal with the standing of *The Lancet* would publish such a statement as that of Dr. Cort in the June 19 issue. Perhaps it is because of your unfamiliarity with American military draft procedure. It would also appear that the University of Birmingham has been misled. This type of reporting is more characteristic of the lay press.

In America medical students are “deferred” from military service during their undergraduate study and for one year afterward while in the internship or other advanced study. Please note that they are deferred and not “exempt.” At the end of this time they are, if physically, mentally, and morally fit, commissioned in the appropriate service for a period of 21–24 months. Loyal citizens do not attempt to evade this obligation. While discharging this obligation several of Dr. Cort's classmates have become casualties in such places as Korea in an attempt to keep the world free so that research may continue.

Dr. Cort's statement is a cleverly worded piece of evasion and diversion which may mislead the British doctor, but it will certainly not confuse any American physician. The issue at hand is not Communism as he would like for you to believe; but instead, it is evasion of military service, or to use the American vernacular simply “draft dodging.” Without attempting to analyse all of his statements I shall comment on only a few.

He mentions several colleagues who were dismissed from their jobs because of Communism. This is untrue. These men were in junior positions and when the terms of their appointments expired they went into the private practice of medicine. He recalls one who remained as being defendant in a suit brought by the State of Massachusetts for “violation of his oath.” The fact that one of his colleagues did remain attests to the fact that Communism was not an issue.

He also mentions that upon his return to America he will be subject to unemployment. This is not true. He is eligible to obtain a licence and enter into the practice of medicine in any of the 48 States, territories, or possessions. If, of course, he expects to obtain a professorship, he may well be unemployed.

As to the loss of citizenship, it is impossible to deprive a natural-born citizen of his citizenship. A naturalised citizen may be repatriated if his citizenship was obtained on the basis of fraud.

As to the 5–10 year prison sentence he mentions, this can be given only upon conviction of a felony. If a felony is involved, he will have ample opportunity to defend himself before an impartial jury of twelve. If the decision is adverse, he may proceed to a court of appeals and in an exceptional circumstance he may even advance to the United States Supreme Court. To put the matter more simply, an honest citizen has nothing to fear.

The proper thing for Dr. Cort to do is to stand up straight on his hind legs like a man and volunteer for his

¹ Zwarenstein, H. *J. Lab. clin. Med.* 1945, 30, 172.

² *Brit. med. J.* 1951, II, 1194.

³ See *Lancet*, May 22, 1954, p. 1088.

military service without hiding behind such statements as "not legally binding," the tolerance of the British Government, and any emotion he may elicit from the ill- or mis-informed public. If at the end of his service he so desired he could return to England as an immigrant if the country would still accept him.

As to his immediate future I am sure that between the American embassy and the Home Office justice will be obtained. The press would do well to stick to the official announcements of these bodies.

AN AMERICAN DOCTOR IN ENGLAND.

ROSE SIMMONDS MEMORIAL FUND

SIR.—In December, 1952, you published an appeal for contributions to the above fund.¹ The object was to provide an educational fund which, through the British Dietetic Association, would offer scholarships to students to train as dietitians, or prizes to students in training.

A sum of £370 has now been contributed. This money has been invested, and the trustees have decided that prizes shall first be available in the autumn of 1955.

DOROTHY S. RUSSELL	E. P. SKINNER
H. G. WIMBUSH	Chairman.
W. R. S. RITCHIE	E. M. GAGE
British Dietetic Association.	

Hon. treasurer.

Medicine and the Law

Death after Tonsillectomy

AT an inquest on a 7-year-old girl at Barnet on June 14 the coroner criticised the emergency arrangements at a local hospital.²

The child's tonsils were removed on May 26 at St. Stephen's Hospital; there were no complications at operation but some four or five hours later, at 8.45 p.m., haemorrhage was noticed. The surgeon, who was at Barnet General Hospital, was kept informed; he ordered an injection which was given at 9.15 p.m., and after a further message went to see the child at 10 p.m., when he ordered her removal by ambulance to Barnet General Hospital. There he operated to stop the haemorrhage and gave blood-transfusions, but the child died.

The bleeding was noticed at a time when day staff was handing over to night staff, and the surgeon was not available on the premises. As there were no facilities at St. Stephen's for the operation and blood-transfusion, the child had to be removed by ambulance, all of which caused delay.

Recording a verdict of death by misadventure the coroner said that the arrangements were perhaps inadequate for an emergency of this sort and he would bring the matter to the attention of the authorities responsible.

Public Health

First Quarter in Scotland

IN the quarter ended March 31 this year³ the birth-rate in Scotland was 18.6 per 1000 population, which was 0.5 above the rate for the corresponding quarter of 1953 and 0.1 above the average in the previous five years. Stillbirths amounted to 25 per 1000 total births. The death-rate was 14.3 per 1000 population—0.6 more than in the corresponding quarter of 1953 but 0.8 below the five-year average. The infant-mortality rate was 38 per 1000 live births, and the neonatal-death rate 24 per 1000 live births. Deaths from tuberculosis amounted to 31 (respiratory 28) per 100,000 population, compared with 32 (27) in the first quarter of 1953 and a five-year average of 56 (49).

1. See *Lancet*, 1952, ii, 1187.

2. *Barnet Press*, June 15, 1954.

3. Quarterly Return of the Registrar-General, Scotland: Births, Deaths, and Marriages registered in the quarter ended March 31, 1954. H.M. Stationery Office. Pp. 32. 2s. 6d.

Obituary

CHARLES COLGATE HOLMAN M.A., M.B. Camb., F.R.C.S.

Mr. C. C. Holman, emeritus surgeon to Northampton General Hospital, died on June 17 at the age of 69.

He was born at East Hoathly, where his father and his grandfather were both in general practice. From Eastbourne College he went to Caius College, Cambridge, where he took the natural sciences tripos in 1905. Following a family tradition he finished his medical education at Guy's, qualifying in 1908 and graduating M.B. in 1909. After serving as house-surgeon at Guy's he held other resident appointments at Addenbrooke's Hospital, Cambridge, at the Norfolk and Norwich Hospital, and at Brighton and Hove Hospital for Women. In 1912 he took his F.R.C.S., and the same year he began his long association with Northampton when he received a house-appointment at the General Hospital. Soon afterwards war broke out and he joined the R.A.M.C., serving for a year in Mesopotamia.

On his return to Northampton he became assistant surgeon to the General Hospital in 1919, and he later joined the staffs of the Manfield Orthopaedic Hospital and the Kettering and District General Hospital. When he retired from the staff of the Northampton General Hospital in 1952 he was appointed emeritus surgeon. During his too short retirement he continued his habit of contributing cogent and incisive letters to our columns, and earlier this year he began his last article with the characteristic words: "After forty years' work I am still seeking the answer to the following questions about cancer of the breast . . ."

R. O. L. writes: "Charles Holman was a modest man who shunned publicity except when he had something of real importance to say. For this reason his merit as a surgeon may not have received full recognition outside his own area, and only those who worked beside him came to know and appreciate his true worth. Thirty-three years of consulting work gave him a vast experience which encompassed the whole range of general surgery and at one time included gynaecology and orthopaedics. In 1939 he formed the first fracture unit at Northampton General Hospital, and from then until 1946, in addition to his general work and with the aid of one houseman, he dealt with all fractures coming to the hospital. His capacity for work was enormous: holidays meant time lost from work and it was an exception for him to be away more than ten days in any year. In operating he was sound and generally conservative; in judgment sure, and in criticism generous."

"A quiet thoughtful man, he kept meticulous records; he also read widely in the medical journals, and his contributions to them were always well balanced and valuable since they were based on his own wide experience. His recreations were simple; lawn-tennis at which, despite a disability resulting from poliomyelitis in childhood, he was an enthusiastic performer and a difficult man to beat, and bridge which he enjoyed and took not too seriously."

"His name was a household word in Northamptonshire and North Bucks and he is mourned by all who knew him."

Mr. Holman is survived by his second wife, Miss V. Lewis, whom he married in 1924. Of the two sons of his first marriage to Miss V. E. Foxell, who died in 1921, one is a doctor.

EDWARD JAMES BOOME
T.D., M.B. Birm., M.R.C.P.

Dr. E. J. Boome, consultant in speech therapy to the London County Council, died on June 12 while on holiday in Devon.

He graduated M.B. from the University of Birmingham in 1907. After holding house-appointments in Birmingham at the General Hospital and the Queen's Hospital, he took the D.P.H. in 1912, and the following year he joined the public-health service of the London County Council. During the 1914–18 war he served in France as a Territorial medical officer, reaching the rank of major and being mentioned in despatches. On demobilisation he

returned to his post with the L.C.C. as assistant school medical officer and his work ranged widely over school medicine. He was an authority on the ascertainment of defective children. For a time he was visiting medical officer to the Farmfield Institution for Mental Defectives and lecturer to the nursing staff. In 1934 he was promoted to be a principal assistant medical officer. A pioneer in the study of speech defects, he was a founder fellow of the College of Speech Therapists. He was responsible for the development of speech therapy in the council's service and he became its consultant on the subject. He was the joint author of several textbooks on the nature and treatment of speech defects, including *Relaxation in Everyday Life* (1938) and *Abnormal Speech* (1939). For several years he also shared in the examination of the council staff, bringing to the work 'clinical skill and charm. His commanding presence, wit, and courtesy will make him difficult to replace.

Mrs. Boome survives him.

Dr. A. L. P. PEENEY

A. V. N. writes: "His fellow consultants will note the great gap caused by Peeney's absence from that mecca for friendly and constructive clinical chat—the warm and welcoming clinical pathology laboratory in the Queen Elizabeth Hospital at Edgbaston. His persistent ability to gather his clinical colleagues together for discussion on research work, and his inclination to leave himself somewhat in the background, were characteristic of the quiet unobtrusiveness of his daily life and work. Many resident officers and medical students have reason to be grateful for the trouble and care he gave to their laboratory work and instruction. Those of us who knew him more intimately came to understand a sound philosophic mind and a man who never withheld kindness and sincere help."

Dr. A. J. M. BUTTER.—Our obituary notice (June 12) contained a personal tribute from J. A. B. Y. This was a shorter and altered version of what was sent to us; and, as the writer informs us that he would not have wished it to appear in that form, we must express our regret that he had no opportunity to correct a proof before publication.

Appointments

BILLINGHURST, MARGARET A., M.B. Lond., D.O.M.S.: refractionist (S.H.M.O.), Westminster Hospital, London, S.W.1.
DREW, D. W. A., M.R.C.S.: anaesthetic registrar, South Devon and East Cornwall Hospital, Plymouth.
EDGAR, WILLIAM, M.B. Edin., D.P.H., D.C.H.: deputy M.O.H., and deputy school M.O., Luton.
GLOVER, J. R., M.B. Camb.: M.O., Westinghouse Brako and Signal Company, Ltd., Chippenham, Wilts.
KENNEDY, C. C. M.D.: consultant clinical pathologist, Belfast City Hospital.
MCGRATH, S. D., M.R.C.P.I., D.P.M.: physician in charge of clinical research, St. Patrick's Hospital, Dublin.
PRESTON, A. E., B.M. Oxf.: deputy director, blood-transfusion service, Oxford.
WINN, J. M., B.A. Camb., M.R.C.P., D.M.R.D.: consultant radiologist, Leeds General Infirmary.

Leeds Regional Hospital Board:

COXON, J. G., M.B. Lond., F.R.C.S.: part-time consultant in general surgery, Dewsbury and Halifax areas.
DONOVAN, J. F., M.R.C.S., D.P.M.: consultant psychiatrist and physician-superintendent, Broadgate Hospital, Beverley.
NEWCOMBE, JOHN, M.B., D.P.M.: consultant in psychiatry, mental deficiency hospitals and hostels, Hull and East Riding areas.
SMART, G. A., M.B. Glasg.: asst. chest physician (S.H.M.O.), chest clinics, hospitals, and sanatoria, Hull area.
WELEMINSKY, ANTONIN, M.D. Prague: asst. chest physician (S.H.M.O.), chest clinics, Pontefract, Goole, and Selby areas.

Liverpool Regional Hospital Board:

EDWARDS, K. C. S., M.R.C.S., D.P.M.: whole-time consultant psychiatrist, Deva Hospital.
GORE, C. P., M.D. Dubl., M.R.C.P.I., D.P.M.: whole-time consultant psychiatrist, Rainhill Hospital.
MARKS, K. L., M.B. Edin., M.C.H.(ORTH.) Lpool, F.R.C.S.E.: consultant orthopaedic surgeon, Chester and central Wirral areas.
STEAD, A. L. M.D. St. And., F.F.A. R.C.S.: part-time consultant anaesthetist, Liverpool city area.
WALKER, ERIC, M.D. Lpool, D.P.H., D.M.R.D.: part-time consultant radiologist, East Liverpool area.

The Hospital for Sick Children, Great Ormond Street, London:

CARTER, C. O., B.M. Oxf., M.R.C.P.: part-time medical geneticist (S.H.M.O.).
CLARK, WENDY A., M.B. Lond., F.F.A. R.C.S.: junior resident anaesthetist.
O'MEARA, P. A., M.B. N.U.I., D.L.O.: registrar, E.N.T. department.
SLOMAN, LIZBETH, M.D.: house-physician to Professor Moncrieff.

Notes and News

OUTPATIENT DEPARTMENTS

At a conference held by the Association of Hospital Management Committees in Scarborough on June 17-19, the Marquess of Normanby (chairman of the board of governors of King's College Hospital) said that, except for casualties, the outpatient department should be reserved for consultative and treatment clinics, to which patients must be referred by the general practitioner: "we should at all costs try to prevent the hospital entering into direct relationship with a member of the public, without going through the general practitioner." Meetings between hospital consultants and general practitioners helped to abate the pressure on this department. Consultants, for their part, might "weigh up in their hearts the value of their membership on each committee as set against the value of their regular and punctual attendance at outpatients." Those in charge of outpatient clinics should give priority to this work over any other, except emergency calls in the wards. As regards the structure of the department, "I am personally not at all impressed by palatial surroundings, but I am deeply impressed if there is someone at hand to discuss any problem arising or to explain to the patient the cause for delay or the cause for any other thing that has gone wrong." Outpatient departments contained much expensive equipment, which should be fully used. It was surely not impossible to envisage a modification of the idea of health centres based on the use of hospital outpatient departments in hours when the hospital doctors were not in attendance.

Mr. G. L. Thompson, as a consultant, spoke of the need for "simple" prescribing not only for inpatients but also for outpatients. Mr. S. Clayton Fryers (formerly chief administrative officer, Leeds United Hospitals) said that nine out of ten complaints came from dissatisfied outpatients. He did not know whether it had been established that the patient had a right to see a consultant: a large number were seen by more junior doctors. Beds might be saved if outpatients were examined thoroughly by consultants: commonly more junior members of the staff felt that they should admit patients, and it might thus be economic to have more consultants.

OUTPATIENT WAITING: THE OTHER SIDE

PATIENTS who do not keep their appointments were the subject of strong comment at a meeting of the Bournemouth and East Dorset Hospital Management Committee reported in the *Bournemouth Times* of June 4. Further facts were given by Mr. E. J. Whitney, secretary of Poole Hospital, in an interview with the *Poole Herald* (June 9). This hospital's house-committee, he said, had long been much concerned to reduce the time that outpatients waste, and by last October had managed to cut the average waiting-time to half an hour. But consultants complained that patients often ignored their appointments, and a check made over a period of five weeks showed that this was done by 88 new patients and 292 old patients—i.e., some 10% of all the patients treated during the period. "Not one of them gave us any warning, or contacted us in any way, in spite of the fact that the appointment card specifically asks them to notify us immediately if for any reason they are unable to attend." The time wasted in this way could have been used to reduce the delay of several weeks before new patients can be seen in some of the departments. Mr. H. R. Rees, deputy group secretary, stated that little could be done except to advise the doctor who fixed the appointment. "Then it is up to him to ask the patients why they did not turn up."

SICK-LEAVE FOR HOSPITAL STAFFS

Mr. G. A. Paines, secretary of the Croydon Hospital Management Committee, comments in the *Municipal Journal* (May 21) on "the apparent decline" in the health of some hospital employees of all grades since the inception of the National Health Service in 1948. "Matrons and hospital secretaries," he declares, "have often been worried, and at times distraught, particularly on the days following public holidays or weekends, by the increased incidence of periodical sickness, which has multiplied each year since 1949." In one group of hospitals, employing under 2000 people, the position became so serious that in 1952 the management committee decided on a special investigation.

An establishment subcommittee, comprising a doctor, a nurse, and a trade-unionist, all members of the management committee

looks into the periodical absences of all grades of staff and then recommends: (a) that the case be reviewed again in three, six, or twelve months; or (b) that the employee be sent for medical examination, after which his own doctor has the right to submit an opinion to the medical referee; or (c) where the medical referee has previously advised that ill health makes a person unsuitable for employment in his present job, and there is no alternative employment available, that reasonable notice be given to terminate employment.

The matter is then considered by the establishment committee, of which the chairman is a doctor not employed in the National Health Service. The investigating group, after further consideration, makes a recommendation to the management committee. A special committee to hear appeals, consisting of three members of the management committee who ordinarily have nothing to do with staff matters in the group, has been set up.

Since this procedure has been in operation 45 employees have had their services terminated. The management committee decided to send for medical examination those members of the staff nominated by the establishment subcommittee.

In the first ten months of the new arrangement the total amount of periodical sick-leave lasting three days or less (without medical certificate) fell by 6%, and sick-leave of over three days (with medical certificate) by 22%.

The inquiry revealed that in 1951 all sickness had increased from the 1947-48 levels as follows: nursing 60%; ancillary staff 25%; other staff 300%. Absences of one, two, or three days without medical certificate had increased by 200%. In 1953 non-resident staff averaged 33% more total sickness than resident; while full-time non-resident staff had a higher proportion of sick-leave than part-timers. Full-time non-resident nurses had 50% more sick-leave than residents; similarly sick-leave among non-resident ancillary staff was 250% greater, and among part-time ancillary staff 300% greater.

Mr. Paines concludes that other employing authorities may wish to collect similar statistical information. "The comparisons may surprise."

A REGISTER OF BENEFITS

The Ministry of Pensions and National Insurance have revised their helpful booklet, *How, When, and Where to Claim Benefit*, which gives a clear summary of the different benefits to which the sick, injured, unemployed, pregnant, or ageing citizen is entitled. As its title promises it gives succinct instructions as to how and where he (or she) should set about making his claim, and it ends with a list of the standard weekly rates offered in each category. Free copies of the booklet may be had from the information division of the Ministry, 10, John Adam Street, London, W.C.2.

FOUNDRY-WORKERS

The general secretary of the Amalgamated Union of Foundry Workers has issued for his members a booklet¹ which tells them what is being done for their health, safety, and welfare. It is divided into five parts, with a preamble which gives a somewhat unbalanced account of the formation of the two committees which have dealt with conditions in steel and iron foundries respectively.

Part 1 contains in full the recommendations of the Joint Advisory Committee on Conditions in Iron Foundries,² but not those of the senior committee on dust in steel foundries which is only mentioned in passing. The new Iron and Steel Foundries Regulations, 1953, are given in full with notes on each regulation. Regulation 7, which deals with the suppression of dust in fumes, is said to be the "most comprehensive in its general effect, dealing as it does with the greatest hazard in the industry." Subsection 6 of regulation 7 says that "all dressing or fettling operations shall be carried out in a separate part of the foundry suitably partitioned off; or in an area of the foundry set apart for the purpose; and shall, so far as reasonably practicable, be carried out with effective and suitable local exhaust ventilation or other equally effective means of suppressing dust, operating as near as possible to the point of origin of the dust." The regulation does not come into operation until Jan. 1, 1956—i.e., twelve years after the setting up of the Dust in Steel Foundries Committee, which was appointed primarily to deal with the problem of dust in the fettling of steel castings. Descriptions and illustrations are given of a new fettling bench to which exhaust ventilation is applied; of an improved exhausted grinding machine; of a swing frame grinder fitted with exhaust ventilation; and also of a new hollow exhausted

pneumatic chisel. We hope that these and other improved machines will speedily be installed in all foundries even before 1956, because the medical branch of the Factory Department has been drawing attention, since before the 1939-45 war, to the serious risk of silicosis in steel fettlers. The risk to health was again emphasised in 1950 in the comprehensive report by A. I. G. McLaughlin and his co-workers.³

In the preamble to the booklet it is stated that a new joint standing committee on non-ferrous foundries has now been appointed. It is added that there is ample scope for intensive investigation into conditions in this group of foundries and that a review of the Brass Casting Regulations, 1908, is overdue. Part 3 contains in full 15 different codes of regulations which apply in varying degree to foundries, and in particular the Blasting (Castings and other Articles) Regulations, 1949, under which the use of sand as an abrasive is prohibited; and the Foundries (Parting Materials) Special Regulations which prohibit the use of siliceous parting powders. Both these codes of regulations were issued as a result of the recommendations of the joint standing committees and constitute real advances in preventive medicine.

In Part 4 extracts are quoted from the Factories Act, 1937, which are relevant to foundries. One important section (119) imposes duties on the workers to use (and not misuse) any appliance which is installed in a factory to secure their health or safety. The general secretary exhorts his members to play their part in using properly the facilities and equipment which the employers are legally obliged to supply. "By mutual appreciation of the benefits to be obtained by the improvements introduced, the foundry can be made a much healthier place than ever before."

Part 5 gives in full the National Insurance (Industrial Injuries) (Prescribed Diseases) Amendment Regulations, 1954; a list of the prescribed diseases; and (rather out of context) a description of some practical measures for reducing the amount of fume from oil-bonded cores.

Altogether, this is a useful compendium of information about the legal and practical aspects of foundry work.

TEETHING-POWDERS

In a memorandum to lay journals the Ministry of Health makes the following observations on "so-called teething-powders":

Babies seldom, if ever, really need powders.

Most powders contain drugs which are harmless in an occasional dose, but which may be harmful if used repeatedly.

No mother should undertake the responsibility of repeated medication of a baby or young child without medical advice.

Babies and young children should never be given a routine "weekly aperient" whether as a "powder" or in any other form.

If a mother thinks her baby needs "powders" it is probable that there is something amiss in the feeding or management. Dosing with "powders" may only lay up trouble for the future, and she should talk things over with her family doctor or the doctor at the clinic, or ask the health visitor to come to see her.

HEALTH STATISTICS

The first International Conference of National Committees on Vital and Health Statistics, held in London last October,⁴ was attended by delegates from twenty-eight countries (members or associate members of the World Health Organisation). The report of the conference, now issued,⁵ deals with the health and vital statistics required by the various countries and methods of improving their quality, and with the implementation of international regulations or recommendations of previous W.H.O. committees.

LONDON MEDICAL ORCHESTRA

About six months ago, a group of doctors, dentists, and nurses formed this orchestra. They gave their first concert in April, and on June 18 some of their members entertained the London Association of the Medical Women's Federation and their friends to an evening's music-making at the Royal Free Hospital School of Medicine. Works by Bach, Purcell, and Mozart were performed with a skill and understanding remarkable for an amateur ensemble. The large audience showed a particular liking for the performance of Bach's Brandenburg Concerto No. 5, in which a young medical student achieved a near-professional standard in playing the difficult part for the solo pianoforte.

3. Industrial Lung Diseases of Iron and Steel Foundry Workers. By A. I. G. McLAUGHLIN (with the assistance of others). H.M. Stationery Office, 1950. See *Lancet*, 1950, ii, 576.

4. See *Lancet*, 1953, ii, 867.

5. *World Hlth Org. techn. Rep. Ser. no. 85*. H.M. Stationery Office. Pp. 27. 1s. 9d.

1. Health, Safety and Welfare in Foundries. Issued by the Amalgamated Union of Foundry Workers, 164, Chorlton Road, Brooks's Bar, Manchester, 16. Pp. 110. 2s. 6d.

2. See *Lancet*, 1947, ii, 292.

RADIO IN CARS

THE Mobile Radio Users Association is seeking to ensure that the frequencies allotted to doctors with two-way radio in their cars shall not be interrupted by other users in the band. Those interested are invited to join the association and use its technical and legal services; the minimum annual subscription is one guinea, which includes a monthly newsletter. Further particulars may be had from Mr. Ronald Simms, secretary of the association, Buckingham Court, Buckingham Gate, London, S.W.1.

THE DORSET COASTLINE

THE lovely stretch of coast between Weymouth and Lyme Regis, with its wealth of tradition and local lore, and its old seaports, churches, and monuments, is handsomely celebrated, with the aid of many fine photographs, by a Dorset ex-Naval Surgeon.¹ Yachtsmen will enjoy the sailing yarns, and lovers of the English countryside and of wild birds will find much to delight them.

University of Oxford

Mr. P. R. Allison, thoracic surgeon to the Leeds United Hospital and the Leeds Regional Hospital Board, has been elected Nuffield professor of surgery from Oct. 1. Since the death of Sir Hugh Cairns in 1952 the chair has been vacant.

In 1927 Mr. Allison took his B.Sc. at the University of Leeds with first-class honours in physiology, and four years later he graduated M.B., again with first-class honours. After holding resident appointments at the Leeds General Infirmary he took his F.R.C.S. in 1932, and the following year he was appointed surgical tutor and registrar at Leeds University and in 1936 clinical lecturer in surgery. The same year he proceeded to the degree of C.H.M. and joined the honorary staff of the infirmary as assistant surgeon. In 1941 his specialist interest in chest surgery was recognised by his appointment as thoracic surgeon to the infirmary and clinical lecturer in thoracic surgery in the university, and he is at present in charge of the thoracic surgical department at the infirmary and regional consultant in his specialty. His numerous publications include papers on the reconstruction of the oesophagus and on the surgical treatment of carcinoma of the lung.

University of Sheffield

The Nuffield Foundation is to establish a research fellowship at the Sheffield centre for the investigation and treatment of rheumatic diseases.

University of Birmingham

Dr. Brian MacMahon has been appointed lecturer in social medicine. The following have been appointed part-time lecturers in obstetrics and gynaecology: Mr. A. L. Deacon, Mr. W. G. Mills, and Miss Dorothy Shotton.

University of Leeds

The council have instituted a new part-time chair of psychiatry and appointed to it Prof. D. R. MacCalman, formerly professor of psychiatry and head of the department of psychiatry.

This change has been made in deference to medical advice given to Professor MacCalman; it will enable him to devote himself to those sections of psychiatry in which he is especially interested, while relieving him of a substantial burden of administrative responsibility. It is expected that in due course a successor to him in the whole-time chair and the headship of the department will be appointed. Meanwhile, Dr. Mary Burbury, senior lecturer in child psychiatry in the university, will act as head of the department.

Royal College of Obstetricians and Gynaecologists

Two public lectures will be given in connection with silver jubilee celebrations which are being held at the college on July 13, 14, 15. On Wednesday, the 14th, Sir William Fletcher Shaw will deliver the William Meredith Fletcher Shaw lecture on The College—its Past, Present, and Future. On Thursday the 15th, Prof. Bruce T. Mayes, of Sydney, who is visiting this country as the Sims-Black professor, will deliver the William Blair-Bell lecture on the Making of an Obstetrician. Both lectures will be given at 11.30 A.M. at 1, Wimpole Street, London, W.1.

International Children's Centre

Some fellowships will be available for those who wish to work at the laboratories of the centre in Paris during 1954–55.

At present the programme of research of the centre is mainly devoted to anti-tuberculosis vaccination and anti-pertussis immunisation. Further particulars may be had from Professor Bugnard, International Children's Centre, Château de Longchamp, Paris 16.

1. The Dorset Coastline. By LLEWELLYN PRIDHAM, M.R.C.S. E.N. ret'd. Photography by Edward Kestin, Dorchester: Longmans (Dorchester) Ltd. 1954. Pp. 126. 25s.

Ophthalmological Society of the United Kingdom

Dr. Robert Leishman (Glasgow) has been awarded the 1954 Treacher Collins prize for his essay on the Eye in General Vascular Disease: Hypertension and Arteriosclerosis.

Royal Medico-Psychological Association

The following have been successful in the association's examinations for the diploma in psychological medicine:

J. K. Arkle, U. B. H. Baruch, N. C. Connell, T. B. Stephens, R. M. Taylor.

British Diabetic Association

The annual scientific meeting of this association is to be held at University College Hospital Medical School, London, W.C.1, on July 16 and 17. On Friday, the 16th, at 2.30 p.m., Dr. K. Hallas-Møller (Copenhagen) will deliver the Banting lecture, on the Chemical and Physiological Background of the new Insulin Zinc Suspensions. The programme will also include discussions on the insulin zinc suspensions (opener, Dr. W. G. Oakley), and plasma-insulin estimations (Dr. P. J. Randle and Dr. J. Vallance-Owen). Further particulars can be had from the secretary of the association, 152, Harley Street, London, W.1.

Service Conference

A joint Services medical-surgical diagnostic and therapeutic conference is to be held at the U.S. Embassy, 5, Grosvenor Square, London, W.1, on July 22, 23, and 24. Speakers will include officers from the U.S. Air Force, the Royal Air Force, the Royal Army Medical Corps, the Royal Naval Medical Service, and the United States Navy, and British civilian physicians and surgeons. The conference is open to Service and civilian doctors. Further information may be had from Colonel L. Render Braswell, Headquarters Third Air Force, Office of the Surgeon, Victoria Park Estates, South Ruislip, Middlesex.

Medical Honours

Captain D. R. Boyns, B.A.M.C., has been appointed M.B.E. in recognition of distinguished services in Malaya.

In announcing the award *The Times* (June 19) relates that Captain Boyns fractured his back in a parachute descent in the Malayan jungle. But from the moment he landed he immediately started to help others who had been injured, moving from place to place over rough country. No-one knew that he had himself been hurt until after the operation was over.

Captain Alasdair Fraser-Darling, R.A.M.C., has been appointed M.B.E. in recognition of brave conduct in Libya on Jan. 15–16.

CORRIGENDUM: *The Disabled*.—The M.R.C. memorandum by Prof. T. Ferguson mentioned in our leading article (June 5) is no. 28.

Diary of the Week**JUNE 27 TO JULY 3**

Tuesday, 29th
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. H. J. Wallace: Endocrine Disorders Affecting the Skin.

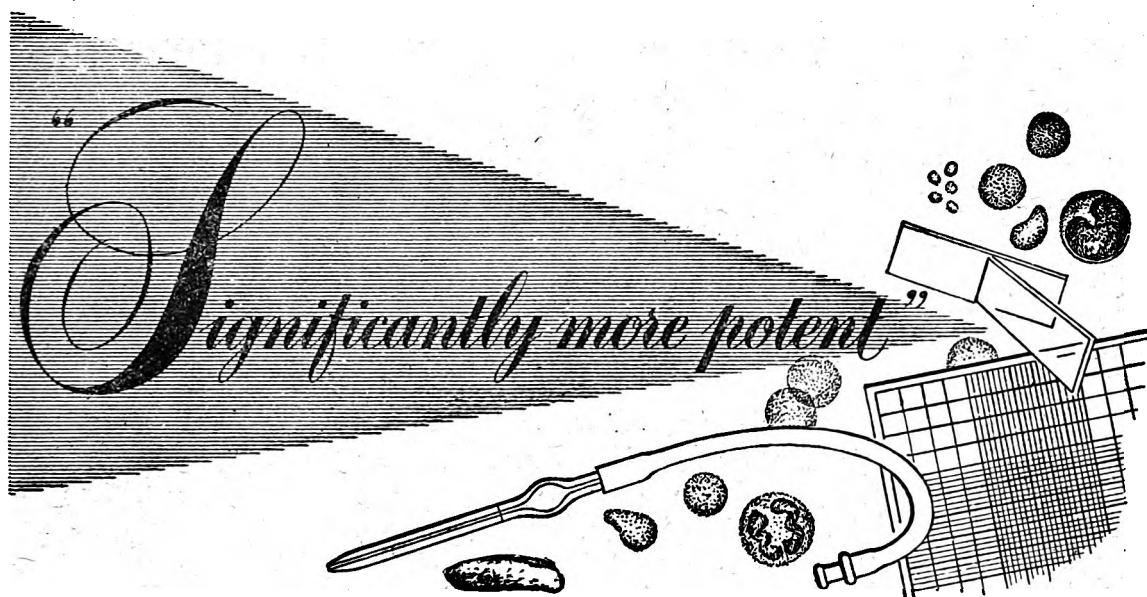
Wednesday, 30th
POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
2 P.M. Prof. T. F. Hewer: Gastritis.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. O. Oliver: Mycobacteria in Skin Disease.

Thursday, 1st
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
6.30 P.M. Mr. J. E. Piercy: Diseases of Thyroid, Parathyroid, and Thymus Glands.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. J. F. Goodwin: Peripheral Vascular Disease.
4.30 P.M. Dr. R. I. S. Bayliss: Adrenal Function in Health and Disease.

Friday, 2nd
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Prof. C. G. Rob: Blood-vessel Grafting.
INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children, Great Ormond Street, W.C.1
5 P.M. Dr. T. Ehrenpreis (Stockholm): Hirschsprung's Disease.

Births, Marriages, and Deaths**BIRTHS**

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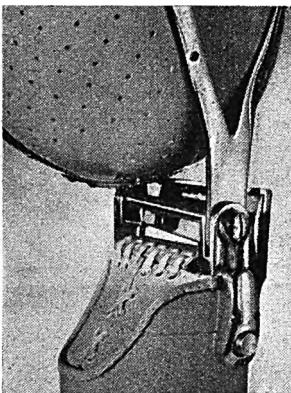
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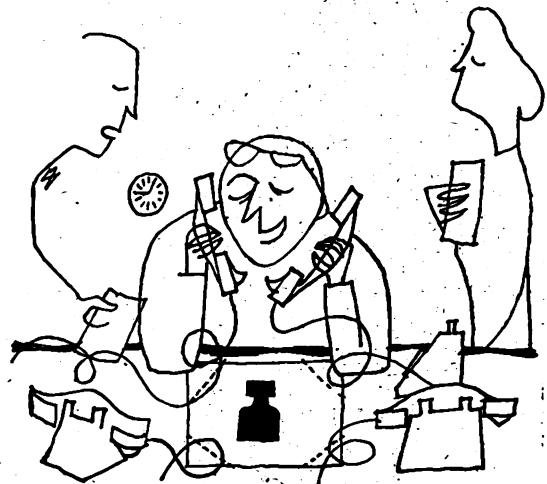
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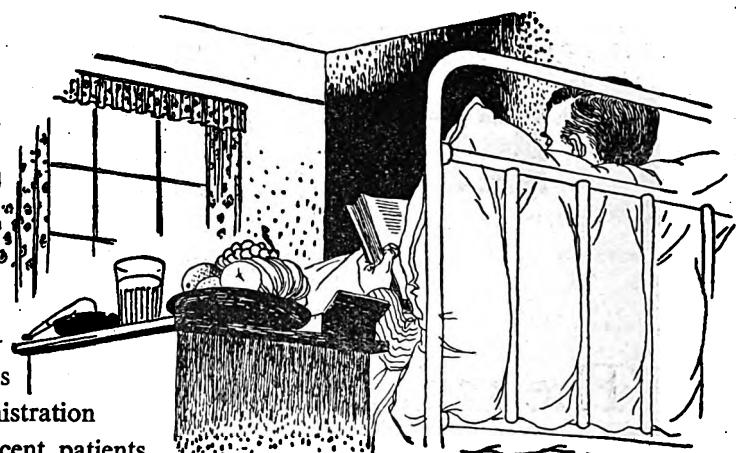
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The first stable, standardised preparation of senna*

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From the 2lb, tax free, dispensing pack,
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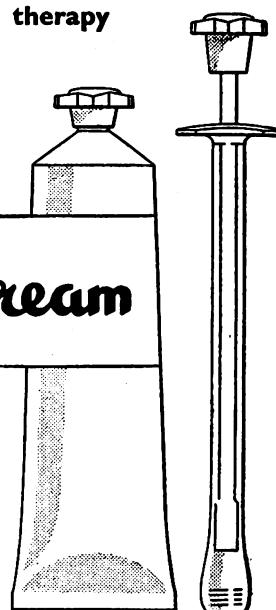


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for maximum effectiveness
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following cervical cautery¹
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* Sulphathiazole
N'Acetyl sulphamamide
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with Urea peroxide
in a highly absorptive
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1. Am.J.Obst. & Gynec. 58:176. 1949
2. Am.J.Obst. & Gynec. 55:511. 1948
3. Am.J.Obst. & Gynec. 61:680. 1951

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LITERATURE ON REQUEST

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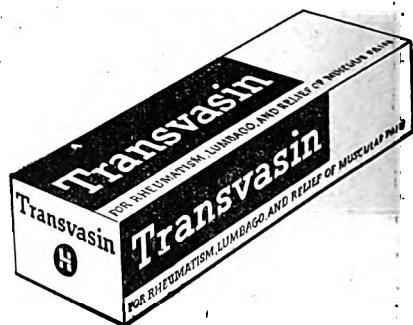
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Contains skin-penetrating esters of salicylic, nicotinic, and p-aminobenzoic acids. It brings real relief to deep-seated muscular rheumatism by simple inunction.

TRANSVASIN, a new preparation developed by Hamol S.A., our Swiss associates, and now available for prescription in this country, contains polar esters of salicylic, p-aminobenzoic and nicotinic acids. These esters readily pass the skin barrier in therapeutic quantities and enable an effective concentration of the drugs to be built up where they are needed. Transvasin not only induces vasodilation of the skin with a superficial erythema, but also brings about a deep hyperaemia of the underlying tissues. It is non-irritant, and can be safely used on the skin.

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<i>Salicylic acid tetrahydrofuryl-ester</i>	14%
<i>Nicotinic acid ethyl-ester</i>	2%
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<i>p-Aminobenzoic acid ethyl-ester</i>	2%
<i>Water-miscible cream base ad</i>	100%

Transvasin is available in 1 oz. tubes at 3/4 $\frac{1}{2}$ plus 7 $\frac{1}{2}$ d P.T., which are obtainable on form E.C.10, and is not advertised to the public.

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are needed for
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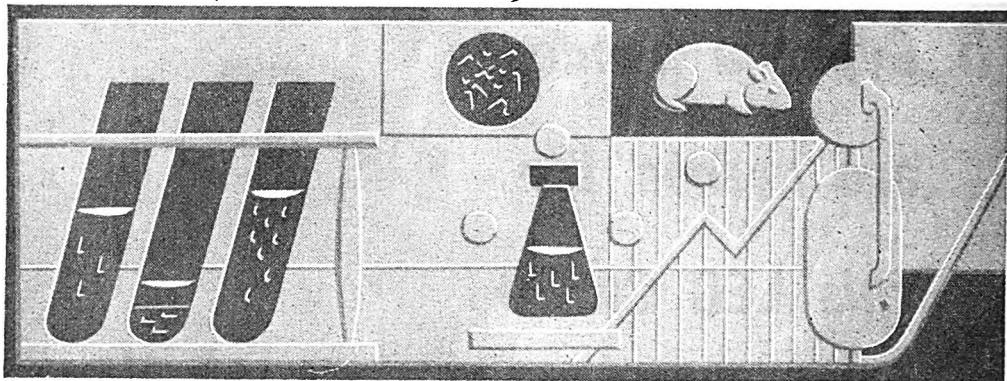
This leg cast was constructed with three 6" x 3 yds. and three 4" x 3 yds. Gypsona bandages. Two 6" bandages were made into a slab and laid down the back of the leg and

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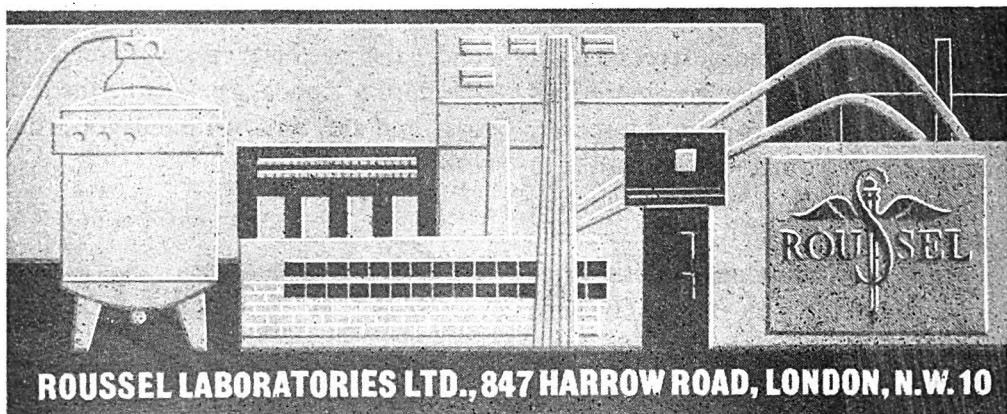
Local injection, 25 mg. per cc.; 5 cc. vials
Skin ointment, 1% & 2.5%; 5 G tubes
Eye drops, 1% suspension; 3 cc. dropper bottles

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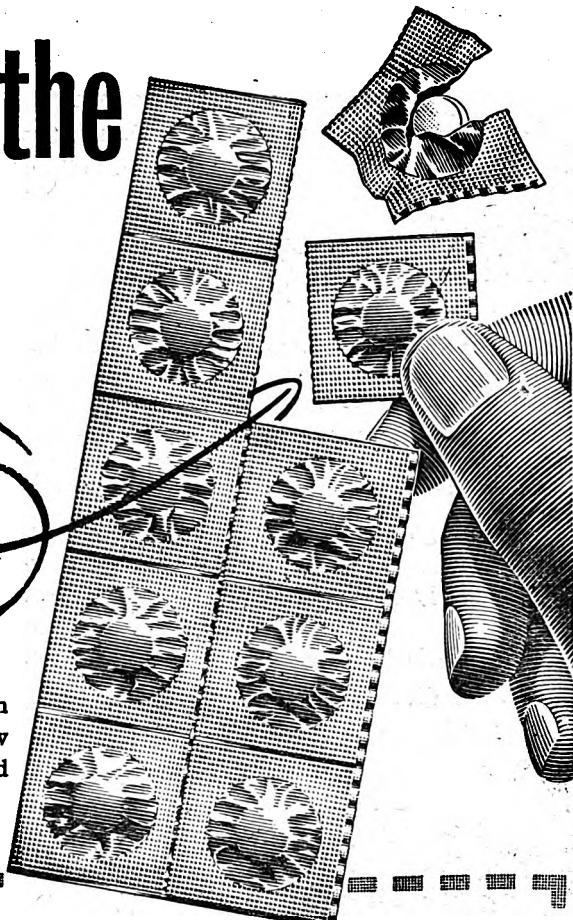
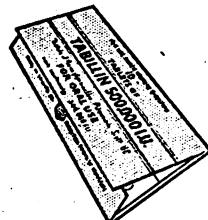


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protects
each tablet
until used*

*individually
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—detached
as required*

— a most important consideration in oral penicillin therapy, which is now established as a satisfactory method of systemic administration.



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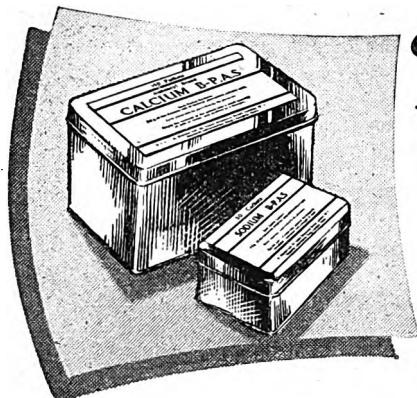
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Bulk Powder1kg. 5kg.

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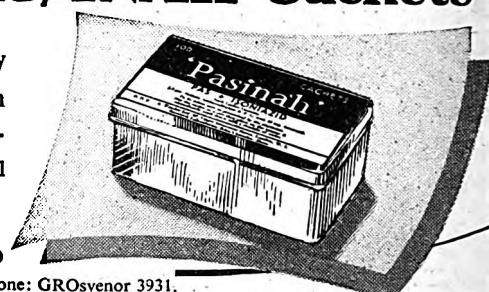
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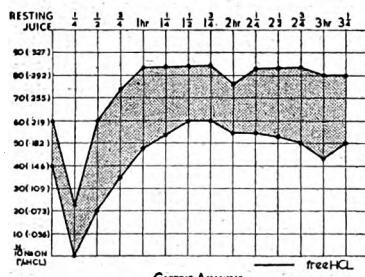


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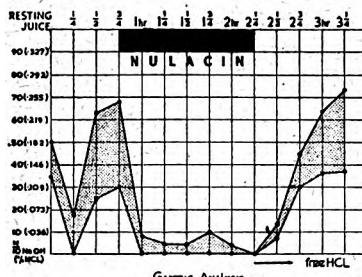


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BIBLIOGRAPHY:

- The Control of Gastric Acidity, 26th July, 1952, Brit. Med. J., 180-182
- Medical Treatment of Peptic Ulcer, 27th February, 1952, Med. Press, 195-199
- The Effect on Gastric Acidity of "Nulacin"

Tablets, 28th November, 1953, Med. J. Aust. 823-824

Control of Gastric Acidity by a New Way of Antacid Administration, (1953), J. Lab. Clin. Med. 42:955

Further Studies on the Reduction of Gastric Acidity, 23rd January, 1954, Brit. Med. J., 183-184

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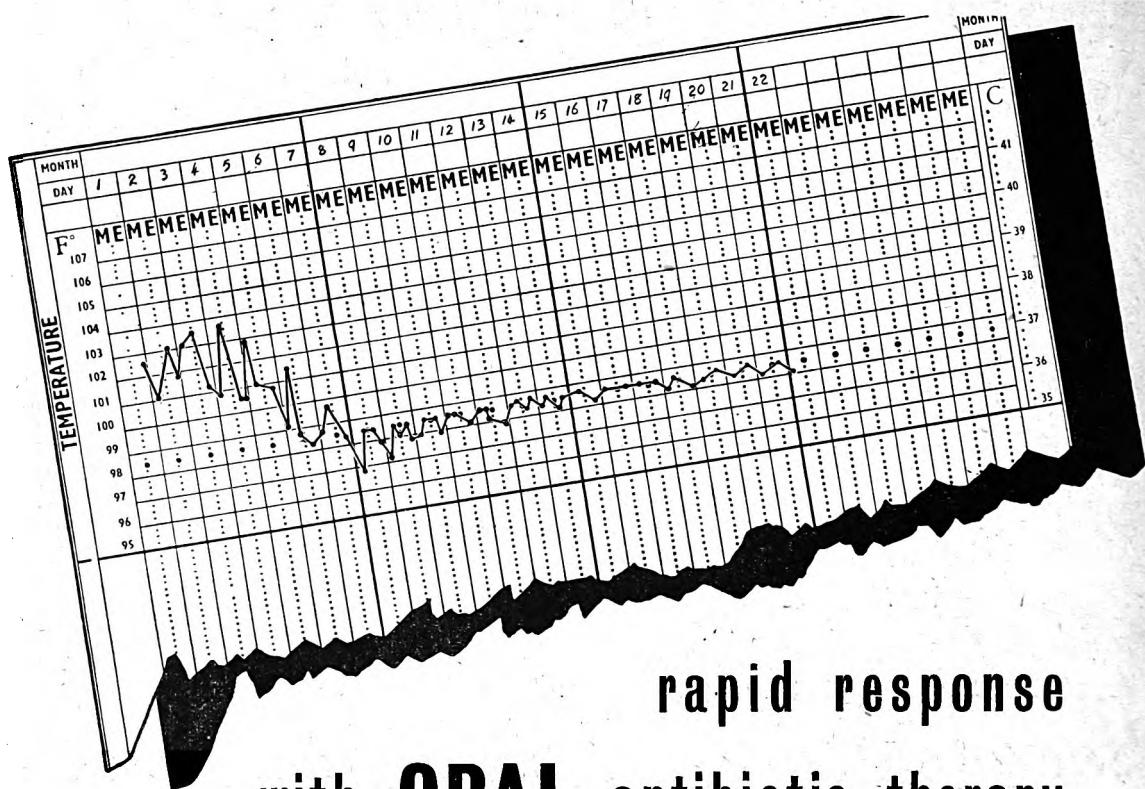
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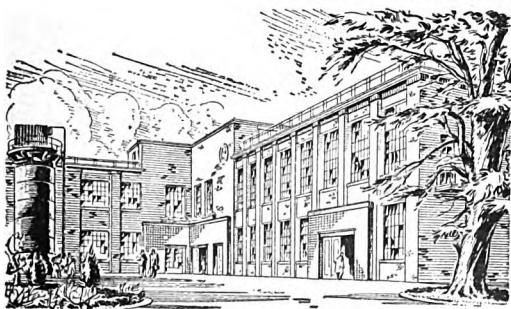
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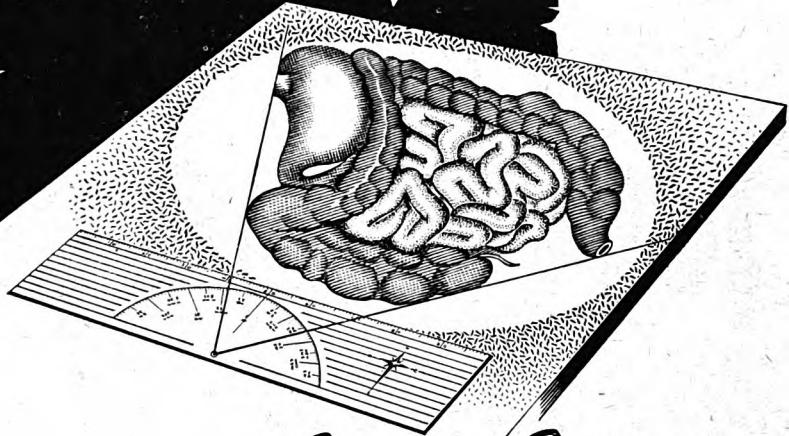
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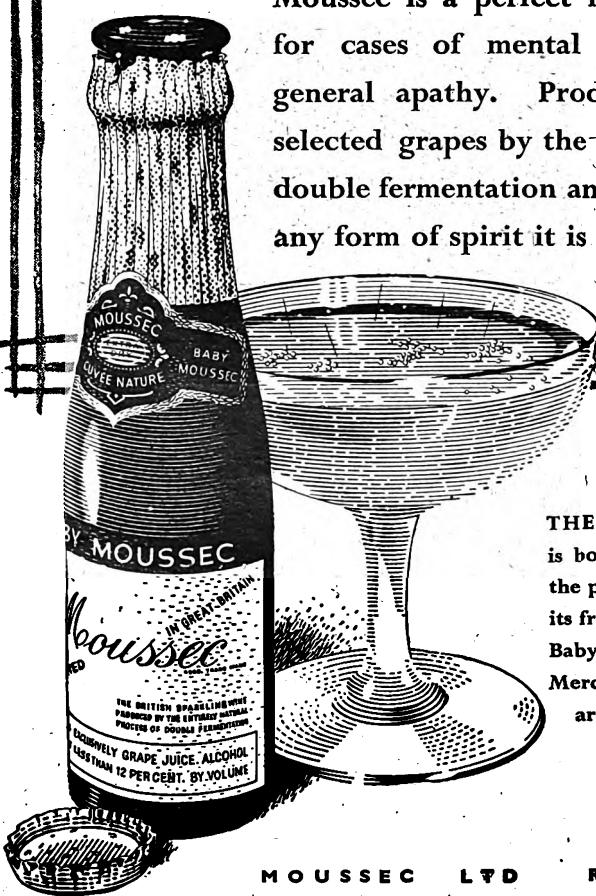
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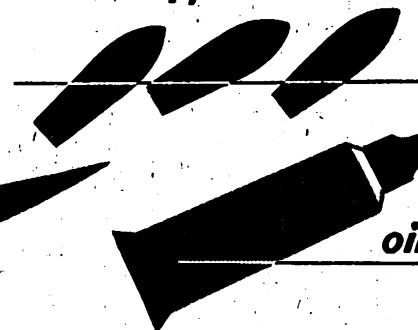


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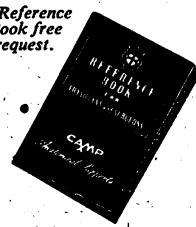


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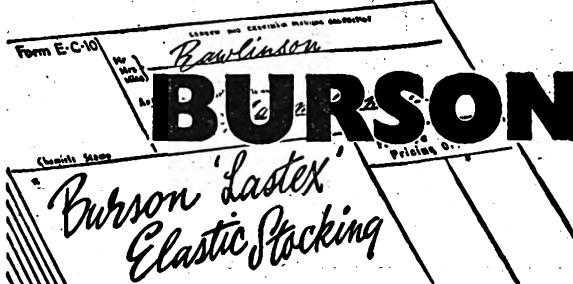
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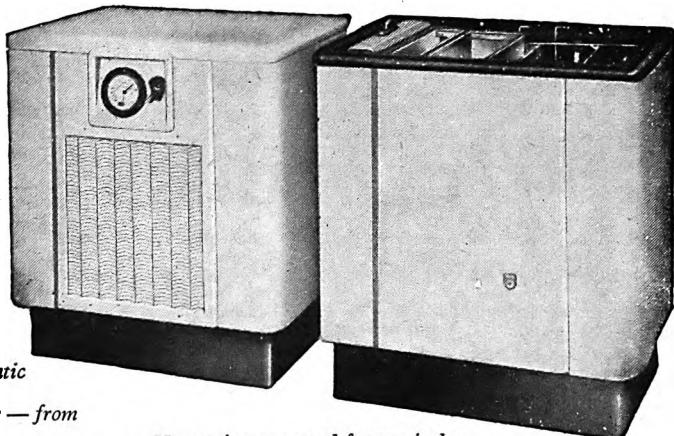
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Stoke-on-Trent. North Staffs Royal Infy. Sr. H.O.	44	St. Leonard's. N.1. H.O.	34	Wolverhampton Group. H.O.'s	46
Wolverhampton Group. Sr. H.O. or H.O.	45	Aberystwyth Gen. Pre-reg. H.O.	34	York A & Tadcaster H.M.C. Sr. H.O.	46
Yorkshire. East Riding H.M.C. H.O.	46	Ashton. Hyde & Glossop H.M.C.	35	Yorkshire. East Riding H.M.C. H.O.'s	46
Ireland. Incorporated Orthopaedic Hosp. of Ireland. R.M.O.	47	H.O.'s	35		
PEDIATRICS		Bedford Gen. Pre-reg. H.O.	35	TROPICAL MEDICINE	
Brentwood. High Wood Hosp. for Child. Temp. Reg.	36	Birmingham. Dudley Rd. H.O.	35	Liverpool. Sefton Gen. H.O.	40
Chelmsford. St. John's. H.O.	37	Birmingham. R.H.B. Regs.	35		
Edgware Gen. H.O.	38	Bishop Auckland Gen. H.O.	36	UROLOGY	
Edinburgh. Princess Margaret Rose. Sr. H.O.	38	Blackburn & Dist. H.M.C. H.O.	36	St. Peter's. St. Paul's and St. Philip's Hosp. & Inst. of Urology. Reg.	34
Edinburgh. Royal Hosp. for Sick Child. Sr. H.O.	38	Bolton Royal Infy. H.O.	36	Leeds United Hosps. Sr. H.O. or Pre- reg. H.O.	39
Halifax Gen. H.O.	38	Brighton. Gen. H.O.	36	South-East Met. R.H.B. Reg.	44
Hastings. St. Helen's. H.O.	38	Burton-on-Trent Gen. Infy. H.O.	36		
Manchester. Duchess of York Hosp. for Babies. H.O.	38	Cambridge. Addenbrooke's. H.O.	37	VENEREOLOGY	
Mid-Glamorgan H.M.C. Sr. H.O.	41	Cardiff. Rookwood. Sr. H.O.	37	Bristol. Cossham/Frenchay H.M.C. Jr. H.M.O.	36
Norwich. Norfolk & Norwich. H.O.	42	Carlisle. Cumberland Infy. H.O. or	37		
30		Locum	37	GENERAL	
		Chelmsford & Essex. Pre-reg. H.O.	37	New York. New Rochelle. Internes	47
		Chesterfield Royal. H.O.'s	37		
		Colchester Group H.M.C. H.O.	37	PUBLIC APPOINTMENTS	
		Colchester Group H.M.C. Sr. H.O.	37		
		Darlington Mem. H.O.	37	GENERAL PRACTICE	
		Derby. Derbyshire Child's. Pre-reg.	37		
		H.O. or Sr. H.O.	37	MISCELLANEOUS	
		Derby. Derbyshire Royal Infy. Pre- reg. H.O. or Sr. H.O.	37		
		Doncaster Royal Infy. H.O.	37	The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.	

Academic and Educational**ROYAL COLLEGE OF PHYSICIANS OF LONDON**

Dr. ERNEST BASIL VERNET, F.R.C.P., F.R.S., will deliver the BERTRAM LOUIS ABRAHAMS LECTURE on THURSDAY, 8TH JULY, 1954, at 5 P.M. at the College, Pall Mall East, S.W.1.

Subject: "Some Aspects of the Renal Excretion of Water and Salt."

Any member of the Medical Profession admitted on presentation of card.

By order of the President.

HAROLD BOLDERO, Registrar.

UNIVERSITY OF LONDON

A LECTURE entitled "Some Observations of Electrical Activity in Normal and Pathological Muscles" will be given by Prof. A. R. MCINTYRE (Nebraska) at 5.30 P.M. on 6TH JULY at Guy's Hospital Medical School, St. Thomas's-street, London Bridge, S.E.1.

Admission free, without ticket.

JAMES HENDERSON, Academic Registrar.

UNIVERSITY OF DURHAM**KING'S COLLEGE, NEWCASTLE UPON TYNE****COURSES OF INSTRUCTION FOR THE POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE**

Part I—A part-time course will be given on 1½ days a week throughout the year, commencing in OCTOBER. Fee £20.

Part II—A full-time 6 months course in Psychiatry and Neurology commences in OCTOBER. Fee £40.

The above courses are integrated with the Newcastle and Sheffield Regional Hospital Board Training Scheme for Psychiatrists. Arrangements can be made for candidates from overseas to complete the requisite clinical experience during the 6 months course.

Separate courses, including clinical experience, are available in Neurology (2 terms; fee £15) and Child Psychiatry (2 months; fee £25).

Further particulars, regulations and syllabus for the Diploma and application forms, may be obtained from the Assistant Registrar, The Medical School, King's College, Queen Victoria-road, Newcastle upon Tyne, 1.

G. R. HANSON, Registrar of King's College.

UNIVERSITY OF EDINBURGH**CHAIR OF PSYCHIATRY**

The University of Edinburgh will shortly proceed to make an appointment to the Chair of Psychiatry which will become vacant on 1st OCTOBER, 1954.

The terms and conditions of appointment may be obtained from the undersigned, with whom applications (8 copies), giving the names of 2 referees and including any testimonials or evidence candidates may wish to offer, should be lodged not later than 15th July, 1954.

Overseas candidates may submit 1 copy of their application which should be received not later than 15th August, 1954.

CHARLES H. STEWART, Secretary to the University.

THE UNIVERSITY OF LEEDS**DIPLOMA IN PSYCHOLOGICAL MEDICINE**

A course for the Diploma in Psychological Medicine will commence in OCTOBER, 1954, if sufficient entries are received. Instruction will be part-time and will occupy 3 half-days a week during 8 academic terms (2½ years).

Further particulars may be obtained from the Sub-Dean, School of Medicine, Leeds, 2, to whom application for admission to the Course should be sent as soon as possible.

SOCIETY OF APOTHECARIES OF LONDON**DIPLOMA IN INDUSTRIAL HEALTH**

The next Examination will begin on MONDAY, 5TH JULY, 1954. The following Examination will be held in December, 1954.

For Regulations apply Registrar, Apothecaries' Hall, Black Friars-lane, London, E.C.4.

CANCER RESEARCH
M.O. GORDON WILL TRUST

Clause 11 of the Will of the late Mrs. M. O. Gordon directs her Trustees to apply her residuary Trust Fund for Cancer Research to be made by investigators of either sex selected by her Trustees, such investigators to be graduates in medicine over 21 and British subjects born in Great Britain.

Applications by any persons interested should be addressed to the undersigned before 24th July, 1954, giving qualifications, proposed research, amount of grant required, the period of time for which the grant is to be effective, and references.

GODWIN, BREMRIDGE & Co., Trustees' Solicitors.

8, St. Thomas-street, Winchester.

THE WELSH NATIONAL SCHOOL OF MEDICINE. (UNIVERSITY OF WALES.) SENIOR LECTURER in the Department of Obstetrics and Gynaecology. Applications are invited for the post of Senior Lecturer in the Department of Obstetrics and Gynaecology of The Welsh National School of Medicine. The person appointed will be required to assist in the work of the Professorial Department as directed by the Professor, and in the care of patients at the Cardiff Royal Infirmary and other hospitals. The post is full-time with salary on the scale £1500-£100-£2000 p.a. Schemes of superannuation and family allowances apply to the appointment.

Further particulars may be obtained from the undersigned, with whom applications should be received within 3 weeks of the appearance of this advertisement.

34, Newport-road, Cardiff.

F. DODSWORTH, Secretary.

THE WELSH NATIONAL SCHOOL OF MEDICINE. (UNIVERSITY OF WALES.) SENIOR LECTURER for Medico-legal Services and for Teaching in Forensic Medicine. Applications are invited for the post of Senior Lecturer in Forensic Medicine. The appointment is full-time and the salary will be on the scale £1500-£100-£2000 p.a., with participation in the superannuation and family allowance schemes. There are facilities for research.

Further particulars may be obtained from the undersigned, by whom applications should be received within 3 weeks of the appearance of this advertisement.

34, Newport-road, Cardiff.

F. DODSWORTH, Secretary.

THE WELSH NATIONAL SCHOOL OF MEDICINE. (UNIVERSITY OF WALES.) Senior Lecturer (Clinical Bacteriologist). Applications are invited for the post of CLINICAL BACTERIOLOGIST (grade—Senior Lecturer). The duties will include hospital bacteriology and teaching. The appointment is full-time and the salary will be on the scale £1500-£100-£2000 p.a., with participation in the superannuation and family allowance schemes. There are facilities for research.

Further particulars may be obtained from the undersigned, by whom applications should be received within 3 weeks of the appearance of this advertisement.

34, Newport-road, Cardiff.

F. DODSWORTH, Secretary.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. BERNARD BARON MEMORIAL RESEARCH LABORATORIES. A REGISTRAR will be required in September at the above Laboratories. Previous specialised experience is not essential. The successful candidate will receive training in serology and bacteriology, and may later assist in the research work. The post is resident, but it may be possible to live out by arrangement.

Applications to the Secretary to the Board of Governors by 5th July on forms obtainable from 339, Goldhawk-road, London, W.6.

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL, BACTERIOLOGY DEPARTMENT. ASSISTANT required, medically qualified, preferably with experience of bacteriology. Duties consist of teaching and research. Salary scale £700-£900 p.a., with superannuation benefits and children's allowance.

Applications should be made immediately to the Secretary of University College Hospital Medical School, University-street, London, W.C.1.

UNIVERSITY OF LONDON KING'S COLLEGE will require on 1st October, 1954, a LECTURER IN PHYSIOLOGY. The appointment will be on the Junior Lecturer scale of £600-£50-£2750, with family allowances and F.S.S.U. benefits.

Particulars and application forms should be obtained from the Registrar, King's College, Strand, W.C.2, whom completed applications should reach by 10th July.

THE UNIVERSITY OF LIVERPOOL. Applications are invited for the post of LECTURER in the Department of Bacteriology. Preference will be given to medically qualified candidates. The salary will be within the range £900-£1200 p.a. according to age, qualifications and experience of the successful candidate.

Applications, stating age, qualifications and experience, together with the names of 3 referees, should be received not later than 3rd July, 1954, by the undersigned, from whom further particulars may be obtained.

STANLEY DUMBELL, Registrar.

THE UNIVERSITY OF SHEFFIELD. Applications are invited for a Part-time RESEARCH ASSISTANT IN CHILD HEALTH to assist in an investigation in the prevention of tuberculosis in children, to begin duties on 1st October, 1954. The appointment will be for 1 year in the first instance and the duties of the post will occupy 4 half-days a week. Salary 12 guineas a week.

Further particulars should be obtained from the Registrar with whom applications (3 copies) should be lodged by 10th July, 1954.

UNIVERSITY OF ABERDEEN. Applications invited for LECTURSHIP IN PATHOLOGY. Salary £600-£100-£2900 or £1000-£100-£1300 (initial placing according to qualifications and experience), with F.S.S.U. and children's allowance. Part of furniture removal expenses to Aberdeen refunded.

Conditions of appointment and forms of application should be obtained from the undersigned, with whom applications (8 copies) should be lodged by 17th July, 1954. Candidates outside the British Isles need submit 1 copy only of their letter of application.

The University, Aberdeen.

W. S. ANGUS, Secretary.

UNIVERSITY OF MALAYA, Singapore. Applications are invited for 2 ASSISTANT LECTURESHIPS IN ANATOMY. Salary £735 p.a. Allowances: expatriation £210 p.a., cost-of-living in range £294-£477 p.a., for medical qualification (temporary) £210 p.a. All paid in Malayan currency. Free passages for appointee, wife, and children under 12 years. Part-furnished quarters at low rent or housing allowance in lieu. Provident fund scheme.

Applications (6 copies), naming 3 referees and stating full qualifications and experience, to be received by 31st July, 1954, by Secretary, Inter-University Council for Higher Education in the Colonies, 1, Gordon-square, W.C.1, from whom further information may be obtained.

UNIVERSITY OF OTAGO, Dunedin, New Zealand. The University of Otago proposes to appoint a PROFESSOR OF MICROBIOLOGY, to take up office as soon as convenient. Salary £2002 8s.-£2502 8s. p.a.

Further particulars are available from the Secretary, Association of Universities of the British Commonwealth, 5, Gordon-square, London, W.C.1. Applications close in London and New Zealand on 31st July, 1954.

Hospital Services : Senior Appointments**NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.**

(1) CONSULTANT OPHTHALMOLOGIST (2 half-days a week; at present Monday and Thursday A.M.), King Edward VII Hospital, Windsor (517 Beds).

Applications by 23rd July, 1954.

(2) CONSULTANT OPHTHALMIC SURGEON (5 hours a week), Royal Northern Hospital, Holloway, N.7 (279 Beds).

Applications by 23rd July, 1954.

(3) CONSULTANT ANAESTHETIST (2 half-days a week), Hendon District Hospital, N.W.4 (63 Beds).

Applications by 26th July, 1954.

(4) ASSISTANT ANAESTHETIST at West Herts Hospital, Hemel Hempstead, Herts (167 Beds). Salary £1500 (at age 32) £1950.

Applications by 12th August, 1954.

(5) MEDICAL DIRECTOR, Mass X-ray Unit 5B, Paddington General Hospital, 285, Harrow-road, W.9, to take charge initially of one unit working in the London area and possibly second unit later. Duties include sessional work at Willesden Chest Clinic. Experience in chest diseases essential. Salary £1500 (at age 32) £1950. Unit and Clinic may be visited by direct appointment.

Applications by 29th July, 1954.

(6) CONSULTANT OBSTETRICIAN AND GYNECOLOGIST (6 half-days a week), Windsor Group of hospitals; mainly King Edward VII Hospital (517 Beds) and Maidenhead Hospital (100 Beds). Successful candidate required to live in area.

Applications by 3rd August, 1954.

(7) CONSULTANT PATHOLOGIST (whole-time or maximum sessions), West Middlesex Hospital, Isleworth, Middlesex (1143 Beds). Good experience in bacteriology and hematology essential.

Applications by 6th August, 1954.

Hospitals may be visited by direct appointment. Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

ROYAL FREE HOSPITAL GROUP. Applications are invited for the post of ASSISTANT PHYSICIAN (Consultant, part-time) to work at The Royal Free and Hampstead General Hospitals. Duties to commence on 1st November, 1954.

Applications, stating age and experience, together with the names of 3 referees, should be forwarded to the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, not later than 13th August, 1954.

BROMSGROVE. BARNESLEY HALL HOSPITAL. (750 Beds.) Whole-time ASSISTANT PSYCHIATRIST. Salary £1500-£1950 p.a. Wide experience specialty essential and specific knowledge or interest in psychotherapy an advantage.

Applications (15 copies), stating name, age, nationality, qualifications, present and previous appointments and details of 3 referees, to Secretary, Birmingham Regional Hospital Board, 10, Augustus-road, Birmingham, 15, before 12th July, 1954.

GATESHEAD-ON-TYNE. DUNSTON HILL HOSPITAL. CONSULTANT ANAESTHETIST required for 1 half-day a week (Tuesday morning). National Health Service terms and conditions of service.

Detailed applications (9 copies), giving nationality, date of birth, qualifications and experience including present appointments and the names of 3 referees, should reach Ministry of Health, Hospital Management Branch, Norcross, Blackpool, Lancashire, by 16th July, 1954.

LEEDS REGIONAL HOSPITAL BOARD. Locum Tenens CONSULTANT in Anesthetics required for the Thoracic Unit, Castle Hill Hospital, near Hull, for a period of approximately 6 months.

Applications, stating age, qualifications and details of previous appointments, together with the names and addresses of 3 referees, should be forwarded to the Secretary to the Board, Park Parade, Harrogate.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the whole-time non-resident post of ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer) to the Group Pathology Laboratory in the Bury and Rossendale Hospitals at Bury General Hospital. Successful candidate will work under general guidance of a Consultant and facilities for gaining experience in all branches of pathology are available.

Application forms from the Senior Administrative Medical Officer to the Board at Cheetwood-road, Manchester, 8, to be returned by 30th June, 1954.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. Whole-time ASSISTANT RADIOLOGIST, to commence as soon as possible. Duties will be divided between Manchester Royal Infirmary and St. Mary's Hospitals for Women and Children, Manchester, under the direction of the Consultant Radiologists. Candidates must possess the D.M.R.D. and must have had wide experience in radiology. Senior Hospital Medical Officer grade.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 14th July, 1954.

F. J. CABLE, Secretary to the Board of Governors.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. ROYAL VICTORIA INFIRMARY. Applications are invited for the appointment of Whole-time or maximum Part-time RADIOTHERAPIST (Consultant), who will be recognised as Deputy to the Head of the Radiotherapy Department.

Applications, giving age, nationality, experience and qualifications, with the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the date of appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of ASSISTANT DIAGNOSTIC RADIOLOGIST on the staff of the Aberdeen General Hospitals. Candidates should have experience in their specialty and hold a Diploma in Radiology. The salary is on the scale £1500-£1950 and the terms and conditions of service for hospital medical and dental officers under the National Health Act (Scotland) will apply to the post.

Applications, together with the names and addresses of 2 referees, should be forwarded by 17th July, 1954, to the Secretary, 1, Albyn-place, Aberdeen, from whom further particulars may be obtained.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time post of SENIOR HOSPITAL MEDICAL OFFICER in Anaesthetics at the Stornoway Hospitals. Duties are mainly at the Lewis Hospital, where a rented house is available for the officer.

Schedules of application and further particulars are obtainable from the undersigned, with whom applications should be lodged by 17th July, 1954.

A. M. FRASER, M.D.,

Secretary and Administrative Medical Officer,
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments:

CONSULTANT SURGEON in charge of wards at the Western Infirmary, Glasgow. The appointment is part-time remunerated on the basis of 7 notional half-days per week.

CONSULTANT E.N.T. SURGEON at Glasgow Royal Infirmary and with other duties elsewhere in the Region as may be arranged. The appointment is part-time remunerated on the basis of 8 notional half-days per week.

Whole-time ASSISTANT E.N.T. SURGEON based at Glasgow Royal Infirmary with duties at the County Hospital, Stonehouse, and elsewhere in the Lanark County Area. Salary on the scale £1500-£50-£1950.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, not later than 30 days after the publication of this advertisement.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT PSYCHIATRIST for the Middlewood Hospital, Sheffield. Salary scale £1500-£50-£1950. A house is available.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 17th July, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. 2 CONSULTANT OPHTHALMOLOGISTS, each for 6 notional half-days per week. Main duties at the Leicester Royal Infirmary. Other duties will include attendance at the Leicester County Borough School Clinic.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 24th July, 1954.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. Whole-time SENIOR CASUALTY OFFICER to have clinical charge of Casualty Department. Salary £1500-£1950 p.a. Tenable up to 4 years. Higher qualification an advantage.

Applications (15 copies), stating name, age, nationality, qualifications, present and previous appointments and details of 3 referees, to Secretary, Birmingham Regional Hospital Board, 10, Augustus-road, Birmingham, 15, before 12th July, 1954.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer grade) for the Portsmouth and Isle of Wight Area Pathological Service. A condition of the appointment is residence in the Gosport and Lee on Solent area.

Applications (5 copies), giving date of birth, qualifications, experience and names of 3 referees, to the Area Secretary, South West Metropolitan Regional Hospital Board, Highercroft, Romsey-road, Winchester, by 12th July, 1954. Applicants may visit the Central Laboratory, Milton-road, Portsmouth, by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. requires Whole-time NON-RESIDENT ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) for the Royal Earlswood Group of (M.D.) Hospitals (1000 Beds approximately). Candidates should possess D.P.M. and preferably have some experience of child psychiatry. Successful candidate required to live within reasonable distance of Royal Earlswood Institution, Redhill, Surrey.

Applications (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, London, W.1, by 17th July, 1954. Applicants may visit hospitals by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. requires a Locum PHYSICIAN (9 half-days per week) immediately for at least 3 months in the Bournemouth and East Dorset Group of hospitals. Remuneration at the rate of 45 guineas per week (if holding National Health Service Consultant grading) otherwise 31½ guineas per week.

Applications immediately to the Area Secretary, South West Metropolitan Regional Hospital Board, Highercroft, Romsey-road, Winchester.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of ASSISTANT SENIOR MEDICAL OFFICER (whole-time) on the headquarters staff of the Board's office. The salary is £1500-£75(4)-£100-£1900, subject to review by the Medical (Whitley) Council for the Health Services. The successful candidate will be engaged on general administrative duties under the Board's Senior Administrative Medical Officer. Experience of public health and hospital administration would be an advantage. The appointment is subject to the provisions of the National Health Service superannuation regulations, and to the conditions of service approved by the Minister of Health.

Applications, stating age, qualifications and experience, and giving the names and addresses of 3 referees, should reach the Secretary of the Board at 27, Tyndalls Park-road, Bristol, 8, not later than 14th July, 1954.

WOLVERHAMPTON. ROYAL HOSPITAL. Whole-time SENIOR CASUALTY OFFICER to have clinical charge of Casualty Department. Salary £1500-£1900 p.a. Tenable up to 4 years. Higher qualification an advantage.

Applications (15 copies), stating name, age, nationality, qualifications, present and previous appointments and details of 3 referees, to Secretary, Birmingham Regional Hospital Board, 10, Augustus-road, Birmingham, 15, before 12th July, 1954.

IRELAND. ST. JOHN OF GOD PRIVATE PSYCHIATRIC HOSPITAL, STILLORGAN, CO. DUBLIN, IRELAND. (Conducted by Brothers of St. John of God. Hospital contains 135 Beds.) Applications are invited for the position of RESIDENT MEDICAL DIRECTOR at above Hospital. Candidates should be of Consultant status and possess the highest qualifications.

Application forms with particulars sent on request. Completed forms to be returned not later than 31st August, 1954, to Brother Secretary, St. John of God Private Psychiatric Hospital, Stillorgan, co. Dublin, Ireland.

IRELAND. ST. JOHN OF GOD PRIVATE PSYCHIATRIC HOSPITAL, STILLORGAN, CO. DUBLIN, IRELAND. Applications invited immediately for position of LOCUM TENENS to the above Hospital, period of employment—3 months; renewal is not guaranteed. Qualifications—D.P.M. essential.

All inquiries directed to Brother Secretary, St. John of God Private Psychiatric Hospital, Stillorgan, co. Dublin, Ireland.

NEW ZEALAND. THE OTAGO HOSPITAL BOARD. DUNEDIN HOSPITAL AND UNIVERSITY OF OTAGO, NEW ZEALAND. Applications are invited for the position of JUNIOR PSYCHIATRIC SPECIALIST AND LECTURER IN PSYCHIATRY from those who hold a Degree in Medicine of an approved University and possess a Diploma of Psychological Medicine. The position is designated as that of Junior Specialist under the Hospital Employment (Medical Officers) Regulations, 1952, Amendment No. 1. Salary scale £NZ1290-£NZ1500 (plus cost-of-living bonus £NZ62 12s. p.a.) by annual increments of £NZ50. Commencing rate of salary according to qualifications and experience. Duties will include the teaching of psychiatry to medical undergraduates. Clinical work is carried out in the Department of Psychiatry, Dunedin Hospital, the general teaching hospital of the Medical School. The Department has 10 Beds in the general medical wards, and a 14-bedded observation and treatment ward. There are adult and child outpatient clinics. The position is a non-resident one.

Applications for this position should be made on the prescribed form obtainable from the Office of the High Commissioner for New Zealand, 416, Strand, London, W.C.2, or from THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2, who can supply further information and conditions of appointment. Applications should be in the hands of the undersigned not later than 10 A.M. on Tuesday, 31st August, 1954.

T. H. MILES, Acting Secretary.

Otago Hospital Board, P.O. Box 946, Dunedin, New Zealand.

SOUTH AFRICAN BLOOD TRANSFUSION SERVICE. Applications are invited from registered medical practitioners with experience in blood-transfusion and bacteriology for the position of SEROLOGIST of the South African Blood Transfusion Service. The appointment will be made on the salary scale £1700-£100-£2400 p.a. but, in determining the commencing salary cognisance may be taken of previous experience and special qualification. The successful applicant will be expected to assume duty in Johannesburg on 1st November, 1954. Membership of the Service's Staff Provident Fund is a condition of employment.

Applications, stating full details of age, qualifications, experience, marital status, &c., should be submitted in writing to the Secretary, South African Blood Transfusion Service, P.O. Box 9326, Johannesburg, so as to be received not later than 15th August, 1954. The Medical Director of the Service will be in London early in September, 1954, to interview applicants at a time and place to be advised.

Hospital Services : Junior Appointments

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE SURGEON (resident), vacant 19th July. Open to registered practitioners and pre-registration candidates. Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 12th July.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in Obstetrics and Gynaecological Department. Post recognised for M.R.C.O.G. Appointment for 6 months from 1st August.

Applications, with copies of 2 testimonials, to Medical Director by 3rd July, 1954.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in Orthopaedic Department. Pre-registration applicants will be considered. Appointment for 6 months from 16th August.

Applications, with copies of 2 testimonials, to Medical Director by 3rd July, 1954.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, London, N.W.10. RESIDENT SENIOR HOUSE OFFICER required for Casualty Department. Successful candidate will work under supervision of Orthopaedic and Traumatic Specialist. Preference given to applicant who has held resident surgical and medical posts in general hospital. Post now vacant. Appointment for 6 months subject to renewal for further 6 months.

Applications, with names of 2 referees or copies of 2 testimonials, to Medical Director by 3rd July.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from registered Women medical practitioners for the appointment of Full-time MEDICAL REGISTRAR for General Medicine and Paediatrics. Appointment for 1 year in the first instance, to commence 1st September, 1954. Salary in accordance with Ministry of Health scale for Registrar grades.

Applications, with names of 3 referees, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 10th July, 1954.

GROUP PATHOLOGICAL LABORATORY, ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD, FULHAM AND KENSINGTON AND CHELSEA HOSPITAL MANAGEMENT COMMITTEES. Applications are invited for appointment as REGISTRAR (pathology), vacant 1st September, 1954. Candidates will be required to work at the Group Laboratory and as required at any other hospital in either of the 2 Groups. Candidates may visit the Laboratory by arrangement with the Director of Pathology.

Applications (5 copies to be completed) to be submitted by 2nd July, 1954, on forms obtainable from the Group Secretary (L.10), Fulham and Kensington Hospital Management Committee, 5, Collingham-gardens, London, S.W.5.

HACKNEY HOSPITAL, London, E.9. (General—844 Beds.) Applications from registered medical practitioners for the posts of HOUSE OFFICERS (casualty) (1 with additional duties in the Skin Department and 1 with additional duties in the E.N.T. Department), should be sent as soon as possible to the Group Secretary at the above address.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Whole-time NON-RESIDENT REGISTRAR (general medicine) required. Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, by 5th July.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. HOUSE SURGEON (orthopaedics) required 16th August.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary, Board of Governors, by 3rd July.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE PHYSICIAN, vacant 4th July, 1954. Preference given to applicants seeking pre-registration post under Medical Act, 1950.

Applications, with copies of 3 testimonials, to Hospital Secretary.

HOSPITALS FOR DISEASES OF THE CHEST. London CHEST HOSPITAL. A vacancy occurs on 1st August, 1954, for RESIDENT HOUSE SURGEON. The appointment is for 6 months at the Hospital's Country Branch, near Hitchin and Letchworth, Herts. The post is graded as Senior House Officer and provides excellent opportunities for experience in thoracic surgery.

Applications from registered medical practitioners, stating age, qualifications with dates and previous appointments held, with copies of 3 testimonials, should be sent at once to—

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

KING'S COLLEGE HOSPITAL, Denmark-hill, S.E.5. Applications are invited for the post of Locum REGISTRAR to the Diagnostic X-ray Department until 30th September when a permanent post becomes vacant. Candidates with or without the Diploma of Radiology will be considered.

If applicants wish to apply for the latter, applications should be received by 30th June. Otherwise applications stating age, qualifications and experience, together with the names of 2 referees, should be addressed to the undersigned by 6th July, 1954.

S. W. BARNES, House Governor.

LAMBETH HOSPITAL, Kennington, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the position of RESIDENT HOUSE SURGEON. The appointment is for 6 months from 23rd July, 1954, and is recognised for the F.R.C.S.

Application forms may be obtained from the Physician-Superintendent at the Hospital.

LAMBETH HOSPITAL, Kennington, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the position of RESIDENT HOUSE PHYSICIAN, vacant 1st August, 1954.

Forms of application from the Physician-Superintendent.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR HOUSE OFFICER to Surgical Outpatient Department.

Applications (6 copies), giving full particulars, together with 6 copies of 3 recent testimonials, to reach the House Governor by 12th July, 1954.

H. BRIERLEY, House Governor.

MILDENHALL MISSION HOSPITAL, Austin-street, London, E.2. (General—56 Beds.) Applications are invited from registered medical practitioners for the posts of HOUSE SURGEON (recognised for F.R.C.S.) and HOUSE PHYSICIAN; both posts recognised for pre-registration. Vacant 5th July. Candidates should be in sympathy with the Evangelical aims of the Hospital.

Apply to the Medical Superintendent, with references, as soon as possible.

MEMORIAL HOSPITAL, Woolwich, S.E.18. Woolwich GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON. 2 vacancies 1st August. Recognised for F.R.C.S. and approved for Pre-registration Service.

Apply, with copies of testimonials, to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

MOTHERS' HOSPITAL (Salvation Army), Clapton, E.5. (Maternity—110 Beds. Recognised for M.R.C.O.G.) Applications are invited for the 12 months appointment of SENIOR HOUSE OFFICER (obstetrics) and should be sent in full detail with copy testimonials to the Group Secretary, Hospital Management Committee, Hackney Hospital, London, E.9, quoting reference MH/SHO.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of REGISTRAR (non-resident) at The National Hospital, Queen-square, W.C.1. This post carries the grade of Senior Registrar. Previous neurological experience and higher medical qualification are desirable. The appointment will be for 1 year in the first instance.

Applications, with names of 3 referees, to be sent to the undersigned not later than 3rd July, 1954.

H. EWART MITCHELL, Secretary.

The National Hospital, Queen-square, W.C.1.

NEASDEN HOSPITAL, Brentfield-road, N.W.10. (Tel. No. WILLESDEN 1850.) Locum Tenens RESIDENT MEDICAL OFFICER (Registrar). Whole-time Resident Registrar required for above Hospital for 19th July, 1954-1st August, 1954, both dates inclusive. This Hospital admits all types of acute infectious diseases and offers a wide clinical experience and opportunity for postgraduate studies.

Applications should be made to the Physician-Superintendent as soon as possible.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. CASUALTY OFFICER (Senior House Officer grade). Post recognised for F.R.C.S. 6 months appointment in the first instance, from 16th August (Locum required 15th July to 15th August). Non-resident.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials and/or names of 2 referees, to Secretary of Hospital by 5th July.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

MEDICAL REGISTRAR (resident or non-resident), German Hospital, E.8. Appointment subject to review after 1 year.

Applications in triplicate detailing date of birth, qualifications, experience, present appointment, grade and salary, with 3 copies of 2 recent testimonials, to Secretary, 11A, Portland-place, W.1, by 10th July, 1954.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in Psychiatry, Department for Children and Parents, Tavistock Clinic, 2-4, Beaumont-street, W.1. Post vacant 1st September, 1954. At least 1 years previous experience in child psychiatry essential. Clinic may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, by 7th July, 1954.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Psychiatry, Department for Children and Parents, Tavistock Clinic, 2-4, Beaumont-street, W.1. Post vacant 1st October, 1954. At least 1 years previous experience in child psychiatry essential. Clinic may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, by 7th July, 1954.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR at Willesden Chest Clinic, Pound-lane, N.W.10, and Clare Hall Hospital, South Mimms, Barnet. The first 2 years will be spent at Chest Clinic, and duties will include work on the district, supervision of beds in Tuberculosis Unit at Central Middlesex Hospital, and teaching, followed by opportunity of further 2 years (approximately) at Clare Hall Hospital. Good training in general medicine and chest diseases essential. Higher medical qualifications desirable. Appointment subject to annual review. Clinic may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, by 17th July, 1954.

REGIONAL NEUROSURGICAL CENTRE. (50 Beds.) BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER (neurosurgeon), vacant 1st August. The post, which is recognised for F.R.C.S., also provides excellent opportunity for training in neurology. Salary £745 p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ROYAL CANCER HOSPITAL, Fulham-road, London, S.W.3. Applications are invited for the post of MEDICAL REGISTRAR. The post, which is for 7 sessions a week, may be filled either in the grade of Registrar or alternatively in the grade of Senior Registrar by a candidate wishing to take a period of advanced training for not more than 2 years, or by a candidate holding a Consultant or Senior Hospital Medical Officer post elsewhere. For appointment as Senior Registrar candidates holding the Diploma of M.R.C.P. will be preferred. If the appointment is in the grade of Registrar some increase in the number of sessions may be considered. The duties include clinical studies of the health of staff, in support of the Hospital's Radiological Protection Service.

Applications, stating whether a Senior Registrar or Registrar post is desired, together with copies of 3 recent testimonials, should be submitted by 7th July on a form which may be obtained from the House Governor.

ROYAL CANCER HOSPITAL, Fulham-road, London, S.W.3. Applications are invited from registered medical practitioners for the 2 posts of HOUSE SURGEON (resident). Salary £525 p.a. The posts are tenable for 6 months from 1st September, 1954.

Forms of application are obtainable from the House Governor to whom applications, together with copies of 3 recent testimonials, should be sent not later than Wednesday, 14th July, 1954.

POPLAR HOSPITAL, East India Dock-road, E.14. (120 Beds.) Required, CASUALTY HOUSE SURGEON. Duties include inpatient, outpatient and casualty work. Post recognised for F.R.C.S. Vacant now.

Applications, stating age, nationality and qualifications, to the Secretary.

PRINCE OF WALES'S GENERAL HOSPITAL, N.15. (219 Beds.) Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER RESIDENT SENIOR HOUSE SURGEON for Casualty, for a period of 6 months, to commence immediately.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. QUEEN CHARLOTTE'S MATERNITY HOSPITAL. JUNIOR OBSTETRIC OFFICER (Senior House Officer), resident post tenable for 6 months from 1st October, 1954.

Applications to the Secretary to the Board of Governors by 10th July on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, E.15. JUNIOR CASUALTY OFFICER (Male or Female) required (House Officer—third post) for 6 months commencing as soon as possible.

Applications, with copies of recent testimonials, to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by 8th July, 1954.

S.E. REGIONAL THORACIC SURGERY UNIT. (46 Beds.) BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER (recognised for F.R.C.S.), vacant now. The Unit treats all types of chest diseases and offers opportunity for comprehensive training in thoracic surgery. Appointment for 6 months in first instance and may be renewed for further period.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. JAMES'S HOSPITAL, Sarsfield-road, S.W.12. Wandsworth HOSPITAL GROUP, SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Post of REGISTRAR vacant in E.N.T. Department.

Application forms (send stamped addressed foolscap envelope) obtainable from Group Secretary, 14, Atkins-road, Balham, S.W.12, to be completed and returned by 3rd July.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (General—182 Beds.) Applications are invited from registered or provisionally registered medical practitioners for the posts of:

HOUSE SURGEON available 16th July, 1954.

HOUSE PHYSICIAN available 5th July, 1954.

Applications, with 2 recent testimonials, to Hospital Secretary by 3rd July, 1954.

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS AND THE INSTITUTE OF UROLOGY. A vacancy will occur on 1st September, 1954, for the combined post of RESIDENT SURGICAL OFFICER at St. Philip's and FOLLOW-UP OFFICER to the Institute. Grading, Registrar first year. Appointment for 6 months with opportunity for extension.

Apply, in writing (6 copies), and names of 2 referees, to the House-Governor, St. Peter's Hospital, Henrietta-street, W.C.2. Closing date 24th July, 1954.

ST. THOMAS'S HOSPITAL, London, S.E.1. Research REGISTRAR to the Department of Psychological Medicine. 1 year in the first instance. Successful candidate to devote whole time to clinical research in psychiatric treatment.

Applications, including names and addresses of 2 referees, to the Clerk of the Governors by 5th July, 1954.

WEST LONDON HOSPITAL, Hammersmith-road, W.6. HOUSE OFFICER (anaesthetics) required 1st September.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary by 10th July.

WHIPPS CROSS HOSPITAL, London, E.11. Leytonstone (No. 10) HOSPITAL GROUP. Applications are invited for the following posts at above Hospital.

ORTHOPÆDIC HOUSE SURGEON. This post, which is recognised for the F.R.C.S. examination, is at present vacant.

ORTHOPÆDIC HOUSE SURGEON (pre-registration post), vacant on 18th July, 1954, but available on a locum basis 2 weeks prior to this date.

Application forms from the Hospital Secretary to be returned within 12 days of the appearance of this advertisement.

ABERDEEN GENERAL HOSPITALS BOARD OF MANAGEMENT. WOODEND GENERAL HOSPITAL. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER in the Thoracic Surgery Department of the above Hospital. The post, which is non-resident, is subject to the conditions of service issued by the Department of Health for Scotland.

Applications, giving details of qualifications and experience, and the names of 2 referees, should be lodged with the Secretary, Aberdeen General Hospitals, 62, Queen's-road, Aberdeen, within 14 days of the appearance of this advertisement.

AYLESBURY, BUCKINGHAMSHIRE. ROYAL BUCKINGHAMSHIRE HOSPITAL. Locum CASUALTY OFFICER for 1 week from 18th July. Salary £13 per week.

Applications, with names of 2 referees, to the Secretary-Superintendent.

AYLESBURY. ROYAL BUCKINGHAMSHIRE AND ASSOCIATED HOSPITALS MANAGEMENT COMMITTEE.

Stoke Mandeville Hospital, Aylesbury

JUNIOR HOSPITAL MEDICAL OFFICER for National Spinal Injuries Centre. Neurological or surgical experience desirable. Vacant 1st July.

Applications, with copies of 2 recent testimonials, to the Administrative Officer.

HOUSE PHYSICIAN (Senior Resident Medical Officer) for Acute General Medical Unit, which comprises 2 Registrars and 3 Resident House Physicians. The post is of Senior House Officer grade and is vacant on 7th July.

Applications, with 3 recent testimonials, to Administrative Officer.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds) with all the usual special departments.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. RESIDENT ANAESTHETIC REGISTRAR (Male) required at above Hospital for general anaesthetic duties at Ashford and such other hospitals within the Group as may be necessary. Post vacant 7th September. Hospital may be visited by direct appointment with the Medical Director.

Application forms obtainable from, and returnable to, the Secretary, Staines Group Hospital Management Committee, Ashford Hospital, Ashford, Middlesex, by 7th July, 1954.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required at Ashton-under-Lyne General Hospital. Preference will be given to pre-registration applicants. Post vacant mid-July.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 testimonials, should be forwarded to the Group Secretary, Astley-road, Stalybridge, Cheshire, as soon as possible.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. 2 HOUSE SURGEONS required at Ashton-under-Lyne General Hospital. Preference will be given to pre-registration applicants. Recognised for F.R.C.S. (Eng.).

Applications, stating age, nationality, qualifications, and experience, if any, together with copies of 3 testimonials, should be forwarded to the Group Secretary, Astley-road, Stalybridge, Cheshire, as soon as possible.

ABERYSTWYTH. GENERAL HOSPITAL. (Hospital recognised for F.R.C.S. examination.) MID-WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from newly qualified medical practitioners seeking pre-registration posts under the Medical Act, 1950, for the resident post of HOUSE SURGEON at the above Hospital. Busy General Hospital. Salary on national scale, less deduction for board and lodging.

Applications, with 2 testimonials, to the Group Secretary, Mid-Wales Hospital Management Committee, General Hospital, Aberystwyth, immediately.

ASCOT, BERKSHIRE. HEATHERWOOD ORTHOPAEDIC HOSPITAL. (212 Beds—Adults and Children.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ORTHOPAEDIC REGISTRAR (resident) required at above Hospital. Hospital is a regional centre for all general orthopaedic conditions, including fractures; there is also a large amount of outpatient work. Post recognised for F.R.C.S. Candidates may visit Hospital by direct appointment.

Application forms obtainable from and returnable to the Group Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, Berks, by 4th July.

BEDFORD GENERAL HOSPITAL. (437 Beds.) Resident HOUSE SURGEON (pre-registration) required immediately. The appointment offers exceptional opportunity for general experience in a busy acute Surgical Unit.

Applications, stating age, nationality, qualifications, previous appointments, together with copies of 2 testimonials, should be forwarded to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (437 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for busy acute Orthopaedic and Traumatic Department at above Hospital. Previous orthopaedic experience desirable. Candidates may visit Hospital by appointment with Group Secretary.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, as soon as possible.

BEDFORD GENERAL HOSPITAL. (437 Beds.) Locum REGISTRAR required for busy acute Orthopaedic and Traumatic Department for approximately 2 months. Previous orthopaedic experience desirable.

Applications, stating age, nationality, qualifications, previous appointments, together with copies of 2 recent testimonials, should be forwarded to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BIRMINGHAM. ROYAL ORTHOPAEDIC HOSPITAL. (Long and short term orthopaedic cases (non-traumatic)—334 Beds and extensive outpatient services.) Applications are invited from registered medical practitioners, preferably with previous orthopaedic experience, for 2 SENIOR HOUSE OFFICER posts vacant shortly.

Apply, to Administrator, 80, Broad-street, Birmingham, 15.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, Solihull, near BIRMINGHAM. HOUSE SURGEON (pre-registration). Obstetrics. General Hospital. 5 other resident Medical staff. Post vacant now.

Applications to Medical Superintendent.

BIRMINGHAM, 13. SORRENTO MATERNITY HOSPITAL. (112 Beds, including 24 premature baby cots.) OBSTETRIC HOUSE SURGEON. Appointment recognised for D.Obst.R.C.O.G. Hospital affiliated to Birmingham Medical School for training of students. Post vacant 1st August, 1954.

Applications to Obstetrician before 30th June, 1954.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (790 Beds.) HOUSE SURGEON (resident) required. Post recognised for pre-registration and F.R.C.S. (Eng.). This appointment, vacant on 10th July, 1954, is in a Unit of General Surgery of approximately 80 adult general surgical beds and 10 children's surgical beds under the control of 2 Consultant Surgeons.

Detailed applications, with copies of 3 recent testimonials, to Secretary.

BIRMINGHAM (near). MARSTON GREEN MATERNITY HOSPITAL, Berwicks-lane, MARSTON GREEN, near BIRMINGHAM. HOUSE SURGEON (obstetrics) required on 1st September, 1954. 128 obstetric and 10 gynaecological beds. Post recognised for Diploma and Obstetric part of Membership of Royal College of Obstetricians and Gynaecologists. Premature Baby Unit. Hospital affiliated to Birmingham Medical School for training of students.

Detailed applications, with copies of 3 recent testimonials, to Hospital Secretary.

BIRMINGHAM REGIONAL HOSPITAL BOARD. 1. The Birmingham Dudley Road Group, Dudley Road Hospital, Birmingham, 18

RESIDENT SURGICAL REGISTRAR for St. Chad's Hospital (50 general surgical beds). Recognised for F.R.C.S. Higher qualification an advantage.

2. Birmingham (Sanatoria) Group Hospital Management Committee, Yardley Green Hospital, Birmingham, 9

REGISTRAR in Tuberculosis for Yardley Green Hospital (413 Beds). Duties also at Birmingham Chest Clinic. Resident accommodation available. Experience specialty desirable.

3. Birmingham (Selly Oak) Hospital Management Committee, Oak Tree-lane, Birmingham, 29

REGISTRAR in Accident Surgery, Birmingham Accident Hospital. Duties as Surgical Registrar to Clinical Director. Hospital recognised for F.R.C.S. Resident. Large Traumatic Unit. 50,000 new patients annually. Opportunity for practical experience in all types of injury.

4. Shrewsbury Group Hospital Management Committee, Royal Salop Infirmary, Shrewsbury

REGISTRAR in Tuberculosis (resident). Duties mainly at Shirledd Sanatorium (65 Beds) and clinics in Shrewsbury area. Experience specialty essential. Vacant 23rd July, 1954.

5. South Worcestershire Hospital Management Committee, Worcester Royal Infirmary

REGISTRAR in Gynaecology and Obstetrics for Worcester Royal Infirmary and Ronskwood Hospital. Unit of 76 Beds recognised for M.R.C.O.G. Single or married quarters available.

6. Walsall Hospital Management Committee, Walsall General Hospital, Wednesbury-road, Walsall

REGISTRAR in General Surgery for Manor Hospital (333 Beds). Experience specialty essential. Resident.

7. Wolverhampton Group Hospital Management Committee, The Royal Hospital, Wolverhampton

(a) RESIDENT SURGICAL REGISTRAR for New Cross Hospital (636 Beds) with some duties at The Royal Hospital (310 beds); preferably F.R.C.S. Vacant now.

(b) REGISTRAR in Diagnostic Radiology for The Royal Hospital. Vacant now. At least Part I of Diploma of Medical Radiology essential. Duties also at other Group hospitals.

(c) CASUALTY OFFICER (Registrar) for The Royal Hospital, Hospital recognised for F.R.C.S. Resident.

Application forms from Group Secretaries, to be returned before 12th July, 1954. Candidates may visit hospitals.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the posts of RESIDENT REGISTRAR in Anaesthetics for duties in the United Hospitals and resident at the Queen Elizabeth Hospital. The appointments are tenable for 1 year in the first instance. Preference will be given to candidates who have passed Part I, D.A., or Primary F.R.A.C.S.

Application forms may be obtained from the Secretary to the Board of Governors, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him not later than 17th July, 1954.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN, Showell Green-lane, SPARKHILL, BIRMINGHAM, 11. Applications are invited from registered medical practitioners for the post of RESIDENT GYNAECOLOGICAL HOUSE SURGEON for duty with the Professorial Unit, vacant 1st October, 1954. The appointment is recognised for the M.R.C.O.G.

Application forms obtainable from the House Governor at the above address, to be returned not later than 10th July, 1954. G. A. PHALE, Secretary.

BIRMINGHAM, 18. WINSON GREEN MENTAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (Male or Female), resident. Salary £745 p.a., less £125 p.a. charge for services. The post, which will be for 1 year in the first instance, will be subject to the terms and conditions of service for medical and dental staffs and subject to the National Health Service superannuation regulations. The Hospital is associated with the University of Birmingham for the teaching of psychiatry, and training for the Diploma in Psychological Medicine will be provided.

Applications, stating age and qualifications, to be sent to the Medical Superintendent at the Hospital.

BISHOP AUCKLAND GENERAL HOSPITAL. (350 Beds.) Applications are invited from registered practitioners or pre-registration candidates for the post of HOUSE PHYSICIAN (vacant early August). Salary £425-£525 p.a. according to previous posts held, less £125 p.a. for full residential emoluments.

Applications, stating age, nationality, qualifications and experience, to be sent, with names of 2 referees, to the undersigned as soon as possible.

K. G. T. LUXFORD, Group Secretary/Finance Officer, South West Durham Hospital Management Committee. The General Hospital, Bishop Auckland.

BISHOP AUCKLAND GENERAL HOSPITAL (350 Beds.) Applications are invited from registered practitioners or pre-registration candidates for the post of HOUSE SURGEON (general surgery—72 Beds). Salary £425-£525 p.a. according to previous posts held, less £125 p.a. for full residential emoluments.

Applications, stating age, nationality, qualifications and experience, to be sent, with names of 2 referees, to the undersigned as soon as possible.

K. G. T. LUXFORD, Group Secretary/Finance Officer, South West Durham Hospital Management Committee. The General Hospital, Bishop Auckland.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following posts, which fall vacant around beginning of July, 1954 :—

Victoria Hospital, Accrington (112 acute beds)

SENIOR HOUSE OFFICER (medicine).

HOUSE SURGEON recognised for pre-registration purposes, and for F.R.C.S.

Apply to Secretary of the Committee, Royal Infirmary, Blackburn.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anaesthetics) required. Residence and duties mainly at Queen's Park Hospital, Blackburn, with sessions at the Blackburn Royal Infirmary and Accrington Victoria Hospital as arranged by the Consultant Anaesthetist. Post recognised for D.A. and F.F.A.R.C.S.

Apply to Secretary of the Committee, Royal Infirmary, Blackburn.

BLACKPOOL. VICTORIA HOSPITAL. (344 Beds.)

(1) SENIOR HOUSE OFFICER (Orthopaedic and Casualty Department), vacant 20th July, 1954. Recognised for 6 months casualty training for Final F.R.C.S. examination.

(2) HOUSE SURGEON (casualty), vacant 1st September, 1954. Recognised for 6 months casualty training for Final F.R.C.S. examination.

(3) RESIDENT HOUSE SURGEON (Surgical Department), vacant 14th September, 1954. Recognised for F.R.C.S.

(4) HOUSE PHYSICIAN, vacant 31st July, 1954.

This is a busy general hospital with a large Outpatient Department and the posts offer excellent opportunities for experience under Consultant staff.

Applications, with names and addresses of referees should be sent to the Hospital Secretary.

BLACKPOOL. GLENROYD MATERNITY HOSPITAL. (60 Beds.) BLACKPOOL AND FYLDE HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (obstetrics), resident, vacant 8th August, 1954.

Applications, together with names of referees, should be sent to the Group Secretary, Blackpool and Fylde Hospital Management Committee, Victoria Hospital, Blackpool.

BOLTON. THE ROYAL INFIRMARY. (237 Beds.)

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER in Orthopaedic Surgery. Tenable for 12 months and recognised for F.R.C.S.

RESIDENT HOUSE SURGEON for general surgical duties. Tenable for 6 months and recognised under the Pre-registration Service Scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience and the names of 2 referees, should be sent immediately to—
H. P. TRAVIS, Group Secretary.

The Royal Infirmary, Bolton.

BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. ROYAL VICTORIA HOSPITAL, Poole-road, WESTBOURNE, BOURNEMOUTH.

Applications are invited for the appointment of HOUSE SURGEON for E.N.T. and ophthalmic duties, vacant 18th July, 1954. In addition to duties at the above Hospital, the successful candidate will be required to assist in the E.N.T. outpatient clinics at the Royal Victoria Hospital, Shelley-road, Boscombe, and the Poole General Hospital. The appointment is recognised for the D.O. and D.L.O. Diplomas but not for pre-registration purposes.

Applications to the Deputy Hospital Secretary, Royal Victoria Hospital, Shelley-road, Boscombe, Bournemouth.

BOURNEMOUTH (near). CHRISTCHURCH HOSPITAL, CHRISTCHURCH, HANTS. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required for General Medicine, post vacant 2nd August, 1954. The Hospital comprises 61 acute medical beds, 188 chronic sick, 34 paediatric and 6 chest diagnostic.

Applications, with copies of testimonials, to the Group Secretary, Hospital Management Committee Office, Royal Victoria Hospital, Gloucester-road, Boscombe, Bournemouth.

BROMSGROVE. ALL SAINTS' HOSPITAL. (423 Beds.) SENIOR HOUSE OBSTETRICIAN AND GYNAECOLOGIST required at the above Hospital, at present 31 maternity, 12 gynaecological beds. Salary £425 p.a. Post vacant early July.

Applications, with the names of 3 referees, to Hospital Secretary.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON to the General Surgical Unit (60 Beds), recognised for F.R.C.S. The post will be vacant about 23rd July, 1954. Salary in accordance with national scale. The post is recognised as a pre-registration appointment.

Applications, stating age, qualifications, experience and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7.

BRIGHTON. NEW SUSSEX HOSPITAL FOR WOMEN. Windlesham-road. HOUSE PHYSICIAN (Female) for a period, of 6 months from 9th August, 1954. Pre-registration candidates may apply.

Applications, stating age, nationality, qualifications and experience, together with copies of recent testimonials, to the Administrative Officer as soon as possible.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL (300 Beds.) Applications are invited for the following posts :—
HOUSE SURGEON. Pre-registration and recognised for F.R.C.S.

CASUALTY HOUSE SURGEON (1 of 3). Duties include work in Orthopaedic and Traumatic Unit. Pre-registration and recognised for F.R.C.S.

Both vacant mid-July.

Applications, stating age, qualifications and experience, naming 2 referees, to be sent to the Administrative Officer.

BRISTOL CLINICAL AREA. The Board of Governors of THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards from registered medical practitioners for the joint appointment of REGISTRAR in Anaesthetics. The appointment will be held for 1 year in the first instance, and be renewable for a further year. The successful candidate will be required to work for the first year mainly at Southmead Hospital, Bristol, but may be required to undertake duties at other hospitals in the Group as circumstances require.

Applications, stating date of birth, qualifications and experience together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 10th July, 1954.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL, (513 staffed beds, expanding.) Applications are invited for the post of SENIOR HOUSE OFFICER in the regional Neurosurgery Department, vacant 1st August, 1954. This post offers useful surgical experience and the opportunity of gaining a working knowledge of neurological diagnosis.

Applications to the Secretary, Frenchay Hospital, quoting "N.S.F." Names of 2 referees required.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a Male JUNIOR ASSISTANT VENEREOLOGIST (non-resident). The duties of the successful candidate will be primarily in connection with V.D. He will be attached to Frenchay Hospital and in addition will be required to undertake duties in the various Bristol area clinics. Previous experience in venereology an advantage. The appointment will be subject to the National Health Service superannuation regulations and terms and conditions for hospital medical staff. Salary scale £700-£750-£1000 p.a.

Applications, with full particulars of age, qualifications and experience, and the names and addresses of 3 referees, should reach the Secretary, Frenchay Hospital, Bristol, not later than 3rd July, 1954.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL. THORACIC SURGERY DEPARTMENT. HOUSE SURGEON required in the above Department, which is the regional Thoracic Surgery Centre (120 Beds) for the South West.

Applications, with full particulars, should be addressed to the Group Secretary, Frenchay Hospital, Bristol, quoting "Thoracic."

BRISTOL. STAPLETON HOSPITAL. (750 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER. Salary £775-£250-£1075. Furnished accommodation available, together with board and laundry, for which a charge of £120 p.a. is made. If a married man is appointed a self-contained flat in close proximity to the Hospital at an economical rent is available. The Hospital caters for acute and chronic illness in the older age groups. All ancillary services available. Consultant staff visit regularly and there is ample time for postgraduate study.

Applications stating age, nationality, whether married or single, experience, qualifications, and names and addresses of 2 referees, to be sent to the Group Secretary, Stapleton Hospital Management Committee, 200, Manor-road, Fishponds, Bristol, within 14 days of the appearance of this advertisement.

BRADFORD ROYAL INFIRMARY. House Officer (anaesthetics), vacant now. Recognised for D.A. and F.F.A.R.C.S. Opportunities for plastic and intra-thoracic experience. Salary £425-£525 p.a., less £125 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to Secretary.

BRADFORD. ST. LUKE'S HOSPITAL. House Officer (anaesthetics), vacant now. Recognised for D.A. and F.F.A.R.C.S. Opportunities for plastic and intra-thoracic experience. Salary £425-£525 p.a., less £125 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRENTWOOD, ESSEX. HIGH WOOD HOSPITAL FOR CHILDREN. Temporary REGISTRAR required for 3 months from 28th June. The Hospital admits cases of pulmonary tuberculosis in children. Possibility of a permanent vacancy later. Please apply to Senior Physician.

BURTON-ON-TRENT GENERAL INFIRMARY. (251 Beds.) RESIDENT HOUSE SURGEON required for General Surgical Unit. Designated for Pre-registration Service. The Hospital is recognised for the F.R.C.S.

Applications, with full details, naming 2 referees, should be sent to the Secretary.

BURY AND ROSENDALE HOSPITAL MANAGEMENT COMMITTEE. ROSENDALE GENERAL HOSPITAL. SENIOR HOUSE OFFICER (obstetrics), resident or non-resident, for Obstetric/Gynaecological Unit consisting of 24 obstetric and 8 gynaecological beds.

Applications to H. WILKINSON Esq., Group Secretary. Bury General Hospital, Bury, Lancs.

CARSHALTON, SURREY. ST. HELENS HOSPITAL Locum DERMATOLOGICAL REGISTRAR (part-time) required for 2 half-days per week for 4 weeks from 3rd July, with possibility of indefinite extension.

Apply to Group Secretary at above address.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. House SURGEON for 6 months from 28th August. Recognised Pre-registration Service.

Apply, stating age, nationality, qualifications, and experience with dates, and copies of 3 testimonials, to Secretary by 10th July. Interviews 14th July.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. Resident ANAESTHETIC SENIOR HOUSE OFFICER for 1 year from 18th August. Anaesthetic experience essential.

Apply, stating age, nationality, qualifications and experience with dates, and copies of 3 testimonials, to Secretary by 10th July. Interviews 22nd July.

CARDIFF. ROOKWOOD HOSPITAL, Llandaff, Cardiff. SENIOR HOUSE OFFICER (surgical) required at the above War Pensioners' Hospital. Whitley Council salary and conditions.

Application forms will be sent on request by Hospital Management Branch, Ministry of Health, Norcross, Blackpool, Lancashire.

CARLISLE. CUMBERLAND INFIRMARY. (340 Beds.) HOUSE OFFICER (general surgery) required immediately for period of 6 months or Locum for shorter period. This post is recognised for the F.R.C.S. examination, and pre-registration practitioners are eligible to apply.

Applications, with 2 names for reference, to be sent to the Secretary.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON (pre-registration post). The post will become vacant on 24th July and offers good surgical experience and is recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD AND ESSEX HOSPITAL, London-road, CHELMSFORD. (161 Beds.) Applications are invited for the post of HOUSE PHYSICIAN (pre-registration post), to work in the general medical wards of the above Hospital. Duties will commence 7th August.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD. ST. JOHN'S HOSPITAL. Applications are invited from registered practitioners for the post of RESIDENT PEDIATRIC HOUSE OFFICER (Male or Female), commencing 17th July, 1954. To work in the Pediatric Unit of the Chelmsford Hospital Group. The Unit includes a Premature Baby Nursery of 10 cots and a Neonatal Department in the maternity block of the Hospital. The work is recognised for the D.C.H.

Applications, together with recent testimonials, should be sent, not later than 8th July, to the Secretary, Hospital Management Committee—Chelmsford Group, Chelmsford and Essex Hospital, London-road, Chelmsford.

CHEPSTOW, MONMOUTHSHIRE. ST. LAWRENCE HOSPITAL. (150 Beds.) PLASTIC SURGERY, JAW INJURIES AND BURNS CENTRE. SENIOR HOUSE OFFICER (resident) in Plastic Surgery required. Previous experience in specialty not essential. The successful candidate will receive a thorough training in plastic surgery and burns. Hospital intakes from most of Wales and post provides extensive experience. Salary £745, less £150 for board-residence.

Write, quoting 2 referees, to Group Secretary, 64, Cardiff-road, Newport, Mon.

CHESTERFIELD ROYAL HOSPITAL. (324 Beds.) CHESTERFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for appointments of 2 HOUSE SURGEONS at the above Hospital. The posts, which are recognised for Pre-registration Service, become vacant early in July. Salary £425, £475, or £525 p.a. according to experience, less £125 p.a. for residential emoluments.

Please apply in detail to M. H. BOONE, Secretary, from whom particulars of the Hospital are obtainable.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the following post:—

Essex County Hospital, Colchester (189 Beds) HOUSE OFFICER (surgical). First, second, third, or pre-registration post; tenable for 6 months.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the following posts:—

Claclton and District Hospital, Clacton-on-Sea (58 Beds) SENIOR HOUSE OFFICER (Resident Surgical Officer). Post tenable for 1 year.

SENIOR HOUSE OFFICER (Resident Casualty Officer) required temporarily during summer months to mid-September.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, 14, Pope's-lane, Colchester, Essex.

CROYDON. ST. MARY'S MATERNITY HOSPITAL. (33 Beds.) SENIOR HOUSE OFFICER (resident). Post, which is recognised for D.Obst.R.C.O.G., vacant from 18th July. Candidate required to undertake certain duties at Mayday Hospital. Post offers opportunity for reading.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Croydon Group Hospital Management Committee, General Hospital, Croydon.

DARLINGTON MEMORIAL HOSPITAL. (210 Beds.) DARLINGTON DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON (resident) which post is recognised for the F.R.C.S. (Eng.). Salary in accordance with national scale.

Apply, giving age and references, to the undersigned forthwith. G. W. BECKWITH, Group Secretary.

CREWE MEMORIAL HOSPITAL. (110 Beds and Annexes 34 Beds—General.) SOUTH CHESHIRE HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER (medical) required at the above Hospital. Salary £745 p.a., less £140 p.a. for board and lodging. Post vacant 1st August, 1954.

Applications, stating age, qualifications and experience, together with copies of recent testimonials, should be sent to the Group Secretary, Barony Hospital, Nantwich, as soon as possible.

DERBY. DERBYSHIRE CHILDREN'S HOSPITAL. (86 Beds.) HOUSE SURGEON (pre-registration) or SENIOR HOUSE OFFICER, vacant now. Recognised for D.C.H.

Applications, with 2 names for reference, should be sent to the Secretary, No. 1 Hospital Management Committee, Babington-lane, Derby.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Senior HOUSE OFFICER (anaesthetics), vacant 1st September, 1954. Recognised for D.A.

Applications, stating full particulars with copies of 2 testimonials, to be sent as soon as possible to the Secretary at the Infirmary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. House SURGEON (pre-registration) or SENIOR HOUSE OFFICER, General Surgery.

Applications, stating full particulars, with copies of 2 testimonials, to be sent as soon as possible to the Secretary at the Infirmary.

DEWSBURY. STAINCLIFFE GENERAL HOSPITAL. (314 Beds.) HOUSE OFFICER (general medicine and paediatrics), first, second, or third post, vacant 1st August, 1954, and tenable for 6 months. Recognised pre-registration appointment. Hospital has 68 adult acute medical and 34 paediatric beds. It is recognised for the D.C.H.

Applications, with full particulars, to the Administrative Officer at the Hospital, quoting Ref. (L).

DONCASTER ROYAL INFIRMARY. (330 Beds.) DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN. The post is approved for Pre-registration Service.

Applications, stating age, qualifications with dates and nationality, and accompanied by copies of 3 recent testimonials, should be forwarded to the Secretary to the Committee at the Doncaster Royal Infirmary.

DONCASTER ROYAL INFIRMARY. (330 Beds.) Recognised under the regulations for the Fellowship examination of the Royal College of Surgeons. DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON. The post is approved for Pre-registration Service.

Applications, stating age, qualifications with dates, and nationality and accompanied by copies of 3 recent testimonials, should be forwarded to the Secretary to the Committee at the Doncaster Royal Infirmary.

DORKING GENERAL HOSPITAL, Horsham-road, Dorking. (234 Beds.) REDHILL GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (surgical), vacant 1st August, 1954. Excellent general surgical experience.

Apply to the Medical Superintendent.

DOVERCOURT. HARWICH AND DISTRICT HOSPITAL. (30 Beds.) Applications invited for post of SENIOR HOUSE OFFICER (resident Surgical Officer). Post tenable for 1 year.

Applications, with copies of 3 testimonials, should be forwarded to the Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

DOVER, KENT. BUCKLAND HOSPITAL. Applications are invited for 2 appointments of HOUSE PHYSICIAN which will shortly become vacant at the above Hospital. Salary £425, £475 or £525 a year, less a deduction of £125 a year for residential emoluments.

Applications, stating age, qualifications, experience, and the names and addresses of 2 referees, should be made to the Group Secretary, South-East Kent Hospital Management Committee, "Ash-Eton," Radnor Park West, Folkestone.

DOVER. ROYAL VICTORIA HOSPITAL. Applications are invited for the post of HOUSE SURGEON at the above Hospital. The post is recognised by the Royal College of Surgeons. Salary £425, £475, or £525 a year, according to experience. A deduction of £125 a year will be made for residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (Fracture Department), vacant 20th August, 1954.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary, by 10th July, 1954.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners, for the appointment of HOUSE PHYSICIAN (medical and paediatrics), vacant 11th August, 1954.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary by 3rd July, 1954.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (E.N.T. Department—31 Beds), vacant now. The post is recognised for the F.R.C.S. examination.

Applications, with copies of 2 recent testimonials, to be forwarded to the Hospital Secretary as soon as possible.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. EXETER AND MID-DEVON HOSPITALS MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners, for the appointment of HOUSE SURGEON (Obstetric and Gynaecological Department), vacant 24th August, 1954.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary by 3rd July, 1954.

EAST CUMBERLAND HOSPITAL MANAGEMENT COMMITTEE. Appointment of House Officers. Applications are invited for the following appointments:

Cumberland Infirmary, Carlisle (340 Beds)

1 HOUSE OFFICER ("Specials"—E.N.T. and Eyes).

1 SENIOR HOUSE OFFICER (orthopaedics).

Applications, with names of 2 referees, should be forwarded immediately to the Secretary, East Cumberland Hospital Management Committee, Cumberland Infirmary, Carlisle.

EAST FIFE HOSPITALS BOARD OF MANAGEMENT. CRAIGTOUN MATERNITY HOSPITAL, ST. ANDREWS (41 Beds), AND ASSOCIATED ANTENATAL CLINICS. Applications are invited for the appointment of 2 RESIDENT HOUSE OFFICERS at the above Hospital. The posts will become vacant on 1st August and 1st October, 1954, and the tenure of each will be for 6 months. At present only 1 of the posts qualifies for pre-registration. Salary on national scale.

Apply, with references, to the Medical Superintendent, East Fife Hospitals Board of Management, 243A, High-street, Kirkcaldy.

EDGWARE GENERAL HOSPITAL. Edgware, Middlesex. (715 Beds.) RESIDENT PAEDIATRIC HOUSE PHYSICIAN for above Hospital. Post vacant 27th July, 1954. Salary according to experience. 6 months appointment.

Applications, stating age, qualifications, experience, and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 3rd July, 1954. Candidates selected for interview will be notified by 10th July, 1954.

EDINBURGH. ROYAL HOSPITAL FOR SICK CHILDREN. Applications are invited from registered medical practitioners for 2 appointments for 12 months of SENIOR HOUSE OFFICER (1 surgical commencing 1st October, 1954; 1 medical commencing 1st September, 1954). Whitley Council scale.

Applications, stating age, qualifications and experience and names of 2 referees, to be sent immediately to Medical Superintendent, Edinburgh Central Hospitals, 18, Rillbank-terrace, Edinburgh, 9.

EDINBURGH. PRINCESS MARGARET ROSE HOSPITAL. Applications are invited from registered medical practitioners for appointment of SENIOR HOUSE OFFICER for 12 months commencing 1st October, 1954. Whitley Council scale.

Applications, stating age, qualifications and experience and names of 2 referees, to be sent immediately to Medical Superintendent, Edinburgh Central Hospitals, 18, Rillbank-terrace, Edinburgh, 9.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. Appointment of RESIDENT HOUSE SURGEON (second or third post), vacant 7th August, 1954. Duties with General Surgical Unit which includes some orthopaedics. 6 months appointment. Post recognised by the Royal College of Surgeons.

Applications, with the names and addresses of 2 referees, to the Secretary of the Management Committee.

EPSOM, SURREY. HORTON HOSPITAL. Horton Hospital MANAGEMENT COMMITTEE, SOUTH WEST METROPOLITAN REGION. Applications are invited for the post of SENIOR REGISTRAR in Psychiatry with duties at above Hospital. Applicants must possess the D.P.M. and have had experience in adult psychiatry. Residential accommodation is available for a single person. Candidates may visit the Hospital by arrangement with the Physician-Superintendent.

Forms of application obtainable from the Secretary, Horton Hospital, Epsom, Surrey, to whom they should be returned, duly completed, not later than 9th July, 1954.

FOLKESTONE. ROYAL VICTORIA HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON which is recognised for Pre-registration Service. The duties will be mainly obstetrical and gynaecological with some general surgery. The post will become vacant on 19th July, 1954. Salary £425, £475 or £525 a year, less a deduction of £125 a year for residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

GLASGOW. HAWKHEAD (MENTAL) HOSPITAL. 510, Crookston-road, GLASGOW, S.W.3. Applications are invited for the post of SENIOR HOUSE OFFICER in Psychiatry (Male or Female), resident or non-resident. The post offers wide experience and training in all aspects of psychiatry (in-patient and outpatient), and all modern methods of treatment are carried out. Recognised for D.P.M.

Applications, together with the names of 2 referees, should be forwarded as soon as possible to Physician-Superintendent at above address.

GLASGOW, N. STOBHILL GENERAL HOSPITAL. PSYCHIATRIC UNIT. HOUSE OFFICERS (resident), Male or Female, required now. (180 Beds.) 1200 admissions yearly. Acute treatable cases. Unit recognised for D.P.M. Salary £50 above standard rate.

Apply to Medical Superintendent.

GLASGOW, N. STOBHILL GENERAL HOSPITAL. Vacancies for HOUSE OFFICERS exist in the following units for the term beginning 1st August, 1954.

Dermatology Unit.

Phthisis Unit.

Surgical Unit.

Ear, Nose and Throat Unit.

Applications should be sent to the Medical Superintendent.

GLASGOW, N. STOBHILL GENERAL HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in the acute Geriatric Unit (70 Beds—for assessment and rehabilitation), supervised by a Consultant Physician specialising in geriatrics. The appointment offers excellent clinical experience in the diagnosis and treatment of acute and other illnesses in the elderly, and will be for 2 years in the first instance.

Applications, stating age, qualifications and experience, with the names of 2 referees, should be sent to the Medical Superintendent.

GLASGOW, S.W.1. DAVID ELDER INFIRmary. (50 gynaecological beds.) JUNIOR HOUSE OFFICER required for 1st August, 1954, for above Gynaecological Unit. Post recognised by University as pre-registration appointment.

Apply, in writing, immediately to Medical Superintendent.

GLASGOW ROYAL INFIRMARY. Senior House Officer in Orthopaedics. Duties at above Infirmary.

Write, giving 3 names for reference, to the Secretary, Board of Management for Glasgow Royal Infirmary and Associated Hospitals, 135, Buchanan-street, Glasgow, C.1.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. SENIOR HOUSE OFFICER in Medicine.

Write to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Gowan-road, Glasgow, S.W.1, naming 2 referees, by 20th July, 1954.

GRIMSBY GENERAL HOSPITAL. (226 Beds.) Grimsby HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER for Orthopaedic, Fracture and Accident Service. Previous surgical and orthopaedic experience would be an advantage. Post recognised for F.R.C.S. Excellent Medical Library facilities.

Applications should be sent immediately to the Hospital Secretary, Grimsby General Hospital.

GRIMSBY GENERAL HOSPITAL. (226 Beds.) Grimsby HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (gynaecological), Male or Female, for duties at the above-named Hospital and Scartho Road Infirmary, Grimsby. A Locum appointment would be considered.

Applications, with the names of 2 referees, to Hospital Secretary, Grimsby General Hospital.

GRIMSBY GENERAL HOSPITAL. (226 Beds.) Grimsby HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR (pre-registration) or SENIOR HOUSE OFFICER (surgical), vacant from 1st August, 1954.

Applications, with names of 2 referees, to Hospital Secretary, Grimsby General Hospital.

HALIFAX GENERAL HOSPITAL. (425 Beds.) House SURGEON required. Approved pre-registration appointment. Post vacant July.

Applications to the Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX GENERAL HOSPITAL. House Physician required for Pediatric Unit of 35 Beds. Approved pre-registration appointment and recognised for D.C.H. Post vacant July.

Applications to the Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX GENERAL HOSPITAL. (425 Beds.) House PHYSICIAN required. Approved pre-registration appointment.

Applications to the Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX GENERAL HOSPITAL. (425 Beds.) Junior HOSPITAL MEDICAL OFFICER in Anaesthetics required. Opportunities for studying for D.A. Board-residence available.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ST. JOHN'S HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER at the above Hospital which has 332 Beds for geriatric cases and chronic sick patients. Good facilities for modern method of treating geriatric cases. Pathological Laboratory; Physiotherapy and Occupational Therapy Departments situated at the Hospital.

Applications to the Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. (301 Beds.) HOUSE SURGEON (E.N.T. and ophthalmology) required. Post now vacant. Approved pre-registration appointment.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. (301 Beds.) SENIOR HOUSE OFFICER in General Surgery required. Post vacant late July.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) SENIOR HOUSE OFFICER (casualty and orthopaedic). Post vacant 1st August. National scale of salary.

Apply to Hospital Administrator.

HASTINGS. ST. HELEN'S HOSPITAL. (497 Beds.) HOUSE PHYSICIAN (resident) for Pediatrics and General Medicine. National scale of salary. Post vacant now.

Apply to Hospital Administrator.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (163 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER for general surgical duties at the above Hospital. Salary in accordance with the approved scales—viz., £745 p.a., less £145 p.a. for residential emoluments.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to Group Secretary, West Wales Hospital Management Committee, Glanwill, Carmarthen.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (163 Beds. Recognised by the Royal College of Surgeons and for Pre-registration Service.) **WEST WALES HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the post of **RESIDENT HOUSE OFFICER (surgical).** Salary £425, £475 and £525 p.a., according to experience (plus special grant of £50 p.a.), less £125 p.a. for residential emoluments.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

HEMEL HEMPSTEAD, HERTFORDSHIRE. West Herts HOSPITAL. (167 Beds.) **HOUSE SURGEON** (pre-registration).

Applications, accompanied by copies of 2 recent testimonials, should be sent to the Hospital Secretary at once.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for the appointment of **HOUSE SURGEON** (General—second post), to commence 5th August, 1954. Pre-registration post; recognised under F.R.C.S. regulations.

Applications to Group Secretary, Hertford Group Hospital Management Committee, Hertford County Hospital, Hertford, Herts.

HITCHIN HOSPITALS, Hitchin, Hertfordshire. Resident SENIOR HOUSE OFFICER (casualty) for duty with the Accident Service and as Orthopaedic House Surgeon, required, for 6 months in the first instance, on 26th July, 1954.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent immediately to the Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, Beds.

HOVE GENERAL HOSPITAL, Sussex. House Surgeon AND CASUALTY OFFICER (recognised for F.R.C.S.) required as soon as possible. Salary £525, less £125 p.a. for residential emoluments.

Applications, stating age, qualifications, experience and naming 2 referees, to the Administrative Officer.

HUDDERSFIELD ROYAL INFIRMARY. (312 Beds.) **HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE.** **HOUSE SURGEON** required, to commence duty immediately. The post is recognised as a pre-registration appointment. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from provisionally registered or registered medical practitioners for the post of **HOUSE SURGEON** to the Princess Royal Maternity Home (57 Beds), to commence duty on 1st August, 1954. The holder of the post, which is recognised for the D.Obst.R.C.O.G., will have access to the abnormal maternity and gynaecological beds at The Royal Infirmary. The Department is under the control of 2 Consultant Obstetricians and Gynaecologists. Salary in accordance with national scale.

Applications to be addressed to—

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HULL. KINGSTON GENERAL HOSPITAL. (447 Beds.) Applications are invited for the post of **RESIDENT SENIOR HOUSE SURGEON** (recognised for the F.R.C.S. examinations). There are 69 general surgical beds and some supervision is required of 17 gynaecological beds. Salary £745, less emoluments. Post now vacant.

Applications, with names of referees, to the Secretary, Hull A Group Hospital Management Committee.

HULL. KINGSTON GENERAL HOSPITAL. (447 Beds.) Applications are invited for the pre-registration appointment of **HOUSE OFFICER** (general surgery). Recognised for the F.R.C.S. examinations. Salary £425, £475, or £525 according to experience. The post is resident and tenable for 6 months. Vacant 1st July, 1954.

Applications, with full particulars, to the Secretary, Hull A Group Hospital Management Committee.

ILFORD, ESSEX. KING GEORGE HOSPITAL. Ilford AND BARKING GROUP HOSPITAL MANAGEMENT COMMITTEE. There will be vacancies for the following at the above Hospital.

HOUSE SURGEON—24th July, 1954.

HOUSE SURGEON—29th July, 1954.

HOUSE SURGEON—20th August, 1954.

Post on pre-registration.

Applications, giving full particulars and accompanied by testimonials, to be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Deputy Group Secretary.

King George Hospital, Ilford.

ILFORD, ESSEX. KING GEORGE HOSPITAL. Ilford AND BARKING GROUP HOSPITAL MANAGEMENT COMMITTEE. There will be a vacancy for a **HOUSE PHYSICIAN** (post or pre-registration) at the above Hospital on 16th July, 1954. The post will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Deputy Secretary.

King George Hospital, Ilford.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) Applications are invited for the post of **SENIOR HOUSE OFFICER** (resident Anesthetist). The post, which is normally of 1 years duration, is recognised for the D.A. and the F.F.A.R.C.S. examinations.

Applications, stating age, nationality, together with recent testimonials, to Hospital Secretary.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) Applications are invited for the post of **SENIOR HOUSE SURGEON** to the Fracture and Orthopaedic Department. The post is graded Senior House Officer and is recognised for the F.R.C.S. examinations. The Department has 2 Consultants, about 60 Beds and a large outpatients attendance and offers a wide experience.

Applications, stating age, nationality, experience and copies of 3 recent testimonials, to the Hospital Secretary.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) Applications are invited for the post of **HOUSE SURGEON** to the Fracture and Orthopaedic Department. Approved pre-registration post.

Applications, with copies of recent testimonials, to the Hospital Secretary.

IRVINE, AYRSHIRE. CENTRAL HOSPITAL. Board of MANAGEMENT FOR NORTHERN AYRSHIRE HOSPITALS. Applications are invited from registered medical practitioners for the post of **ASSISTANT BACTERIOLOGIST AND CLINICAL PATHOLOGIST** (Junior Hospital Medical Officer) at the County Laboratory, at above Hospital, vacant now. National terms. Applicants should have had some experience in bacteriology and preferably also in haematology.

Apply immediately, enclosing copies of 3 testimonials, to Area Medical Superintendent, 1, Hill-street, Kilmarnock.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. **SENIOR HOUSE OFFICER** required for Specials Unit which comprises E.N.T. Plastics and Ophthalmic Departments. Candidates should have held medical and surgical house posts.

Applications, stating age, nationality, qualifications and experience, with copies of up to 3 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, by 7th July, 1954.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. **SENIOR HOUSE OFFICER** required for Maternity Department. Must have held medical, surgical, obstetrical and gynaecological house posts.

Applications, stating age, nationality, qualifications and experience, with copies of up to 3 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, by 8th July, 1954.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. **SENIOR HOUSE OFFICER** required for Dermatological Unit. Candidates must have held medical and surgical house posts and previous experience in dermatology desirable. Post suitable for anyone intending to specialise in this subject.

Applications, stating age, nationality, qualifications and experience, with copies of up to 3 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, by 7th July, 1954.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. **SENIOR HOUSE OFFICER** required for Psychiatric Unit. Duties mainly in observation wards. Post recognised by Conjoint and R.M.P.A. as D.P.M. training post.

Applications, stating age, nationality, qualifications and experience, with copies of up to 3 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, by 6th July, 1954.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. Pre-registration **HOUSE OFFICERS** (2) required for general medicine.

Applications, stating age, nationality, qualifications obtained with copies of up to 2 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, Middlesex, by 6th July, 1954.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. Pre-registration **HOUSE OFFICER** required for Maternity Unit.

Applications, stating age, nationality, qualifications obtained with copies of up to 2 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, Middlesex, by 6th July, 1954.

KIDDERMINSTER AND DISTRICT GENERAL HOSPITAL. (112 Beds.) **HOUSE SURGEON** required at the above Hospital. Post vacant early July. Salary £425-£525 according to experience.

Applications, with the names of 3 referees, to the Hospital Secretary.

LEEDS A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of **SENIOR HOUSE OFFICER** (anaesthetics) for duties mainly at St. James's Hospital. The appointment, which is recognised for the D.A. and the F.F.A.R.C.S., will be for a period of 1 year, and the salary will be in accordance with the agreed terms and conditions of service of hospital medical and dental staffs—namely, £745 p.a. with an appropriate deduction in respect of board, lodging, and other services provided.

Applications, stating age, qualifications, experience, &c., together with the names of 2 referees, to be forwarded to the undersigned as soon as possible.

J. FOLKARD, Secretary to the Committee.

Administrative Offices, St. James's Hospital, Leeds, 9.

LEEDS. UNITED LEEDS HOSPITALS. Applications are invited for the post of **SENIOR HOUSE OFFICER** or **HOUSE OFFICER** (pre-registration post) to the Department of Urology at the General Infirmary at Leeds. The post, which is resident, will be for a period of 6 months in the first instance.

Applications, stating age, qualifications and previous posts with dates, should be forwarded to the undersigned not later than 7th July, 1954.

J. ARNOLD TUNSTALL, Secretary to the Board.

The General Infirmary, Leeds, 1.

LEEDS. UNITED LEEDS HOSPITALS. Applications are invited for the post of REGISTRAR in Anaesthetics. The appointment will be for 1 year in the first instance.

Applications, giving full details of previous experience, together with the names of 3 referees, should be forwarded to the Sub-Dean, School of Medicine, Leeds, 1, not later than 5th July, 1954.

LEEDS REGIONAL HOSPITAL BOARD invites applications for the following REGISTRAR posts :—

Anæsthetics

Duties in the Harrogate and Ripon Group, mainly at Harrogate General Hospital (resident/non-resident).

General Surgery

St. Luke's Hospital, Bradford (150 general surgical beds) (non-resident). Recognised for the F.R.C.S.

General and Plastic Surgery

St. Luke's Hospital Bradford (150 general surgical beds). Half the duties will be in the Plastic Unit (20 Beds) (preferably resident).

Orthopaedic Surgery

(a) Hull A Group (50 orthopaedic beds), Hull B Group and East Riding Group (50 orthopaedic beds) (non-resident). Includes some duties in the Casualty Department at the Hull Royal Infirmary.

(b) Huddersfield Royal Infirmary and other hospitals in the Huddersfield Group (34 orthopaedic beds) (non-resident).

(c) The General Hospital, Batley (36 orthopaedic beds) and other hospitals in the Dewsbury Batley and Mirfield Group (resident).

Psychiatry

Psychiatric Unit, St. James's Hospital, Leeds (resident). Offers special opportunity for experience with neurotic and psychosomatic patients.

Thoracic Surgery

Pinderfields General Hospital, Wakefield. Experience in thoracic surgery desirable. 53 Beds under the Consultants to the Teaching Hospital. (Resident.)

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later than 1st July, 1954.

LEEDS. SEACROFT HOSPITAL, York-road. House SURGEON required immediately for above Hospital for children's wards for general, ophthalmic and E.N.T. surgery. Recognised pre-registration post.

Apply, giving full details and names of 2 referees, to Group Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP. RESIDENT HOUSE SURGEON (general surgery). Post vacant now. Recognised for pre-registration. Post provides excellent experience. Good accommodation available.

Apply Hospital Secretary.

LLANELLY HOSPITAL, Llanelli, Carmarthenshire. (164 Beds.) GLANTAWE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER for duty in the E.N.T., Ophthalmic and Gynaecological Departments.

Full particulars, stating age, qualifications and experience, should be addressed to the Hospital Secretary, Llanelli Hospital, Marble Hall-road, Llanelli.

LOWESTOFT AND NORTH SUFFOLK HOSPITAL. LOWESTOFT. (99 Beds.) Applications are invited for the appointment of SENIOR HOUSE SURGEON. Salary £745 p.a., less £150 for residential emoluments. The Hospital is staffed by Consultant General Surgeons and visiting Consultants in all specialties from the Norfolk and Norwich Hospital.

Applications, stating age, qualifications and experience with names of 2 referees, to Hospital Secretary, immediately.

LINCOLN. COUNTY HOSPITAL. (200 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in Surgery and E.N.T.

Applications, giving full particulars, should be addressed to—
R. W. HOWICK, Group Secretary.

LINCOLN. ST. GEORGE'S HOSPITAL. (178 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (resident) to assist the Resident Medical Officer at the above Hospital which has medical, surgical, orthopaedic, and geriatric beds.

Applications, giving full particulars, together with 3 names for reference, should be addressed to—
R. W. HOWICK, Group Secretary.

County Hospital, Lincoln.

LIVERPOOL. BOOTLE HOSPITAL. (119 Beds.) HOUSE SURGEON (general surgery) required 1st July, 1954, or as soon after as possible. Recognised pre-registration post.

Applications to Secretary, North Liverpool Hospital Management Committee, Walton Hospital, Liverpool, 9.

LIVERPOOL. 15. SEFTON GENERAL HOSPITAL. (995 Beds, 116 Cots.) Applications are invited for the following resident appointments which will become vacant at the above-named Hospital on 1st September, 1954, and will be for a period of 6 months. These posts are approved as pre-registration posts.

5 HOUSE PHYSICIANS (general).
2 HOUSE PHYSICIANS (psychiatric).

2 HOUSE SURGEONS (general).

2 HOUSE SURGEONS (obstetric).

1 HOUSE PHYSICIAN (tropical).

The terms and conditions of service will be in accordance with the regulations of the Ministry of Health.

Application forms may be obtained from the undersigned, to whom they should be returned not later than Thursday, 8th July, 1954.

GARNET CHAPLIN, Secretary to the Committee,
South Liverpool Hospital Management Committee.

LIVERPOOL. WALTON HOSPITAL. (1321 Beds.) The following resident posts are vacant from the dates stated :—
Vacant now.

HOUSE SURGEONS (general surgery).

1st September, 1954.

HOUSE PHYSICIANS (general medicine).

HOUSE SURGEONS (general surgery).

HOUSE SURGEON (orthopaedics).

1st October, 1954.

HOUSE SURGEONS (gynaecology).

All these posts are recognised for Pre-registration Service.

Applications, stating age, date of qualification, experience and enclosing 2 copies of recent testimonials, to the Physician-Superintendent, Walton Hospital, Liverpool, 9.

LIVERPOOL. WALTON HOSPITAL. (1321 Beds.) SENIOR HOUSE OFFICER (neurosurgery), vacant now.

Applications, stating age, date of qualification and experience, with copies of 2 recent testimonials, to Physician-Superintendent.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. Applications are invited for the post of HOUSE SURGEON, vacant 1st July, 1954. Recognised as pre-registration post and for F.R.C.S. The appointment will be for 6 months in the first instance.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Secretary by 28th June.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. Applications are invited for the post of HOUSE SURGEON, vacant 9th July, 1954. Recognised as pre-registration post and for F.R.C.S. The appointment will be for 6 months in the first instance.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Secretary by 5th July.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. SENIOR HOUSE OFFICER (resident) in Medicine required.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Secretary by 30th June.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE.

Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months appointment. Post vacant July, 1954. Salary at the rate of £425, £475 to £525 according to experience. A deduction at the rate of £125 a year is made in respect of board and lodging and other services provided.

Applications should be forwarded as soon as possible to the Administrative Officer at the Hospital.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE.

Applications are invited for the appointment of RECEIVING-ROOM OFFICER. Post now vacant. Salary £745 a year, with deduction at present of £150 a year for residential emoluments.

Applications to Administrative Officer at Hospital as soon as possible.

MANCHESTER ROYAL EYE HOSPITAL. United MANCHESTER HOSPITALS. Applications are invited for post of SENIOR HOUSE OFFICER. Salary £670 p.a., less £130 p.a. for residential emoluments.

Application forms may be obtained from the undersigned.
H. R. NORTE, General Superintendent.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time resident post of REGISTRAR in General Surgery (recognised for F.R.C.S.(Eng.)) in the Ashton, Hyde and Glossop Group of hospitals.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 testimonials, should be forwarded to the Group Secretary, Astley-road, Stalybridge, Cheshire.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for a post of SURGICAL REGISTRAR (resident or non-resident) at the North Lonsdale Hospital, Barrow-in-Furness. Post recognised for F.R.C.S.

Applications to Group Secretary, Barrow and Furness Hospital Management Committee, 52, Paradise-street, Barrow-in-Furness, not later than 10th July, 1954.

MANCHESTER REGIONAL HOSPITAL BOARD. Royal MANCHESTER CHILDREN'S HOSPITAL. SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Surgical Registrar), falling vacant 1st July, 1954. Previous experience in surgery essential. Experience in paediatric surgery and the Diploma of F.R.C.S. desirable. The Hospital is the chief teaching unit of the University Department of Child Health.

Applications, stating age, nationality and experience, together with names of 3 referees, to be forwarded to the Group Secretary, Salford Royal Hospital, Chapel-street, Salford, 3, to be received within 7 days of appearance of this advertisement.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. The Board invite applications for the post of REGISTRAR in E.N.T. Surgery in the South Manchester Group, with principle duties at the Manchester Ear Hospital.

Applications, stating age, qualifications, present post and names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of RESIDENT REGISTRAR in Obstetrics and Gynaecology in the West Manchester Group of hospitals with main duties at Park Hospital, Davyhulme. There are 73 obstetric beds, 31 gynaecology beds, and a special care Baby Unit of 7 Beds at Park Hospital. Post recognised for the M.R.C.O.G. Vacant 31st August, 1954. Appointment for 1 year, renewable.

Application forms from Secretary, Park Hospital, Davyhulme.

MANCHESTER REGIONAL HOSPITAL BOARD. Resident REGISTRAR (obstetrics/gynaecology) required early September in the Blackburn and District Hospital Group. Recognised post for F.R.C.O.G. based on Queen's Park Hospital, Blackburn (a general hospital with 83 obstetric/gynaecological beds) with duties at Blackburn Royal Infirmary and Accrington Victoria Hospital.

Application forms obtainable from and returnable to the Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

MANCHESTER. UNITED MANCHESTER HOSPITALS.

MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of REGISTRAR (resident). Tenable for 12 months, subject to renewal. Previous experience in ophthalmology essential. The terms and conditions of service for hospital medical and dental staffs will apply.

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS.

SAINT MARY'S HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER in Obstetrics. Applicants must have had previous hospital experience in general medicine and surgery, and in obstetrics. The post is recognised for purposes of the M.R.C.O.G. examination. The duties involve clinical responsibility for mothers and babies, and supervision of the work of pre-registration House Officers is also included. The appointment is for 12 months from 1st September, 1954. National scale.

Application forms may be obtained from the undersigned and returned not later than 5th July, 1954.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

MANCHESTER. UNITED MANCHESTER HOSPITALS.

MANCHESTER ROYAL INFIRMIARY, MANCHESTER, 13. SENIOR REGISTRAR to the Department of Psychiatry, to commence as soon as possible. Applicants must have held house appointments and possess a higher qualification. Whole-time non-resident appointment for 12 months, renewable. The successful applicant will be expected to participate in the teaching of the department and engage in research work. He will also be required to undertake duties in connection with a small unit shortly to be opened in 1 of the Mental Hospitals in the Region.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 14th July, 1954.

F. J. CABLE, Secretary to the Board of Governors.

MANCHESTER. UNITED MANCHESTER HOSPITALS.

MANCHESTER ROYAL INFIRMIARY, MANCHESTER, 13. REGISTRAR to the Department of Cardiology, to commence on 7th August, 1954. Whole-time non-resident post, tenable for 12 months, renewable for a further 12 months.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 14th July, 1954.

G. H. TAYLOR, Secretary.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE.

PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) HOUSE OFFICER (general surgery) required, pre- or post-registration. Post vacant 18th July, 1954.

Forms from Secretary.

MANCHESTER. DARBISHIRE HOUSE HEALTH CENTRE.

A General Practitioner LOCUM is required for short or long periods up to 4 months commencing immediately. Accommodation in the Centre is available, if required. 20 guineas weekly. Experience in this teaching Health Centre would be valuable for later practice.

Further particulars from the Secretary, Darbshire House Health Centre, 295, Upper Brook-street, Manchester, 13 (Telephone No. Manchester Rusholme 6322).

MANCHESTER, 19. DUCHESS OF YORK HOSPITAL FOR BABIES. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered practitioners (Male or Female) for the post of HOUSE PHYSICIAN for 6 months from 1st August, 1954. The Hospital is associated with Manchester University for teaching purposes.

Applications, with copies of 3 testimonials, to be forwarded to the Administrative Officer of the Hospital by 10th July, 1954.

MID-GLAMORGAN HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following Medical staff appointments, vacant on the dates stated:—

Neath General Hospital (412 Beds)

HOUSE SURGEON (E.N.T. and ophthalmology); immediately.

HOUSE SURGEON; 1st August, 1954.

HOUSE PHYSICIAN; 1st August, 1954.

HOUSE PHYSICIAN (obstetrics and gynaecology); 24th August, 1954.

Port Talbot General Hospital, Hospital-road, Port Talbot (85 Beds) (in association with Neath General Hospital)

SENIOR HOUSE OFFICER (general medicine); immediately.

Bridgend General Hospital, Quarella-road, Bridgend (364 Beds)

SENIOR HOUSE OFFICER (paediatrics); 1st August, 1954.

HOUSE SURGEON (obstetrics and gynaecology); 1st August, 1954.

HOUSE SURGEON; 1st August, 1954.

HOUSE SURGEON (orthopaedic and traumatics); 1st August, 1954.

HOUSE PHYSICIAN; 1st August, 1954.

Neath General Hospital and Bridgend General Hospital are recognised for the principal Diplomas and are both approved by the General Medical Council for Pre-registration Service under Section 2 of the Medical Act, 1950.

Applications, naming 2 referees, to be addressed to the Group Secretary of the Committee, 8, Wind-street, Neath.

MARGATE. ROYAL SEA BATHING HOSPITAL. (241 Beds.) SENIOR HOUSE OFFICER. This post, which becomes vacant on 6th July, 1954, is primarily an orthopaedic one and affords experience in the treatment of tuberculous and non-tuberculous orthopaedic conditions. There are also beds for the treatment of genito-urinary tuberculosis. The post is suitable for candidates for the Primary and the Final F.R.C.S. examinations. Salary £745 p.a., less £150 for residential emoluments.

Applications, with copies of testimonials, to the Medical Superintendent.

NEWARK GENERAL HOSPITAL. Newark. (82 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL OFFICER with general duties required at Registrar rate of pay. This post offers good experience to anyone preparing to enter general practice. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 5th July, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

NEWMARKET GENERAL HOSPITAL. Newmarket, SUFFOLK. Applications are invited for the post of HOUSE SURGEON, vacant 26th July. Duties include surgical house charge of general surgical, E.N.T. and eye cases. The post is resident and available for 6 months, and is recognised for pre-registration.

Applications, with copies of 3 recent testimonials, should be addressed to the Physician-Superintendent.

NEWPORT, MONMOUTHSHIRE. ROYAL GWENT HOSPITAL. (280 Beds, 10 residents. Recognised F.R.C.S.) SENIOR HOUSE OFFICER required for Casualty Department beginning of July. This is the base Hospital in the Group and all medical and surgical emergencies are admitted through casualty, which is under the full-time charge of a Senior Hospital Medical Officer, there being also 2 Senior House Officers. Post recognised for F.R.C.S. for 6 months and tenable 6 or 12 months as desired. Salary £745, less £120 for board-residence.

Write, quoting 2 referees, to T. A. JONES, Group Secretary, 64, Cardiff-road, Newport, Mon.

NEWPORT, I.W. ST. MARY'S HOSPITAL. (380 Beds.) ISLE OF WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required as Casualty Officer and House Officer to Consultant Obstetrician and Gynaecologist, vacant August. Salary £745, less residential charge. Modern flat available for married candidate.

Applications, with names of 2 referees, to Hospital Secretary.

NORTHAMPTON. ST. CRISPIN HOSPITAL. Duston, NORTHAMPTON. (1250 Beds.) SENIOR HOUSE OFFICER required. Salary according to national scale. A well-appointed flat is available at the Hospital at moderate rental. The Hospital is approved for training for the D.P.M. of the Conjoint Board and facilities are available in child psychiatry and outpatient clinics locally, and in neurology (at Oxford). There is a modern Admission Unit and an annual admission-rate of over 600 patients annually. Regular case conferences are held.

Applications, giving full details and names of 3 referees, to be sent to the Physician-Superintendent at the Hospital within 14 days.

NORTHWOOD, MIDDLESEX. MOUNT VERNON HOSPITAL. Locum ANAESTHETIC REGISTRAR required for 4 weeks commencing 4th July, 1954.

Applications to the Secretary and House Governor.

NOTTINGHAM CHILDREN'S HOSPITAL. (136 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON (post recognised for pre-registration), which is vacant immediately. The post is tenable for 6 months.

Applications, with copies of 2 testimonials, should be sent to the Secretary, Nottingham Children's Hospital, Chestnut-grove, Nottingham.

NOTTINGHAM CITY HOSPITAL. (804 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (medical). Post vacant 1st August. The appointment will be for 1 year.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent immediately to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered general practitioners for the post of THIRD CASUALTY OFFICER (Senior House Officer grade). Salary (less £150 emoluments) and conditions of service in accordance with those laid down by the Ministry. Duties to commence as soon as possible. This post offers wide experience of casualty work. The Staff establishment requires only 1 night in 3 emergency work, and off duty permits time for study for higher examinations.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—General Hospital, Nottingham. HENRY M. STANLEY.

NOTTINGHAM GENERAL HOSPITAL. 2 Resident HOUSE SURGEONS required (Male or Female, also open to pre-registration candidates) at the above Hospital; duties to commence as soon as possible. Salary and conditions of service in accordance with published regulations. The appointment is for a term of 6 months.

Applications, stating age, qualifications, and experience, to be sent to HENRY M. STANLEY, Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Required, SENIOR SURGICAL HOUSE OFFICER for the above Hospital, duties to commence at beginning of July, 1954. Salary (less £150 residential emoluments) and conditions of service in accordance with those laid down by the Ministry.

Applications, stating age, qualifications and experience together with copies of testimonials, to be sent to—General Hospital, Nottingham. HENRY M. STANLEY.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR ORTHOPÆDIC AND FRACTURE HOUSE OFFICER. (Locum Tenens considered.) The post offers exceptional experience in traumatic and orthopaedic surgery. Duties to commence as soon as possible. Salary and conditions of service in accordance with Ministry regulations. If resident £150 deducted for emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—
HENRY M. STANLEY, Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners (Male or Female—locum tenens considered) for the post of RESIDENT SENIOR ANAESTHETIC HOUSE OFFICER; duties to commence as soon as possible. Terms and conditions of service in accordance with published regulations of the Ministry of Health. £150 deducted for residential emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—
HENRY M. STANLEY, Group Secretary.

NOTTINGHAM AND MIDLAND EYE INFIRMARY. Required, SENIOR HOUSE OFFICER for the above Hospital. Duties to commence on or about 9th August. Salary £745 p.a., less deduction of £150 for residential emoluments.

Applications, stating age, qualifications and experience, together with testimonials, to be sent to—
HENRY M. STANLEY, Group Secretary.

General Hospital, Nottingham.

NORWICH. NORFOLK AND NORWICH HOSPITAL. Applications are invited for the following appointments vacant on 1st August, 1954. All are pre-registration posts and the salaries in each case are at the rate of £425, £475, or £525 p.a. according to experience, less £125 p.a. for residential emoluments:

(1) **Norfolk and Norwich Hospital, Norwich**
(a) JUNIOR CASUALTY OFFICER (2 Casualty Officers employed in Department).

(b) HOUSE SURGEON (Male or Female). Post recognised for Final F.R.C.S. examination. Duties entirely general surgical.

(2) **Jenny Lind Hospital for Children, Norwich**
(a) RESIDENT MEDICAL OFFICER (Male or Female).

(b) HOUSE SURGEON (Male or Female).

At Jenny Lind Hospital which forms the entire Paediatric Department of the United Norwich Hospitals. The duties are under the direct supervision of the Consultant staff of the Norfolk and Norwich Hospital.

(3) **West Norwich and Norwich Isolation Hospitals**

HOUSE PHYSICIAN (Male or Female). Duties include acute medical, geriatric and infectious diseases. The beds at these units are under the control of the Consultant Physicians of the Norfolk and Norwich Hospital and the successful candidate will be required to undertake general medical duties under their supervision.

(4) **West Norwich Hospital**
HOUSE SURGEON (Male or Female). Post recognised for Final F.R.C.S. examination. The beds at this Hospital are under the control of the Consultant staff of the Norfolk and Norwich Hospital.

Applications for all the above posts, stating age, qualifications and experience, with names of 2 referees, to be sent to Group Secretary, No. 6 Group Hospital Management Committee, St. Stephen's-road, Norwich.

OXFORD. WARNEFORD AND PARK HOSPITALS. SENIOR HOUSE OFFICER wanted. Warneford Hospital (140 Beds) is developing as an acute Psychiatric Unit, specially related to research and postgraduate teaching. The adjacent Park Hospital is a Neurosis Centre (30 Beds) with daily outpatient clinics. Previous psychiatric experience not essential. This post is specially suitable for training for D.P.M., for which full facilities are available, including neurology and child psychiatry. The post is resident with accommodation for a single man.

Further particulars may be obtained from the Physician-Superintendent, Warneford Hospital, Oxford, to whom application should be sent, with the names of 2 referees, within 14 days.

OTLEY, YORKSHIRE. THE GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT MEDICAL OFFICER in the grade of Junior Hospital Medical Officer or alternatively in the grade of Senior House Officer. This appointment is at a busy 170-bedded hospital with full Consultant staff who are members of the Teaching staff of Leeds University, offers good experience in acute general medicine and paediatrics. Duties to commence on or about 25th July, 1954.

Applications, stating full particulars of age, nationality and experience, together with the names of 2 referees to the undersigned as soon as possible.

E. W. BEST, Group Secretary,
Ilkley and Otley Hospital Management Committee.

PETERBOROUGH MEMORIAL HOSPITAL. East ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR at above Hospital. The successful candidate will be required to undertake duties in Casualty Department. Post offers wide experience. Appointment for 1 year, renewal for second year.

Detailed applications, including age and names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 5th July, 1954. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

PAISLEY. BARSHAW AND THORNHILL MATERNITY HOSPITALS. MATERNITY UNIT. OBSTETRIC HOUSE SURGEONS (2) required for period commencing 1st August, 1954. Salary according to scale.

Applications should be submitted as early as possible to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS (2) required for period commencing 1st August, 1954. Salary according to scale.

Applications should be submitted as early as possible to Group Medical Superintendent at above address.

PLYMOUTH. MOUNT GOLD ORTHOPÆDIC HOSPITAL (with Annex 122 Beds). PLYMOUTH SPECIAL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER for the Orthopaedic and Fracture Service, centring on Mount Gold Orthopaedic and associate hospitals. Vacancy commences from 1st August, 1954.

Applications, stating age, qualifications with dates, &c., and with copies of 2 recent testimonials, to be forwarded to the Secretary, Mount Gold Hospital, Plymouth, within 14 days of this advertisement appearing.

PLYMOUTH AND DEVONPORT. SOUTH DEVON AND EAST CORNWALL HOSPITAL. HOUSE SURGEONS, required immediately, also 1st and 15th July, 1954, recognised for the F.R.C.S.

ENTRAL HOUSE SURGEON, vacant 1st July, 1954, recognised for the Fellowship.

Applications, stating age, nationality, qualifications and experience, with names of 3 referees, to be sent to—
ARTHUR R. CASH, Group Secretary.
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH, SOUTH DEVON AND EAST CORNWALL GENERAL HOSPITAL GROUP. AREA PATHOLOGICAL DEPARTMENT. Applications invited from duly qualified and registered medical practitioners for the appointment of RESIDENT SENIOR HOUSE OFFICER in Pathology, vacant 27th July, 1954. The appointment will be for a period of 12 months, in the new area laboratory at the South Devon and East Cornwall Hospital, Greenbank-road, Plymouth, which provides excellent modern working facilities.

Applications, stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees, to be sent to ARTHUR R. CASH, Group Secretary.

7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. Applications invited from duly qualified registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in Surgery, vacant about 1st August, 1954. The appointment will be for a period of 12 months. The Hospital is recognised for the F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees, to be sent to the undersigned, closing date 10th July, 1954.

ARTHUR R. CASH, Group Secretary.
7, Nelson-gardens, Stoke, Plymouth.

PONTYPOOL AND DISTRICT HOSPITAL. Pontypool, MONMOUTHSHIRE. (115 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (surgical) required immediately. This is the senior resident post, and resident staff consists of 2 House Surgeons, a House Physician and this post. This is a busy acute general hospital with a good Outpatient Department and regular visits from Consultants. Post affords good practical experience in surgery. Salary £775-250-2107, less £150 board-residence.

Write, quoting 2 referees, to T. A. JONES, Group Secretary, 64, Cardiff-road, Newport, Mon.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000.) SENIOR HOUSE OFFICER (surgical).

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent as soon as possible to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000.) HOUSE OFFICERS (surgical) to commence 1st August, 1954 (to include duties at the Porth and District Hospital).

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent as soon as possible to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000. Recognised for the F.F.A.R.C.S. and D.A.) SENIOR HOUSE OFFICER (anaesthetics).

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000.) SENIOR HOUSE OFFICER (pathology).

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000. Recognised for D.C.H.) HOUSE OFFICER (paediatrics) to commence 1st August, 1954.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent as soon as possible to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000. Recognised for D.Obst.R.C.O.G.) 2 HOUSE OFFICERS (obstetrics) to commence 1st August, 1954.
Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent as soon as possible to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000. Recognised for Membership and D.Obst.R.C.O.G.) 2 SENIOR HOUSE OFFICERS (obstetrics and gynaecology).

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent as soon as possible to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 177,000.) 2 HOUSE OFFICERS (medical) to commence 1st August, 1954.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent as soon as possible to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PORTRSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments:

SENIOR HOUSE OFFICER required in the Traumatic and Orthopaedic Department (105 Beds). Duties mainly at the Royal Portsmouth Hospital. Vacant now.

Saint Mary's Hospital (74 acute medical beds)
HOUSE PHYSICIAN, vacant 25th July, 1954. Pre-registration post.

Royal Portsmouth Hospital (65 acute medical beds)
HOUSE PHYSICIAN, vacant 20th July, 1954. Pre-registration post.

Applications, stating age, experience, and qualifications, and names of 2 referees, should be submitted as soon as possible to—
35, Grove-road South, Southsea. E. H. Hurst.

PORTRSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of GYNAECOLOGICAL HOUSE SURGEON for duties at Queen Alexandra Hospital, Portsmouth, vacant 1st July, 1954. Post recognised for M.R.C.O.G. After expiration of 6 months the successful candidate may be offered House Surgeoncy in obstetrics and gynaecology, at Saint Mary's Hospital, Portsmouth. This post is recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Applications, stating age, experience and qualifications, and names of 2 referees, should be forwarded as soon as possible to—
35, Grove-road South, Southsea. E. H. Hurst.

REDHILL COUNTY HOSPITAL, Earlswood Common, REDHILL, SURREY. REDHILL GROUP HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR in Clinical Pathology for appointment to Group Laboratory. Visits by arrangement with Group Pathologist (Telephone : Redhill 3581).

Application forms from Group Secretary at above address.

READING. ROYAL BERKSHIRE HOSPITAL. (403 Beds.) Applications are invited from provisionally registered medical practitioners (Male or Female) for the resident post of JUNIOR HOUSE SURGEON (E.N.T.) vacant 1st August, 1954. Salary £225-£475, less £125 board-residence.

Write, stating age, qualifications with dates, nationality, with copy of 1 recent testimonial, to the Secretary.

READING. ROYAL BERKSHIRE HOSPITAL. (403 Beds.) Applications are invited from registered medical practitioners (Male or Female), for the appointment of RESIDENT ANAESTHETIST (Senior House Officer grade) vacant immediately for period of 12 months. Recognised for F.F.A.R.C.S. Salary £745 p.a., less £125 p.a. board-residence.

Write, stating age, qualifications with dates, nationality and present post, with copy of 1 recent testimonial, to Secretary.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (603 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Geriatric and Psychiatric Units at the above Hospital. A wide range of facilities are available at the Hospital for the investigation, treatment and rehabilitation of acute and chronic cases.

Applications, stating age, &c., to be sent to the undersigned by 30th June, 1954.

J. C. FIELD, Secretary.

ROCHDALE INFIRMARY. Rochdale and District Hospital Management Committee. SENIOR HOUSE OFFICER (orthopaedics). Post recognised for 6 months for F.R.C.S. examination.

Apply at once to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROCHDALE, BIRCH HILL HOSPITAL. Rochdale and District Hospital Management Committee. Applications are invited for the position of SENIOR HOUSE OFFICER (obstetrics and gynaecology) now vacant at the above Hospital. The post is for 12 months in the first instance and is recognised for the D.Obst.R.C.O.G.

Applications to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, at once.

ROCHDALE, BIRCH HILL HOSPITAL. Rochdale and District Hospital Management Committee. Applications are invited for the position of HOUSE OFFICER (obstetrics and gynaecology) now vacant at the above Hospital. The position is pre-registration or post-registration and is for 6 months. Recognised for D.Obst.R.C.O.G.

Applications to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, at once.

ROCHDALE, BIRCH HILL HOSPITAL. Rochdale and District Hospital Management Committee. HOUSE PHYSICIANS (available for pre-registration). Posts vacant July at above Hospital.

Apply at once, with names and addresses of 2 referees, to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROCHESTER. ST. BARTHolemew's HOSPITAL. (Recognised for F.R.C.S.) MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of CASUALTY OFFICER, vacant now. Post offers good experience with fractures and emergency surgery, and is tenable for 12 months. Salary £670 p.a.

Applications, stating age, nationality, qualifications and experience, together with recent testimonials, to be addressed to the Hospital Secretary.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) ORTHOPAEDIC HOUSE SURGEON (resident) required in the Orthopaedic and Accident Unit, vacant from 1st July, 1954. The service consists of 100 Beds divided equally between traumatic surgery and "cold" orthopaedics. Post is recognised for pre-registration purposes and for F.R.C.S.

Applications to be sent to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) SENIOR HOUSE OFFICER required in Neurosurgical Department. Post now vacant. Suitable for candidates seeking higher qualification as it offers excellent experience in neurology.

Apply to Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford, Essex, as soon as possible.

ROMFORD, ESSEX. RUSH GREEN HOSPITAL. (301 Beds.) SENIOR HOUSE OFFICER in Anaesthetics required from 15th July, 1954. Resident post for Male or Female. Married quarters are available. Good experience, modern equipment. Recognised for D.A. and F.F.A.R.C.S.

Applications to Medical Superintendent. Hospital may be seen by arrangement. Tel. : Romford 7711.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE SURGEON (Male) required immediately. Post not approved for pre-registration purposes.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required from 1st July, 1954. Post not approved for pre-registration purposes.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

RYDE, I.W. ROYAL I.W. COUNTY HOSPITAL. (116 Beds.) ISLE OF WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE PHYSICIAN, vacant mid-July. Post recognised for Pre-registration Service.

Applications, with names of 2 referees, to Hospital Secretary.

SALFORD. HOPE HOSPITAL. Salford Hospital Management Committee. Applications are invited for the following House Officer posts : which become vacant 26th July, 1954.

3 HOUSE SURGEONS (pre-registration).

3 HOUSE PHYSICIANS (pre-registration).

1 PEDIATRIC HOUSE OFFICER (post-registration).

1 OBSTETRICAL HOUSE OFFICER (pre-registration).

1 OBSTETRICAL HOUSE OFFICER (post-registration).

Applications, stating age, qualifications, experience and the names of 2 referees, to be forwarded to the Hospital Secretary immediately.

SALFORD. LADYWELL HOSPITAL. Salford Hospital Management Committee. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital. Duties will be mainly in the Tuberculosis Unit, but the successful applicant will also be engaged on the geriatric and acute infectious disease wards. The post offers opportunities for study and access to other hospitals within the Group. Salary in accordance with scale. A deduction of £140 p.a. will be made for the cost of board-residence.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be submitted immediately to the Hospital Secretary, Ladywell Hospital, Salford, 5, Lancs.

SELBY (near). GATEFORTH HOSPITAL. Senior House OFFICER. Post vacant 1st August. Appointment for 1 year. 100 male tuberculosis beds. Associated with Thoracic Surgical Unit. Charge for board and lodging £150 p.a. (subject to review).

Applications to Group Secretary, Seacroft Hospital, York-road, Leeds.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time post of MEDICAL REGISTRAR at the Inverness Hospitals. Main duties are at Raigmore Hospital, Inverness.

A form of application and a note of further particulars are obtainable from the undersigned, to whom applications should be submitted by 10th July, 1954.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR HOUSE OFFICER for duties in Infectious Diseases at Ruchill Hospital, Glasgow. The appointment will be for 1 year in the first instance.

Applications, stating age, qualifications, experience and present appointment and naming 3 referees, to be lodged immediately with the Secretary, Board of Management for Glasgow Northern Hospitals, 13, Woodside-place, Glasgow, C.3.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of SENIOR REGISTRAR in Tuberculosis based at Dumfries and Galloway Sanatorium, Lochmaben, which will be for 1 year in the first instance. This appointment is subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, by 20th July, 1954.

SALISBURY GENERAL HOSPITAL. **Salisbury Group HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the appointment of RESIDENT HOUSE SURGEON for a period of 6 months from 6th August, 1954. The post is open to pre-registration candidates.

Apply, naming 2 referees, to Group Secretary, Odstock Hospital, Salisbury.

SALISBURY GENERAL HOSPITAL. Children's Department. **SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the post of PEDIATRIC HOUSE OFFICER to the above Department, situated at Odstock Hospital and containing 55 medical and surgical beds. Post recognised for D.C.H.

Applications, stating age, nationality, qualifications, previous posts held, with relevant testimonials, should be submitted immediately to Group Secretary, Odstock Hospital, Salisbury.

SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR for the Area Pathological Service based on the Salisbury General Infirmary. Post vacant 1st September.

Further details and applications forms obtainable from, and must be returned to, the Group Secretary, Odstock Hospital, Salisbury, within 14 days of the appearance of this advertisement.

SHOTLEY BRIDGE GENERAL HOSPITAL. Shotley Bridge, Consett, Co. Durham. NORTH WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE OFFICER (obstetrics and gynaecology) required for 6 months commencing 1st August for duties in Obstetrical (30 Beds) and Gynaecological (43 Beds) Departments. Resident at Richard Murray Maternity Hospital. Recognised for D.O.B.R.C.O.G. Second pre-registration or post-registration appointment.

Apply to the Group Secretary stating age and experience and enclosing copies of 3 recent testimonials.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. JESSOP HOSPITAL FOR WOMEN. Applications invited from registered medical practitioners for the resident post of SENIOR HOUSE OFFICER (obstetrics) at the above Hospital from 1st October, 1954.

Applications, stating age, qualifications and experience together with 3 recent testimonials, should be forwarded immediately to The Superintendent, Jessop Hospital for Women, Leavygreave-road, Sheffield, 3.

SHEFFIELD. CITY GENERAL HOSPITAL. Applications are invited for the resident appointment of HOUSE SURGEON (general surgery). Recognised pre-registration post. Vacant on 15th July, 1954.

Applications, giving full details of age, nationality, qualifications, present and previous appointments if any, and the names of 2 persons to whom reference can be made, should be forwarded to W. STANSFIELD at Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. CITY GENERAL HOSPITAL. Applications are invited for the resident appointment of HOUSE PHYSICIAN (general medicine)—recognised pre-registration post, vacant on 15th July, 1954.

Applications, giving full details of age, nationality, qualifications, present and previous appointments if any, and the names of 2 persons to whom reference can be made, should be forwarded to W. STANSFIELD at Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. CITY GENERAL HOSPITAL. Applications are invited for the resident appointment of HOUSE SURGEON (orthopaedics). Recognised pre-registration post. Vacant on 15th July, 1954.

Applications, giving full details of age, nationality, qualifications, present and previous appointments if any, and the names of 2 persons to whom reference can be made, should be forwarded to W. STANSFIELD at Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. CITY GENERAL HOSPITAL. Locum SENIOR HOUSE OFFICER (anaesthetics) required.

Apply, stating period for which available, to the undersigned at Nether Edge Hospital, Sheffield, 11.

W. STANSFIELD, Secretary.

SHEFFIELD. CITY GENERAL HOSPITAL. (Recognised for D.C.H.) Applications are invited for the resident appointment of HOUSE PHYSICIAN (paediatrics). Recognised pre-registration post. Vacant 1st July, 1954.

Applications, giving full details of age, nationality, qualifications, present and previous appointments with dates, and the names of 2 persons to whom reference may be made, should be forwarded to W. STANSFIELD, at Nether Edge Hospital, Sheffield, 11.

SHEFFIELD REGIONAL HOSPITAL BOARD. Applications are invited for the posts of REGISTRAR in Psychiatry in the following hospitals: Carlton Hayes, near Leicester; Mapperley, Nottingham; Pastures, near Derby; and Middlewood, Sheffield; to commence in October, 1954. These posts form a part of the joint training scheme in psychiatry sponsored by the Newcastle and Sheffield Regional Hospital Boards. Full particulars of the posts may be obtained from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield.

Applications should be made to the Secretary of the Board, by 12th July, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SENIOR REGISTRAR in Chest Diseases for the Leicester Isolation Hospital and Chest Unit, Groby-road, Leicester. Clinical duties mainly concerned with chest work but candidates should have general medical experience and special experience in the treatment of chest diseases and tuberculosis. Appointment for 1 year in the first instance, reviewable annually.

Applications giving age, nationality, qualifications, present and previous appointments with dates, and naming 3 referees, to the Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 12th July, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Resident LOCUM SURGICAL REGISTRAR required immediately at King's Mill Hospital, Sutton-in-Ashfield. Remuneration at rate of £16 per week with a deduction for residence.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, naming 2 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Resident LOCUM REGISTRAR (chest diseases) required immediately at Oakwood Hall Sanatorium and Chest Clinic, Rotherham. Remuneration at the rate of £16 per week with a deduction for residence.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, naming 2 referees.

SHREWSBURY. ROYAL SALOP INFIRMARY. (241 Beds.) SHREWSBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from general registered practitioners (Male or Female) for the appointment of RESIDENT HOUSE SURGEON in General Surgery. Now vacant. Recognised for the F.R.C.S., and approved for Pre-registration Service.

Applications, with references, should be sent to the Secretary, Group 15 Hospital Management Committee, Royal Salop Infirmary, Shrewsbury.

SOUTHAMPTON CHEST HOSPITAL. South West METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of Whole-time REGISTRAR in Anaesthetics to the Thoracic Surgical Unit of the above Hospital, becoming vacant in October, 1954. This Unit deals with all types of thoracic surgical cases. Candidates are invited to visit the Unit, if they so desire.

Forms of application may be obtained from the undersigned, to whom they should be returned not later than 10th July, 1954.

FRANK JENNINGS, Group Secretary,

Southampton Group Hospital Management Committee.

Bullar-street, Southampton.

SOUTHAMPTON GENERAL HOSPITAL. (471 Beds—80 surgical.) 2 HOUSE SURGEONS required middle and end of July, 1954. Posts tenable for 6 months. Both recognised for F.R.C.S. and Pre-registration Service.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (278 Beds.) CASUALTY OFFICER/SENIOR HOUSE OFFICER (orthopaedic) required for the above Hospital (Orthopaedic Unit 74 Beds). This Hospital is the centre to which all trauma from a large industrial town and port is directed thus providing excellent experience in the treatment of traumatic conditions.

Applications, with copies of testimonials, to be submitted as soon as possible, to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (278 Beds) AND **SOUTHAMPTON GENERAL HOSPITAL** (471 Beds).

SENIOR HOUSE OFFICER (E.N.T.) required immediately. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work, including audiometry. The Group includes a diagnostic and distributing hearing-aid centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as a Whole-time REGISTRAR in Urology to fill a vacancy in the Canterbury Group of hospitals, for duty mainly at the Kent and Canterbury Hospital, Canterbury, and also at the Royal Sea Bathing Hospital, Margate, in the Isle of Thanet Group of hospitals, where there is work in genito-urinary tuberculosis. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 10th July, 1954.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Part-time REGISTRAR in Dermatology required from 1st August for:—

(i) 2 half-day sessions a week at St. Heller Hospital, Carshalton, Surrey;

(ii) 1 half-day session a week at Kingston Hospital.

Application forms obtainable from, and returnable to, Group Secretary, St. Heller Hospital, Carshalton, Surrey, by 10th July.

SUTTON-IN-ASHFIELD. KING'S MILL HOSPITAL. (172 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required. Appointment for 1 year in first instance. Apart from the Surgical Unit there are also E.N.T. and Gynaecological Units at this Hospital.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 5th July, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. (475 Beds.) GYNAECOLOGY DEPARTMENT. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER or HOUSE OFFICER according to experience. Post recognised for M.R.C.O.G. and/or for pre-registration (surgery). Experience in abnormal obstetrics available, but the work is mostly gynaecological.

Applications, together with copies of 3 testimonials, to Hospital Secretary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (casualty) required (1 of 2) for busy Casualty Department. Experience provided in orthopaedic and plastic cases.

Applications, stating age and qualifications, together with names of 2 referees, to Hospital Secretary.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (382 Beds.) LOCUM JUNIOR HOSPITAL MEDICAL OFFICER required for the Gynaecological and Obstetric Department at the above Hospital from 21st July to 10th August, 1954.

Applications to the Group Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (382 Beds.) HOUSE SURGEON (House Officer grade) required for 1 of the 2 general surgical teams. (Recognised for the F.R.C.S.) Post vacant about 2nd August, 1954, and tenable for 6 months. Preference given to candidates seeking pre-registration posts under the Medical Act, 1950.

Applications to the Group Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (382 Beds.) HOUSE PHYSICIAN (House Officer grade) required for 1 of the 2 medical teams for duties mainly on the acute wards. Post vacant about 28th July, 1954, and tenable for 6 months. Preference given to candidates seeking pre-registration posts under the Medical Act, 1950.

Applications to the Group Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

STROUD GENERAL HOSPITAL, Stroud, Gloucestershire. 2 SENIOR HOUSE OFFICERS required. 1 for medicine and 1 for surgery.

Applications, naming 2 referees, to the Hospital Secretary, Stroud General Hospital, Stroud, Glos.

STAFFORD. STAFFORDSHIRE GENERAL INFIRMARY. (176 Beds.) HOUSE PHYSICIAN (Male or Female). Post or pre-registration candidate considered. Post vacant 1st July.

Applications, giving full particulars and copies of 3 recent testimonials, to the Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STAFFORD. STAFFORDSHIRE GENERAL INFIRMARY. (175 Beds—32 Bed Recovery Unit.) STAFFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (Male or Female). Post or pre-registration candidates considered. Post vacant 17th July.

Applications, giving full particulars and copies of 3 recent testimonials, to the Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (paediatrics) required. Recognised pre-registration post, vacant 7th July.

Detailed applications, with copy testimonials, should be forwarded to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Pediatrics. Post recognised for D.C.H. Vacant 21st August.

Applications, with copy testimonials, and details of previous experience, should be forwarded to the Group Secretary, Hospital Management Committee, Stoke-on-Trent, as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER (medical), vacant 7th August. Recognised for experience during pre-registration period.

Apply, with copy testimonials, stating age, nationality and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for HOUSE OFFICER (general surgery), vacant now. Hospital recognised for F.R.C.S. examinations, and the post is recognised for experience during the pre-registration period.

Apply, with copy testimonials, stating age, nationality and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for SENIOR HOUSE OFFICER (orthopaedics). Post recognised for F.R.C.S.

Apply, stating age and nationality, together with details of previous service, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (medical) required. Post vacant 1st July, 1954. Recognised for pre-registration experience.

Applications, with copy testimonials, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

SWANSEA HOSPITAL. (403 Beds.) Giantawie Hospital MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident appointment of SENIOR HOUSE OFFICER in the Surgical Unit of the above Hospital. Vacancy 1st July, 1954. The Hospital is recognised for the F.R.C.S. (Eng.) examinations.

Applications, stating age, qualifications and experience, should be forwarded to the Group Secretary, Giantawie Hospital Management Committee, St. Helen's-road, Swansea.

TAUNTON HOSPITAL MANAGEMENT COMMITTEE. TAUNTON AND SOMERSET HOSPITAL. (Musgrave Park and East Reach Branches.) Applications are invited for the appointment of SENIOR RESIDENT OFFICER (surgical) in the grade of Senior House Officer. The Officer appointed would be the Senior Resident Officer of both branches of the Hospital. The post, which gives excellent experience in surgery, including operating work according to qualifications and experience, is recognised by the Royal College of Surgeons as a qualifying appointment for the Final Fellowship examination.

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to reach the Secretary, Taunton and Somerset Hospital, Musgrave Park Branch, Taunton, Somerset, not later than 2nd July, 1954.

TREDEGAR GENERAL HOSPITAL. (20 miles from Newport and 24 from Teaching Hospital in Cardiff; 6 miles from the Vale of Usk, Surgical Unit of 50 Beds, with also 6 orthopaedic beds, under daily supervision of Consultant Surgeon and visiting supervision of Orthopaedic Surgeon. Busy Out-patient and Casualty Departments.)

1 JUNIOR HOSPITAL MEDICAL OFFICER.
1 HOUSE SURGEON (pre-registration if suitable candidate available).

Junior Hospital Medical Officer: salary £775-£250-£21075, less agreed deduction for married quarters (if required). House Officer post tenable 6 months: salary £425-£2525, less agreed deduction for married quarters or £125 p.a. for single residential emoluments.

Apply, with full particulars, to the Group Secretary, Hospital Management Committee, St. Martin's-road, Caerphilly, near Cardiff.

TYNEMOUTH VICTORIA JUBILEE INFIRMARY. Hawkeye's-lane, NORTH SHIELDS. The resident post of HOUSE PHYSICIAN becomes available in July. Appointment recognised for Pre-registration Service.

Applications should be sent to the Group Secretary, Preston Hospital, North Shields, Northumberland.

VENTNOR, ISLE OF WIGHT. ROYAL NATIONAL HOSPITAL FOR DISEASES OF THE CHEST. (249 Beds.) Required: JUNIOR HOSPITAL MEDICAL OFFICER, and SENIOR HOUSE OFFICER.

Resident posts. Hospital has all facilities for major thoracic surgery.

Applications, with names of 2 referees, to Physician-Superintendent.

WARRINGTON GENERAL HOSPITAL. (368 Beds.) Applications are invited for the post of HOUSE SURGEON (Male or Female), recognised for pre-registration, at the above Hospital. National Health Service terms and conditions. The staffing of the Surgical Unit consists of a Senior Registrar, Registrar and 2 House Surgeons. The post offers a comprehensive training in surgery.

Apply, giving full particulars, to—
H. L. Boot, Group Secretary,
Warrington and District Hospital Management Committee,
c/o General Hospital, Warrington, Lancs.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (Resident Casualty Officer). The commencing salary is in accordance with the scale £700-£450-£1000, less a deduction of £130 for residential emoluments. Applications will also be considered for a short-term period on a week-to-week basis.

Applications, stating age, experience and qualifications, should be forwarded or telephoned to—
H. L. Boot, Group Secretary,
Warrington and District Hospital Management Committee,
c/o General Hospital (Tel. No. 1868), Warrington, Lancs.

WARRINGTON INFIRMARY. Warrington and District HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from qualified practitioners for the vacancy of RESIDENT ANAESTHETIST (Senior House Officer grade), Male or Female, at the Warrington Infirmary. Scale of salary £2670 p.a., less £130 p.a. for residential emoluments.

Applications to—
H. L. Boot, Group Secretary,
Warrington and District Hospital Management Committee,
c/o General Hospital, Warrington.

WARWICK HOSPITAL. (264 Beds.) South Warwickshire HOSPITAL GROUP. Applications are invited for the resident appointment of HOUSE SURGEON (House Officer), pre-registration, vacant end of July. Good experience in general surgery available. Candidates taking final examination may apply.

Applications, with 2 testimonials, to be forwarded to the Medical Superintendent, Warwick Hospital, Lakin-road, Warwick.

WARWICK HOSPITAL. (264 Beds.) South Warwickshire Hospital Group. HOUSE PHYSICIAN (resident) required. Post vacant end of July. Pre-registration or registered candidates may apply.

Applications, together with 2 testimonials, to be forwarded to the Medical Superintendent, Warwick Hospital, Lakin-road, Warwick.

WARWICK (near). CENTRAL MENTAL HOSPITAL. SENIOR HOUSE OFFICER required on 1st September in this Mental Hospital of 1400 Beds with Neurosis Unit, 4 adult and 2 child psychiatry clinics recognised for the D.P.M., and Departments of Electro-encephalography, Occupational Therapy, Psychology and social work. A modern house is available.

Applications, together with the names and addresses of 3 referees, to the Medical Superintendent within 14 days of the appearance of this advertisement.

WARWICK (near). KING EDWARD VII MEMORIAL SANATORIUM. Hertford Hill, near WARWICK. (Diseases of the Chest—225 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP. Applications are invited for the post of SENIOR HOUSE OFFICER at the above Sanatorium, which is a modern building, to take up duties in July. All forms of therapy and minor surgery are carried out and the Sanatorium works in close association with a major Thoracic Surgery Unit in a nearby hospital, which will be transferred to the Sanatorium in the near future.

Applications, together with the names of 3 referees, should be forwarded to the Medical Superintendent as soon as possible.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments, vacant 1st August:

Manor Hospital (333 Beds)

HOUSE SURGEON (1 vacancy).

HOUSE PHYSICIAN (2 vacancies).

General Hospital (181 Beds)

HOUSE SURGEON (2 vacancies).

HOUSE PHYSICIAN (1 vacancy).

All above posts recognised pre-registration.

Applications to Secretary, with names of 2 referees.

WELLINGBOROUGH. PARK HOSPITAL. (201 Beds.) KETTERING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER to the Geriatric Unit of 40 Beds, at present non-resident, and vacant now. The unit is in close association with a similar larger unit at Kettering.

Applications, stating age, nationality, qualifications, and past experience, should be sent to the Group Secretary, General Hospital, Kettering.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) CASUALTY OFFICER (pre-registration post), vacant 1st July, 1954. Recognised for F.R.C.S. examinations.

Applications, together with names of 2 referees, to Secretary, Royal Infirmary, Wigan.

WINDSOR. KING EDWARD VII HOSPITAL. House SURGEON in General Surgery required (Male or Female), for post vacant 13th August. Recognised for F.R.C.S. Preference given to persons seeking pre-registration House Officer post under the Medical Act, 1950. Applicants required to be members of a Medical Protection Society.

Applications, stating age, nationality, qualifications with dates and experience with copies of 3 testimonials, to Hospital Secretary by 11th July.

WOLVERHAMPTON GROUP.

The Royal Hospital, Wolverhampton (an Associated Hospital of the University of Birmingham Medical School) SENIOR HOUSE OFFICER or HOUSE OFFICER (Fracture and Orthopaedic Department), vacant now.

SENIOR HOUSE OFFICER (Anesthetist), vacant now.

HOUSE OFFICER (Casualty Department), vacant now.

*3 HOUSE OFFICERS (general surgery), 2 vacant 30th June, 1 vacant now.

*HOUSE OFFICER (paediatrics). Appointment recognised for D.C.H. Vacant 16th July.

New Cross Hospital, Wolverhampton

*HOUSE OFFICER (general surgery), vacant now.

SENIOR HOUSE OFFICER (obstetrics). Appointment recognised for D.Obst.R.C.O.G. Vacant 5th July.

*Approved for Pre-registration Service.

Wolverhampton Eye Infirmary

Part-time NON-RESIDENT CLINICAL ASSISTANT required, 3 sessions weekly, Monday, Wednesday, and Friday mornings. Duties in association with Consultants, mainly refection work at morning outpatient clinics. D.O. an advantage.

Applications, with copies of 3 recent testimonials, to be sent to Group Secretary.

The Royal Hospital, Wolverhampton.

WESTON-SUPER-MARE GENERAL HOSPITAL. (110 Beds.) Applications are invited from registered medical practitioners for the resident appointment, vacant mid-August, of HOUSE PHYSICIAN (non pre-registration). The appointment is for 6 months in the first instance and may be renewed for a further 6 months.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WESTON-SUPER-MARE GENERAL HOSPITAL. (110 Beds.) Applications are invited from registered medical practitioners for the resident appointment of HOUSE SURGEON (non pre-registration). The appointment will be for a period of 6 months in the first instance and may be renewed for a further 6 months.

Applications, stating age, qualifications and experience, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WEST BROMWICH AND DISTRICT GENERAL HOSPITAL, Edward-street, WEST BROMWICH. (144 Beds.) WEST BROMWICH AND DISTRICT HOSPITALS MANAGEMENT COMMITTEE GROUP NO. 18. Applications are invited for the post of HOUSE SURGEON, vacant immediately. Salary, terms and conditions in accordance with the Ministry of Health regulations. The post is tenable for 6 months, resident, and is recognised for Pre-registration Scheme.

Applications, together with 3 recent testimonials, should be submitted to J. O. ROBINS, Esq., Group Secretary.

WEST BROMWICH. HALLAM HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (pathology), for the Group Laboratory at this Hospital. Duties at other hospitals in the Group may be included. Previous experience in pathology not essential.

Applications, stating age, nationality, qualifications, and experience, with copies of 3 recent testimonials, to the Pathologist, as soon as possible.

WATFORD AND DISTRICT PEACE MEMORIAL HOSPITAL. (189 Beds.) Applications are invited for the post of HOUSE PHYSICIAN. Post recognised for pre-registration. Vacant middle of July. Salary according to National Health Service scale.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, should be sent to—
CYRIL HOPKINSON, Administrator.

YORKSHIRE. EAST RIDING HOSPITAL MANAGEMENT COMMITTEE.

Westwood Hospital, Beverley, E. Yorks (207 Beds)

(a) HOUSE SURGEON (first, second, or third post), vacant now. General surgical duties, some orthopaedics. Offering good opportunity for general experience in busy acute General Hospital. Recognised for F.R.C.S. Approved pre-registration post. Married accommodation available.

(b) ORTHOPAEDIC HOUSE SURGEON (first, second, or third post), vacant now. Offers good opportunity for general experience in busy acute General Hospital. Approved pre-registration post. Married accommodation available.

(c) ASSISTANT PATHOLOGIST (Senior House Officer grade) required in Area Laboratory, with attendance at Branch Laboratory, Driffield. Offers experience all branches pathology.

East Riding General Hospital, Driffield, Yorks (269 Beds)

(d) HOUSE SURGEON (first, second, or third post), vacant now. Approved pre-registration post. General surgical duties. Recognised for F.R.C.S.

Broadgate (Mental) Hospital, Beverley, E. Yorks (650 Beds)

(e) HOUSE PHYSICIAN (first, second, or third post), vacant now.

Salary for (a), (b), (d) and (e) £425-£525, and for (c) £745. Fully qualified practitioners may apply for the pre-registration posts.

Detailed applications to Group Secretary, Westwood Hospital, Beverley, Yorks.

YORK AND TADCASTER HOSPITAL MANAGEMENT COMMITTEE.

York County Hospital (Acute Hospital of 269 Beds with full Consultant staff)

CASUALTY OFFICER (with charge of orthopaedic beds), resident or non-resident. Junior Hospital Medical Officer grade, vacant immediately. Salary £775-£250-£1075, less £153 if resident. Recognised for F.R.C.S.

York. Fairfield Sanatorium (63 Beds); **City Hospital** (265 Beds)

Required immediately, SENIOR HOUSE OFFICER in Chest Diseases and General Medicine to spend half time at Fairfield Sanatorium, (63 Beds) and at the City Hospital, where 8 Beds are reserved for investigation of chest cases, and where outpatient refill clinics are held, the remainder of time at County and City General Hospitals (269 and 265 Beds respectively), in Department of General Medicine. Previous experience in treatment of tuberculosis an advantage. Salary £745. A furnished flat is available at a reasonable rental, or accommodation may be provided temporarily.

York Military Hospital (Civilian Wing) (60 Beds)

Required immediately, SENIOR HOUSE OFFICER (resident or non-resident). There are 18 gynaecological beds, 30 general surgical beds, and 12 medical beds. The Hospital is associated with the County Hospital (general hospital of 269 Beds) where relief casualty and emergency work and relief work for House Surgeons may be undertaken and where residence can be provided. Salary £745, less £153 if resident. A furnished flat is available at reasonable rental.

Applications, giving age, nationality, experience, qualifications, and names of 2 referees, immediately to the Secretary, York A and Tadcaster Hospital Management Committee, Bootham Park, York.

CASTLEREA. ST. PATRICK'S REGIONAL CHEST HOSPITAL. ROSCOMMON COUNTY COUNCIL. Applications are invited from suitably qualified persons for the temporary post of REGISTRAR to the Thoracic Surgical Unit at above Hospital. Applicants must since registration have had not less than 3 years practice, including 2 years satisfactory experience in surgery. It is preferable that 6 months of this 2 years shall have been spent in a recognised teaching hospital. Previous experience in thoracic surgery is desirable but not essential. Salary £800 p.a. inclusive of all existing temporary bonuses, subject to a deduction of £150 p.a., in respect of full residential emoluments, where provided in kind.

Applicants should communicate with the undersigned at once, giving full particulars as to date and place of birth, qualifications and experience, and state how soon could take up duty, if appointed.

T. D. WYER, County, Secretary.
Courthouse, Roscommon, 14th June, 1954.

NEWFOUNDLAND PROVINCIAL DEPARTMENT OF HEALTH

ST. JOHN'S GENERAL HOSPITAL (475 Beds)
ST. JOHN'S, NEWFOUNDLAND
DEPARTMENT OF ANAESTHESIA

Applications are invited to fill the post of RESIDENT ANAESTHESIA REGISTRAR. Previous experience in anaesthetics desirable. Salary is \$3600 (approximately £1292) p.a., less \$600 (approximately £215) for maintenance, &c. Passage will be paid to St. John's as well as return fare to the United Kingdom on completion of 12 months service.

Applications with full details should be forwarded immediately to Dr. E. Wilson, Superintendent, General Hospital, St. John's, Newfoundland.

LEONARD MILLER, M.D., Deputy Minister of Health.

NEWFOUNDLAND PROVINCIAL DEPARTMENT OF HEALTH

ST. JOHN'S GENERAL HOSPITAL (475 Beds)
ST. JOHN'S, NEWFOUNDLAND
DEPARTMENT OF PATHOLOGY

Applications are invited to fill the post of RESIDENT REGISTRAR in Pathology. Duties will include clinical, surgical and autopsy pathology. Previous experience in pathology desirable but not essential. The post is recognised for postgraduate training and towards Certification in Pathology by the Royal College of Surgeons and Physicians of Canada and the American College of Surgeons. Excellent opportunities exist for gaining extensive experience. Salary is \$3200 (approximately £1149) p.a., less \$480 (approximately £172) for maintenance, &c. Passage will be paid to St. John's as well as return fare to the United Kingdom on completion of 12 months service.

Applications with full details should be addressed to Dr. E. Wilson, Superintendent, General Hospital, St. John's, Newfoundland.

LEONARD MILLER, M.D., Deputy Minister of Health.

IRELAND. INCORPORATED ORTHOPÆDIC HOSPITAL OF IRELAND, Castle-avenue, CLONTARF, DUBLIN. (142 Beds). Applications are invited from registered medical practitioners for the post of RESIDENT MEDICAL OFFICER, vacant now. Post offers good experience and opportunities for post-graduate study. Tenable for 12 months. Salary according to experience, minimum £250 p.a.

Applications, stating age, qualifications and experience, to be addressed to the Hospital Secretary.

NEW YORK. ALBANY HOSPITAL, Albany, New York, U.S.A. NEUROLOGY RESIDENCIES available in 700-Bed University-Teaching, General Hospital. Salary range \$1620-\$2220 annually, plus laundry, uniforms and room.

Address inquiries to Medical Director.

NEW YORK. NEW ROCHELLE HOSPITAL, New Rochelle, New York, U.S.A. (360-Bed general community hospital). Approved by the Joint Commission on Accreditation of Hospitals. Also approved by American College of Surgeons and American Medical Association for Internship and Residency Training. Only graduates from approved university schools accepted. Term of Internship: 1st July, 1954-30th June, 1955. INTERNES—\$150 per month plus full maintenance. Return passage to England paid by Hospital after completion of internship.

Apply Superintendent.

UNITED STATES. MOUNT AUBURN HOSPITAL, CAMBRIDGE, MASSACHUSETTS. Applications are invited for anesthesiology approved 2-year RESIDENCY beginning 1st September, 1954, 1st April, 1955, and 1st July, 1955. This is a 250-Bed community hospital. Teaching programme included. Salary \$1800 first year and \$3000 second year and full maintenance. Travel expense to and from the United States will be paid.

Apply: Director of Anesthesiology, P.O. Box 115, Cambridge, 38, Massachusetts.

Public Appointments

ANGLESEY. COUNTY OF ANGLESEY. Applications are invited from medical practitioners holding the D.P.H. or similar qualification for the appointment of ASSISTANT COUNTY AND SCHOOL MEDICAL OFFICER AND MEDICAL OFFICER OF HEALTH for the Borough of Beaumaris, the Urban Districts of Llangefn and Menai Bridge and the Rural District of Aethwy. Salary in accordance with the national award for a mixed appointment—£1368 15s., rising to £1687 10s. Starting-point according to experience. The national conditions of service, travelling allowances, &c., apply.

Application forms to be returned to the undersigned by 10th July, 1954, may be obtained from the County Medical Officer, Shire Hall, Llangefn.

WILLIAM JONES, Clerk of the County Council.

Shire Hall, Llangefn.

DERBYSHIRE COUNTY COUNCIL. County Health Department. ASSISTANT MATERNITY AND CHILD WELFARE MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER. Applications are invited from registered medical practitioners for this whole-time superannuable post. Salary £950 p.a. by annual increments of £50 to £1300 p.a., plus a car allowance.

Application forms are obtainable from Dr. J. B. S. MORGAN, County Medical Officer, St. Mary's-gate, Derby, to whom they should be returned by 14th July.

BAHRAIN, PERSIAN GULF. GOVERNMENT OF BAHRAIN MEDICAL DEPARTMENT invites applications from British Women Doctors for the post of ASSISTANT to the Lady Medical Officer in charge of Women's medical services. Age 30-40. Minimum salary £1584, no allowances, rising by annual increments of £45. Starting salary on incremental scale according to age up to 40. Non-contributory gratuity on retirement. Private practice among Europeans only. No income-tax. Agreement for 2 years, renewable by mutual consent. Free quarters with hard furniture and car. Home leave amounts to 2½ months on full pay for every years service. Free return air passage every 2 years.

Applications should be addressed to Messrs. CHAS. KENDALL & PARTNERS LTD., 7, Albert-court, Kensington Gore, London, S.W.7.

BOARD OF CONTROL. Whole-time Deputy Medical SUPERINTENDENT (Consultant), at Rampton Hospital, near Retford, Notts (1143 Beds), for patients exhibiting conduct disorders with mental deficiency. Excellent opportunities for study, treatment and training of behaviour disorders of all kinds and degrees. Applicants must be registered medical practitioners, with experience in psychiatry and the D.P.M.; post is clinical, but experience in hospital administration an advantage; duties may involve attendance at outpatient clinics. Appointment on National Health Service conditions of service and superannuation regulations. House on the estate available at appropriate rental.

Applications, stating name, date and place of birth, nationality, details of education, professional qualifications, war service, present and previous appointments, and names of 3 referees, to Medical Superintendent, Rampton Hospital, Retford, Notts, by 16th July, 1954. Envelopes to be marked A/DMS. Canvassing in any form leads to disqualification. Candidates may visit Hospital by appointment with Medical Superintendent.

HER MAJESTY'S COLONIAL SERVICE. TRINIDAD MEDICAL OFFICERS OF HEALTH required. Duties include matters relating to sanitation, public health education, venereal diseases, tuberculosis, maternity and child welfare, school medical work, housing and town planning. Appointment can be made on a permanent basis with pension (non-contributory) at the age of 60, or on short-term agreement. A candidate in the National Health Service may resign from the National Health Service but retain his superannuation rights during his time in the Colonial Service (up to 6 years) and receive a resettlement grant of 20% of the aggregate of his Colonial salary on leaving the Colonial Service at the end of his engagement. Salary scale ranges from B.W.I. \$5280 to B.W.I. \$5760 (£1100-£1200) p.a. A temporary variable cost-of-living allowance is at present payable at the rate of \$108 p.a. (1 B.W.I. \$ equals 4s. 2d.) Starting salary is determined in accordance with the candidate's age, qualifications and experience. A revision of salaries is being undertaken in Trinidad and Officer selected would benefit from any increase granted. Pension is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. Provision of quarters not guaranteed, but if government quarters are provided a small rental is charged. Where government quarters are not provided an allowance in lieu is payable. Free passages on first appointment are provided for Officer and family not exceeding 5 persons in all, also free passages on leave subject to a maximum of 3 adult fares. Income-tax at local rates. Local leave is permissible and generous home leave is granted after each tour. Tour of service is 3½ years. Educational facilities are available. Candidates must possess qualification registrable in the United Kingdom and must also hold the Diploma in Public Health.

Application forms can be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. BCD. 117/38/014).

HER MAJESTY'S COLONIAL SERVICE. NIGERIA. A SPECIALIST (Alienist) is required in the Medical Department, Eastern Region, Nigeria. Duties comprise organisation of mental services, training of staff and advising on establishment of new mental hospitals in the Region; investigation, diagnosis and classification of the various forms of mental cases and advice on their treatment and disposal; administration of preventive medicine and clinical work. Appointment, which is for 5 years, may be made as follows:

(a) From the National Health Service. Candidates may resign from the National Health Service, but retain their superannuation rights during their time in the Colonial Service and receive a resettlement grant of 20% of the aggregate of their Colonial salary on leaving the Colonial Service at the end of their engagement. Salary, including expatriate allowance, amounts to £2025 a year.

(b) On contract with inclusive salary of £2195 a year. On completion of contract a gratuity is paid at the rate of £37 10s. for each completed period of 3 months service (including leave).

Extramural Consultant practice permitted under certain conditions.

Tours of service are from 18 to 24 months. Quarters are provided at low rents. Free passages in both directions are provided for officer and his wife. Payment of the cost actually incurred on 1 outward and 1 homeward passage for each of 2 children under age of 18, subject to a maximum of £75 in respect of the return journey for each child, is also granted. Income-tax at local rates. Local leave is permissible and generous home leave is granted after each tour. Candidates must possess a medical qualification registrable in the United Kingdom, and a Diploma in Psychological Medicine, and have had at least 3 years experience in the diagnosis and treatment of mental cases.

Application forms can be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. BCD. 117/14/025).

COATBRIDGE. BURGH OF COATBRIDGE. Applications are invited from registered medical practitioners possessing the Diploma in Public Health for appointment as ASSISTANT MEDICAL OFFICER OF HEALTH of the Burgh. The salary scale is £950 p.a. rising by annual increments of £50 to £1300 p.a. Placing on the scale may be granted according to qualifications and experience. Main duties will be in respect of Child Welfare, Immunisation and Vaccination Services and such other duties as may be required by the Medical Officer of Health. The post is superannuable and the successful applicant will be required to pass a medical examination.

Applications, giving particulars of qualifications, experience and appointments held, with copies of testimonials, should be lodged with the undersigned within 14 days of the appearance of this advertisement. ALEXANDER S. THOM, Town Clerk.

Municipal Buildings, Coatbridge, 14th June, 1954.

DEWSBURY. COUNTY BOROUGH OF DEWSBURY. Applications are invited for the appointment of DEPUTY MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER of the County Borough of Dewsbury. Applicants should be registered medical practitioners and possession of a Diploma in Public Health is desirable but not essential. Preference will be given to candidates approved previously by the Ministry of Education for ascertainment of educationally subnormal children. The salary will be within the scale £1100-£250-£1300 p.a., the commencing salary being fixed in accordance with qualifications and experience, plus a car allowance (at present £108 p.a.). Housing accommodation will be available if required. The appointment is permanent and superannuable and the successful candidate will be required to pass a medical examination.

Particulars of the duties and other conditions of the appointment, together with application forms, may be obtained from the Medical Officer of Health, Municipal Buildings, Halifax-road, Dewsbury, Yorkshire, to whom applications should be sent within 14 days after the appearance of this advertisement.

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Town Hall, Dewsbury, 16th June, 1954.

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Latest date for receipt
of applications

District	County	
PERSHORE	WORCESTER	10TH JULY, 1954

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Town Hall, Ipswich. J. C. NELSON, Town Clerk.

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PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.

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PRINTED IN GREAT BRITAIN—Entered as Second Class at the New York, U.S.A., Office.

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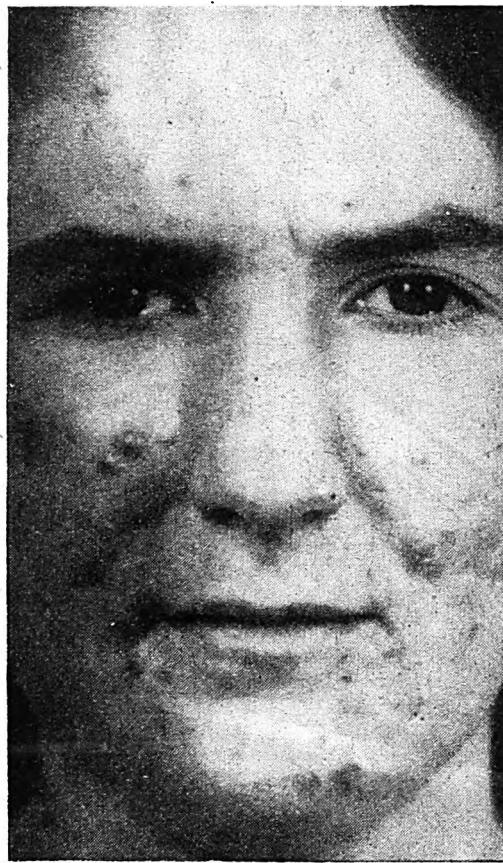
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for Smith Kline & French International Co., owner of the trade mark 'Eskamel'

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Applications, giving particulars of qualifications, experience and appointments held, with copies of testimonials, should be lodged with the undersigned within 14 days of the appearance of this advertisement. ALEXANDER S. THOM, Town Clerk.

Municipal Buildings, Coatbridge, 14th June, 1954.

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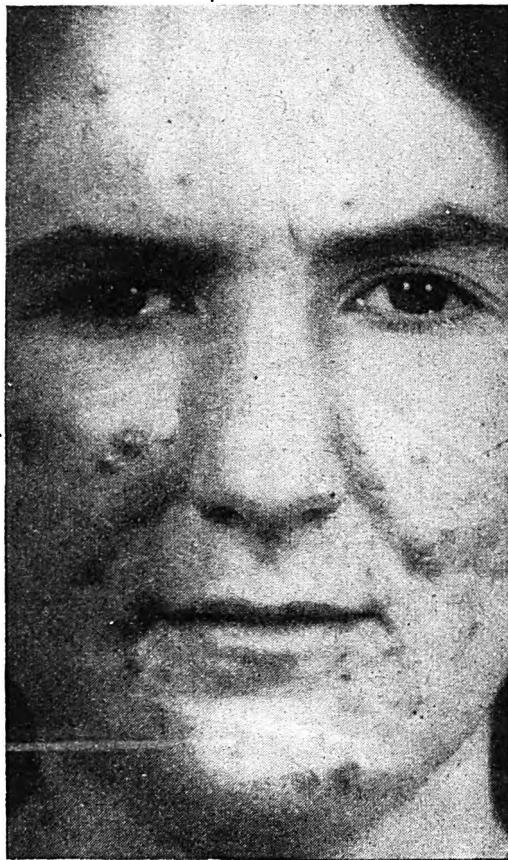
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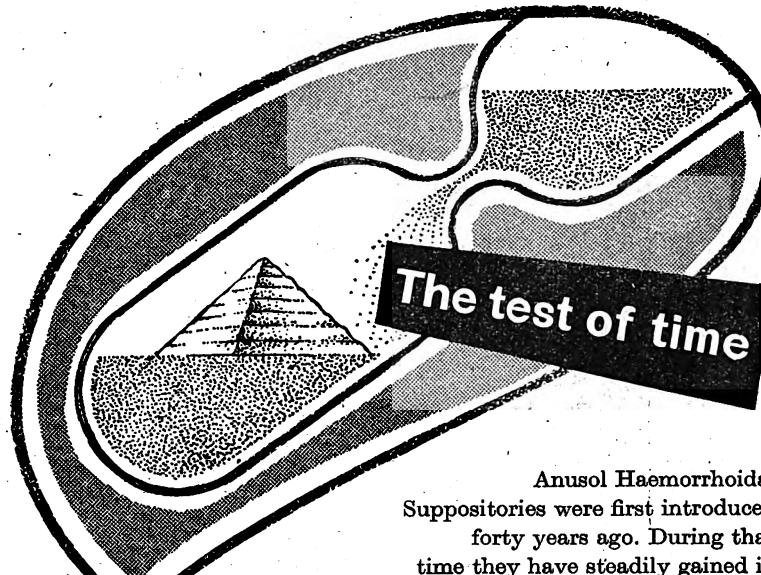
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Anusol Haemorrhoidal Suppositories were first introduced forty years ago. During that time they have steadily gained in popularity as a mildly astringent and antiseptic remedy for haemorrhoids and simple ano-rectal inflammations. They meet all the essential requirements — economy in use, ease of insertion, decongestive effect, lubrication, mild antiseptic action and prompt relief without narcotics or analgesics.

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Resorcin, 0.87%, Balsam of
Peru, 1.77%, Zinc oxide,
10.60%, Boric acid, 17.85%,
Base of cacao butter and
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PACKING:

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dispensing purposes at 16/8d.
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