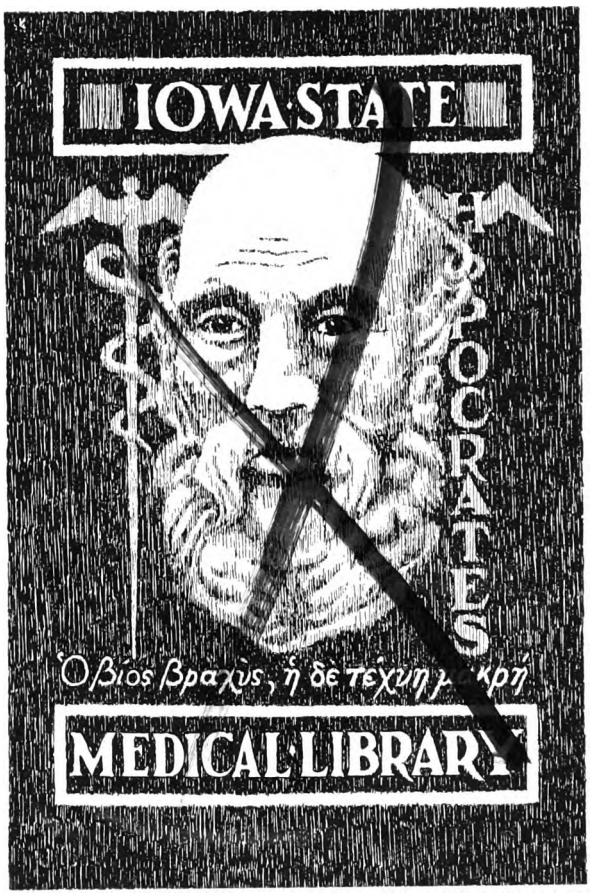

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No. 6532 LONDON: SATURDAY, NOVEMBER 6, 1948 CCLV

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THE VOCATION OF MEDICINE *

LORD HORDER
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YOU are, I suppose, at various stages of your medical training. Some of you are in the preclinical stage. Some are in the wards and post-mortem room. Some are in the special departments. And some of you have, no doubt—I won't say finished your training, because in Medicine, as in life, one never finishes one's training—a few of you are what the law euphemistically calls "qualified."

What I say today applies chiefly to those who are at the beginning of their training and will later be engaged in doctoring, whether as general practitioners—assuming, as I must in the public interest, that this particular genus continues to exist—or as consultants and specialists. A few, no doubt, will drop out by the wayside, changing over to industry, politics, or even to one of the other "liberal" professions, finding that doctoring is not, after all, and speaking in the vernacular, their "cup of tea."

Many years ago, Sir James Paget analysed 1000 medical students from the point of view of what happened to them. It was an interesting but rather a disappointing study.

For two reasons Paget's analysis is not applicable today. In the first place it is possible to break away from the straight line of doctoring at a number of points in the course of training, a fact which should be borne in mind when any one of you begins to doubt if you are sufficiently interested in your human fellow creatures to make a good doctor. You can teach in the preclinical subjects; you can take up X-ray or radium work; you can be a clinical or an academic pathologist; you can engage in public health.

In the second place there is more thought being given now than formerly as to whether you should "go in" for Medicine at all. The whole outlook has received rather a jostle. If a boy or a girl is individualist in temperament, and is keen upon a spice of adventure, he or she may today well hesitate. Sons and daughters of doctors, making, as they generally do, good doctors themselves, will pause and think, as indeed their parents also will. This position may, of course, adjust itself; as an optimist (or is this wishful thinking in the public interest?) I believe that it will. Anyway, when I am asked if there is a future for doctors I still answer Yes. "All that a man hath will he give for his skin." The machinery of doctoring isn't working very smoothly at the moment, but the individual doctor cannot be dispensed with, and it is for the individual doctor, with the public backing, to see to it that mere machinery does not handicap his best work, or, should I say, these days, does not find him "frustrated."

But there is another question that I am frequently asked. That is, whether a boy or a girl will *make* a good doctor.

Now although I hold strongly that a good doctor, like a good poet, is born and not made, I do not mean by this what those parents mean who see a budding doctor in their child as they watch him pulling a fly to pieces, or what the child himself means when, later on, he says, with the emerging ego of youth, "I always wanted to be a doctor." It is true that I have no statistical evidence as to the efficiency of these two groups in actual practice, but I gravely mistrust the incident, and the sentiment, as indicating fitness for doctoring. I don't regard the essentials for an efficient doctor as either exceptional or dramatic. Good health is a primary requisite, and I am glad to note that here in Sheffield some assurance as to this is obtained before a student is admitted. A good general education is also essential. Some *nous*, as it is called, is very helpful and a humanist approach to other folk. Indeed, I don't find it difficult, after an interview, to answer the question with a Yes or No in the majority of cases.

But all this is too late on this occasion. You are committed—though, as I said, by no means irrevocably committed to that branch of Medicine which I regard as its most valuable branch, the form which entails a "close up" between doctor and patient.

A wise man once gave a definition of what he called successful Medicine in the words "Successful Medicine is sympathy armed with understanding." I entirely agree, and I think the definition would lose none of its truth if it ran "successful Medicine is understanding touched with sympathy." I shall assume in the beginners amongst you a modicum of cleverness and goodness—to use very homely words—that will make the journey you have embarked upon a successful one. With this basis let me tell you some things that seem to me to be useful as you proceed. And you must forgive the use of the imperative tense in which I shall speak. The privilege of being exhortative is one of the few compensations allowed to those who have arrived at that stage in their professional life when they are invited to give addresses like this.

Understanding

READING

My first effort to help you will probably be hailed with acclamation. It is to warn you against studiousness. (Yes, but you must hear me through!) It was Francis Bacon, I believe, who first uttered what is only apparently a paradox, that "to spend too much time in studies is sloth." I am quite sure, from my own personal experience, that excessive reading may be a form of laziness and I shall presently tell you why. If you spend most of your time in reading you are likely to be left, not only with no time for the more important occupations of observing and thinking, but with no mind wherewith to do these essential things.

"Knowledge is valuable according as it helps us in action"—a maxim which I commend to those who are responsible for your curriculum. Froude might well have had our science and art in his mind when he said "the knowledge which a man can use is the only real knowledge that has life and growth in it. The rest hangs like dust about the brain, or dries like raindrops on the stones." Broussais applied this to Medicine: "facts which cannot be used for healing," he said, "do not belong to the physician, they belong to the naturalist."

OBSERVATION

Then as to how you should spend most of your time: the first essential is that you must cultivate the power of observation, without which—nothing. If you say this advice is a "hardy annual" on occasions like this, I should retort that hardy annuals are the only annuals worth growing. If you ask me, observe what? My reply is, observe anything, everything, and begin to do it at once. From the moment you made the decision to be a doctor everything should have become "clinical." But observe especially men and women and children and the things connected with them, for these are to be the future life of most of you. Observe the colour of their eyes, the shape of their head, the length of their hair, the clothes they wear, the way they walk and hold themselves, how they shake hands, how they say good-morning—and a hundred other things. Do this whilst

* Address in opening the winter session of the medical school at Sheffield on Oct. 13. In his opening passages Lord Horder paid tribute to some of his distinguished predecessors who have addressed the school.

you are engaged in your preclinical studies. Train your attention to be active rather than passive, and so break up that useless reverie in which the untrained mind spends the greater part of its life, yes, even when it is studiously reading: "Sometimes I reads and thinks and sometimes I just reads." This reverie can, with discipline, be changed for an alertness, an awareness, that supplies the mind with food on which it may ruminate. Someone in authority has said that we only use one-third of our brain for the ordinary affairs of life. I do not know how he arrived at this conclusion, but speaking for myself I should regard this estimate as being too liberal.

By the time you enter the wards and the outpatient rooms this habit of active attention, which is by this time becoming more and more effortless, will enable you to observe many things about your patients that do not need instruments and yet are as valuable, often more valuable, than those that do require them.

At first, and probably for some time, you will observe a lot of things that are quite useless, things that are quite dissociated. How can it be otherwise? But later it will be found that your observations tend to become systematised, purposeful, and synthetically useful. In time you will develop the power of observing things that are not obvious, you will look not only *at* things but *for* things—associated things, that together make sense, that make, in the fullest meaning of the word, a diagnosis.

In this exhortation to train yourselves to observe I am not thinking of your eyes only. Your ears, also, are important, and not only in the field of auscultation. The character of a cough, the rhythm of breathing, the lack of overtones in a voice, even on the telephone, these are observations that are full of meaning to the initiated. Then I might expand all this by reference to touch and smell. These large, but vitally important observations are all the more important nowadays when instruments of precision have become so numerous and so popular. Instruments of precision enable us to measure the degree of the defects which our trained senses tell us are present. It is this clinical acumen which should suggest to us in what directions we may most profitably employ these instruments. But you cannot achieve this facility unless you have made observation a familiar habit. Then, when you have done this, that common expression, "I became aware of," does not wait until sights and sounds are shattering your senses and hammering at the door of your consciousness; you are aware almost *un*consciously. You have developed mental antennæ.

When this faculty has arrived you will find that two other things happen. You make many observations without knowing it and your observations take on a selective character: they group themselves in terms of affinity and you develop the faculty of distinguishing the essentials from the non-essentials.

I believe that those people who possess what is called a "clinical sense" really owe it to these two facts; they make many observations of which they are unconscious, and they effect a synthesis of those observations that are causatively associated. At the same time they are able to discard those that do not possess these characters.

Herein lies the nearest explanation I can give of the mental processes involved in diagnosis. And diagnosis is, of course, the end to which all observations should tend. Diagnosis, like ripeness, is all.

But side by side with the development of this facility in observation there goes necessarily the basic facts of anatomy, of physiology and of chemistry. These form the touchstone by which we are able to recognise the morbid from the healthy. Facility in observation, combined with experience of the healthy, enables us to pick out the unusual from the usual, to note deviations from the average. I use the word "average" rather than the word "normal" because normality is a concept which involves us in a number of more or less agreed theoretical considerations; the average is a summation of actual experience.

RECOGNISING THE AVERAGE

My third exhortation, therefore, is to train yourselves to recognise the average, so that your attention is at once struck by any deviation from it. The deviation may be physiological or it may be pathological; it should be assumed to be pathological unless there are adequate reasons to the contrary. If pathological it may be trivial and therefore negligible, or it may be important and therefore informative. It should be assumed to be important until proved otherwise.

Let me illustrate. The height of the great majority of persons of the same age and sex varies within a few inches, and their weight varies within a few pounds. So that we quickly notice that this man is tall and that one short, this woman fat and that one thin. Not so readily, however, do we notice deviations from the average complexion, nor from the average gait, nor mode of sitting on a chair, nor of lying in bed, nor of shaking hands, nor of reaction to conversation, though there is an average, too, in all these things. As indeed, there is an average in the more elaborate forms of behaviour: how else do we recognise, when we see them, the bachelor, the spinster, and the only child?

The value of recognising even slight deviations from the average in these and other matters is seen in the early stages of a number of diseases which, but for this training, might otherwise go unsuspected. To those of you who already have some clinical experience I need only mention hypo- and hyper-thyroidism, chorea, nephritis, heart disease, general paresis, and parkinsonism.

And there is more "to it" (if you will forgive the vulgarism) than this. You must observe people's faces for other things than complexion—for the expression of pain, physical and mental, for happiness and unhappiness, and especially for anxiety and fear. What, in short is the dominant emotional state, and whether this is only of recent origin or has been in existence for a long time.

The value of this kind of observation is incalculable. It enables us to "check up" the things that patients tell us: that agonising pain, those sleepless nights, those days and weeks of so little food that it is a wonder life is not extinct. Look at their faces—and of course put them on the scales, and on the couch—but *look at their faces.*

After a time, if you have become sensitive to deviations from the average, it will sometimes be borne in upon you that the person with whom you are in contact is not average, but for the moment you cannot say in what way. You must not pass that doubt off lightly, you must accept the challenge, you must revise your observation and seek to explain it, for it may prove to be a clue to the main position.

By this kind of mental discipline you will develop a power that unthinking folks call "uncanny." It isn't really uncanny; it merely means that you have trained your mind but that the onlooker does not see it working. The prestidigitator's legerdemain is just as "uncanny" after years of training of his hands.

You have now become expert, which means that you possess a power which the layman has not got. If this were not the case the layman's ideas of health would be as sound as the doctor's; and they aren't. The man who "looks the picture of health" may not be healthy at all: he may be a case of polycythæmia. And the proud possessor of that "broad chest," which he displays in such military fashion, may be showing us one of the committal signs of emphysema.

If I have made myself clear and my premises are sound, I think you will see that mere industry, whether with books or with instruments, useful though both of these are in the acquirement of knowledge, can never supply us with the fundamental wisdom that Medicine, of all human pursuits, really demands.

So much for understanding. And now a few words about the second essential in a good doctor—*sympathy*.

Sympathy

Industry can never be a substitute for sensitivity. When you begin the study of Medicine many of you possess the power of fine appreciation and delicate discrimination. Don't try to "douse" it. Don't be ashamed of it. It is of tremendous service if transmuted through the personality of a good doctor. But it will be of even greater service if you cultivate it and discipline it, when you are face to face with your patients. How many people have need of your *spiritual* sensitivity you will not realise until you make close contact with them as doctor and patient. And many of your patients (and among these will be some of the nicest) will cover their need with a spurious brusqueness which you must not fail to put aside, gently, of course, because they are just as much ashamed of their need as some of you may be of your power to supply it.

Begin to cultivate this gift of sympathy early. Sit down on the lockers of the patients who are allotted to you and talk to them. The experience will surprise you—and it will probably surprise the patient! A good deal has been said about the doctor-patient relationship; I've said a good deal about it myself. But since it is the very soul of good doctoring its importance can never be exaggerated. One of my chief reasons for distrusting the "new look" recently given to British Medicine is its tendency to disregard the "close-up" which is so important between doctor and patient. Availability of Medicine to all the people is a good idea. I am "all for it," as the expression goes. But *what* Medicine? Seeing 85 patients in a doctor's "surgery hour"—the operative word is clearly "seeing"—isn't Medicine. This is one of the results of the switch-over that it is to be hoped will soon be adjusted. There are other knots to unravel. But the standard of doctoring is the thing that matters and no one can maintain that except the doctor himself.

It is easy to level down; it can be done with a stroke of the pen; it is difficult to level up, and that takes time. If it be found that the machine will not enable good work to be turned out, then the machine must be reconstructed.

Meantime, the "new look" hasn't changed my view of fundamental Medicine. I still think it is a good thing that you are committing yourselves to. You will find that Medicine presents life to you in its full range. If you are a realist like old Montaigne, you will be able to "find a ravishing kind of satisfaction in pleasing another, and in doing a just action." And if you are an idealist, then, at the risk of being thought sententious, I would like to read you part of a lecture by a great clinician, Peter Mere Latham, because it traces in far better language than I can do, the history of the soul of the good doctor.

> "Diseases are not abstractions; they are modes of acting, different from the natural and healthy modes—modes of disorganising, modes of suffering, and modes of dying; and there must be a living, moving, sentient body for all this. This body must be your study and your continued care. Nothing must make you shrink from it. In its weakness and infirmities, you must still value it,—still stay by it—to mark its hunger and thirst, in sleeping and waking, its heat and its cold; to hear its complaints, to register its groans. And is it possible to feel an interest in all this? Indeed it is. Whence comes this interest? At first it seldom comes naturally; a mere sense of duty must engender it. Presently, the quick, curious, restless spirit of science enlivens it; and then the deliberate choice of the mind.
>
> "When the interest of attending the sick has reached this point, there arises from it a ready discernment of disease, and a skill in the use of remedies. And the skill exalts the interest, and the interest improves the skill, until, in process of time, experience forms the consummate practitioner. But does the interest of attending the sick necessarily stop here? No. What if humanity shall warm it? Then this interest, this excitement, this intellectual pleasure is exalted into a principle, and invested with a moral motive, and passes into the heart. . . ."

Whether you push straight through and become a general practitioner, or whether you specialise, or whether you branch off at any of the points in the curriculum where the science, rather than the art, attracts you, you will not repent your main decision. I believe that you can lose your soul with less ease along this path than any other I know. You will frequently be rewarded by people's gratitude and affection on account of services you scarcely thought about when you rendered them, and some of your labours that you reckoned hardest and most worthy of applause will go unrecognised. But you have your stalwarts to stimulate you, should you lack courage, and you have their examples to light you on your way. Are you doubtful of success? "I have a key in my bosom called Promise (said Christian) that will, I am persuaded, open any lock in Doubting Castle. Then, said Hopeful, that's good luck, good brother; pluck it out of thy bosom and try."

THROMBO-ANGIITIS OBLITERANS

RESULTS OF SYMPATHECTOMY AND PROGNOSIS

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In a recent review of cases of thrombo-angiitis obliterans treated in fourteen years it was possible to trace 77 patients in whom the diagnosis was confirmed and of whom records were complete; 8 patients could not be traced. Attention was particularly directed to the natural course of the malady over a period of years, and the effects of sympathectomy in different clinical types of the disease.

A generally acceptable definition of thrombo-angiitis obliterans, or Buerger's disease, is an obliterating disease of the arteries and veins, usually affecting segments of vessels in the extremities, and occurring almost always in young men. The cause of the vascular lesion remains unknown.

DIAGNOSIS

The main features of the disease are usually clear enough to permit of diagnosis by simple methods. The history is characteristic, and clinical examination gives clear evidence of ischæmia, particularly the loss of the arterial pulses in the limbs. Special investigations are occasionally needed to make or to confirm the diagnosis, but they are not essential in the average case. Oscillometry is a useful refinement in the detection of arterial pulsation, particularly in œdematous limbs where swelling makes it difficult to feel the pulse. Arteriography is sometimes of great help in uncertain cases but is unnecessary and unjustifiable as a routine measure. Microscopy of vessels obtained from amputated digits or limbs or by arterectomy is often valuable in diagnosis. It is important to cut sections over a sufficient length of the affected vessel, because unrepresentative portions containing consecutive thrombus, and presenting a picture of clot in the lumen of an apparently normal vessel, will cause confusion if this precaution is not taken.

Thrombosis of superficial veins occurred in 24 of the 77 cases, and in 19 patients it was the first symptom of the disease. Superficial phlebitis, or a history of it, is

important in diagnosis, but microscopy of an affected vein is not usually of great value, unless the nature of the swelling is in doubt, as when short lengths of small veins are involved. These may present as tender cutaneous nodules, the nature of which is discovered by biopsy and microscopy, as in the following case.

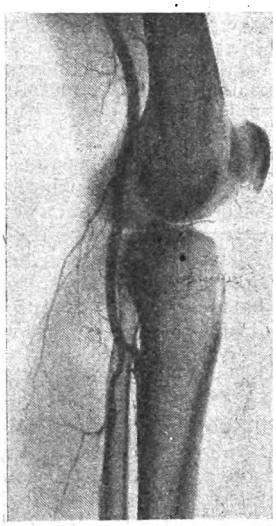

Fig. 1—Normal arteriogram of leg, showing arterial branches to calf muscles.

A man, aged 22, sustained an injury to his left knee in a car accident. Six years later the foot became cold, and he had pain in the calf after walking a few miles. The walking distance gradually diminished to 300 yards, when he sought medical aid. He was found to have a left popliteal thrombosis and no evidence of disease elsewhere. This was thought to be entirely post-traumatic, though the long interval before developing claudication was difficult to explain. Small tender cutaneous nodules next appeared spontaneously on the left leg. One of these, when removed and examined histologically, proved to be a focus of thrombophlebitis with changes usually considered typical of thrombo-angiitis obliterans.

ÆTIOLOGICAL FACTORS

An attempt was made to assess statistically the connexion between smoking and Buerger's disease. It proved impossible because the patients could not be separated into clear categories of those who stopped smoking and those who continued; too many merely reduced their smoking or continued to smoke sporadically. The one non-smoker in the series was also the only female patient. Two patients gave up smoking entirely but had fresh attacks of Buerger's disease in different parts of the body in subsequent years. Though smoking is not regarded as the cause of the disease, patients were advised to give it up because of its known vasoconstrictive effect on peripheral vessels.

This series, unlike some others, did not include an unduly high proportion of Jews.

Only 1 of the 77 patients had a positive Wassermann reaction. Syphilitic infection, when present, appears not to be of ætiological significance.

NATURAL COURSE

The average age of the patients at the onset of the disease was 35 years. The oldest patient was 48 and the youngest 16 when the disease started. The first episode in the history of this youngest patient was an isolated phlebitis several years before any arterial symptoms arose, but there were several patients whose initial manifestation was an arterial one, such as claudication starting at the age of 20 or 21.

Episodes of Activity.—It is well recognised that Buerger's disease tends to run its course in a series of episodes of activity, separated often by months or years of quiescence. Therefore all the histories were carefully analysed so that the periods between active episodes were known for every patient. The longest of these periods was fourteen years. Many other patients experienced fresh attacks of activity after an interval of ten years.

It has been suggested that Buerger's disease can burn itself out completely; but, since we know that it can manifest itself afresh after many years, it seems doubtful whether it can ever be said to be completely cured.

Duration.—There were 7 fatal cases, in which the duration of the disease and the causes of death were said to be as follows:

Duration of disease at death (yr.)	*Cause of death*
5 ..	Coronary thrombosis
11 ..	Widespread gangrene
31 ..	Widespread gangrene, including iliac thrombosis
13 ..	Mesenteric thrombosis
4 ..	Buerger's disease (no more exact information)
2 ..	Cerebral hæmorrhage
2 ..	Coronary thrombosis, embolism, gangrene

Average 9·9

It will be seen that all the deaths were due to manifestations of the disease, and that the duration of the disease varied widely, the longest history from onset to death being 31 years. One patient still alive has lived 30 years since his first symptom.

CLINICAL TYPES

The cases fell naturally into three groups according to the initial site of the disease, for it sometimes started in large vessels, sometimes in the small vessels, and sometimes in both simultaneously. The main criterion of differentiation was the presence or absence of the popliteal pulse. Prognosis varied in the three groups as regards alleviation of symptoms by sympathectomy and survival of the limb.

Obstruction of a Main Vessel.—In this group thrombosis occurs in the femoral or in the popliteal artery, the popliteal pulse is not palpable, and the main symptom is intermittent claudication in the calf. As a rule there are pronounced postural colour changes, and wasting of the calf muscles is often evident. Provided the thrombosis does not extend downwards into the smaller distal vessels, the collateral circulation is usually adequate to prevent gangrene of the foot, the skin of which remains comparatively healthy.

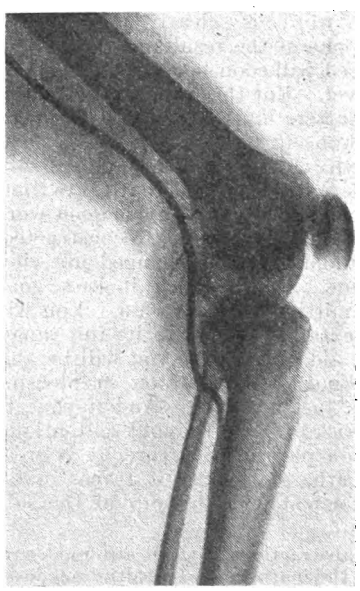

Fig. 2—Arteriogram showing Buerger's disease affecting smaller arteries to calf muscles in a patient with a palpable popliteal pulse and claudication pain in the calf.

Obstruction of Small Vessels.—When the smaller vessels are the first to be attacked, the popliteal pulse remains palpable, but the pulses at the ankle are diminished or absent. As one would expect, symptoms appear in the foot—claudication in the sole, rest pain, constant erythrocyanosis of the skin, and coldness followed by ulceration or gangrene of the toes. Some of the patients in this group have claudication in the calf, which, in the presence of a popliteal pulse, must be attributed to obstruction of the muscular branches of the main vessels.

Mixed Type.—The clinical picture in this group is a combination of the other two, since the disease attacks the main and the smaller arteries simultaneously, and so claudication in the calf, loss of the popliteal pulse,

and rest pain in the foot, with the premonitory signs of gangrene, all come on together.

EFFECTS OF SYMPATHECTOMY

Claudication pain in the calf is one of the prominent symptoms from which these patients may suffer. Reports of results of sympathectomy are infrequent in the otherwise extensive literature of Buerger's disease, and the statements made about its effect on claudication are often vague and unsatisfactory. Telford and Stopford [1] stated that the disability had been entirely abolished in some of the milder cases, but that the average result was persistence of claudication, often with a considerably lengthened walking distance.

Fig. 3—Arteriogram showing Buerger's disease affecting smaller arteries in the foot in a patient with a palpable popliteal pulse but no distal pulse, and with rest pain in the foot, claudication pain in the sole, and ulcerated toes.

Others have tried to assess improvement on a percentage basis, but this may give a very misleading impression of results—in the case, for example, of a patient who could walk 15 yards before operation and 30 yards afterwards, who would be rated as "100% improvement." In the present series a patient was not classed as "improved" unless his walking distance was increased by a really useful amount after operation, a quarter of a mile being taken as a minimum. Patients were closely questioned or tested on their postoperative walking distance, and this was compared with the preoperative distance noted in the records. This often showed that the patients entertained a somewhat optimistic idea of the amount of improvement, and that close and critical assessment was necessary.

Claudication.—The effect of sympathectomy on claudication pain in the calf was as follows:

Type of disease	*No. of limbs affected*	*No. improved*
Main vessels	23	9
Small vessels	19	16
Mixed	14	0
Totals	56	25

These figures indicate that the best results are to be expected when the smaller vessels are affected—i.e., when the popliteal pulse is palpable. Improvement was not observed in the mixed type.

Survival of the Limb.—The fate of the limb in the three types of disease for all cases in the series in which a sympathectomy was performed was as follows:

	Sympathectomised lower limbs		
Type of disease	*Total*	*Lost*	*Preserved*
Large vessel	23	10	13
Small vessels	72	17	55
Mixed	16	10	6
Totals	111	37	74

It will be seen that the prognosis is best when the small vessels alone are affected. Limbs classed as preserved are those in which, though a minor amputation, such as that of a toe, may have been necessary, a major amputation was not required.

1. Telford, E. D., Stopford, J. S. B. *Brit. med. J.* 1935, i, 863.

The fate of the limb in the three types for all cases in the series, including those which were not submitted to sympathectomy, was as follows:

	All lower limbs		
Type of disease	*Total*	*Lost*	*Preserved*
Large vessel	26	12	14
Small vessels	81	18	63
Mixed	16	10	6
Totals	123	40	83

The limbs not submitted to sympathectomy were too few to be compared with those operated on, and they also included the mildest cases. The figures for the whole series emphasise still further the better prognosis when the small vessels alone are affected.

It is clear that in the cases of obstruction of a main vessel the onset of gangrene indicates the spread of the disease to the smaller vessels—i.e., the cases have become of mixed type in spite of sympathectomy. It is impossible to say exactly what effect sympathectomy has had in stopping or slowing this process of spread, since no control series of similar untreated cases is available.

In the limbs preserved the average duration of arterial symptoms at the follow-up examination was seven years in disease of the small vessels and four years in disease of a large vessel. Only 1 limb is known to have survived with the mixed type of disease for more than two years.

Other Effects of Sympathectomy.—Besides claudication pain in the calf, other symptoms less amenable to statistical demonstration were benefited, including claudication in the sole, rest pain, and the superimposed vasospastic attacks in the extremities characterised by coldness and numbness, often resembling Raynaud's disease. It seemed also that ulcers and minor amputations healed better after sympathectomy.

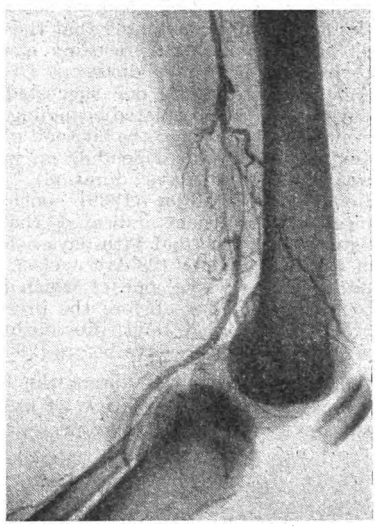

Fig. 4—Arteriogram showing Buerger's disease affecting larger arteries in a patient with impalpable popliteal pulse, claudication pain in the calf, and a relatively healthy foot.

"*Prophylactic*" *Sympathectomy.*—In some early cases of unilateral Buerger's disease bilateral sympathectomy was performed. In several of these the disease subsequently appeared in what had been the sound limb. Hence "prophylactic" sympathectomy did not give complete protection, though it possibly delayed the onset of symptoms.

SUMMARY

Buerger's disease is episodic and may recur after many years of quiescence. Without a very long follow-up, therefore, it is impossible to be certain that any particular form of treatment has cured the disease.

Cases may be divided into three groups according to the initial site of the disease in the arterial tree. The effects of sympathectomy and the prognosis for the limb are best when the smaller vessels are the first to be attacked.

I wish to thank Prof. J. Paterson Ross for his great help and advice in the preparation of this paper.

OVULATION AND THE MENSTRUAL CYCLE

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THERE is much divergence of opinion concerning both the time of ovulation in the menstrual cycle and the subdivision of that cycle into phases with characteristic endometrial histology. A considerable body of opinion holds that, whereas the commonest time of ovulation is about midway in the cycle (of 28 days), there is a wide range of variation in different individuals, and that even in the same individual the day of ovulation may vary in different cycles (Asdell 1927, Evans and Swezy 1931, Weinstock 1934, Burr and Musselman 1938, Stein and Cohen 1938, Seymour 1939, Altmann et al. 1941). Some investigators claim that ovulation is more closely related to the succeeding than to the preceding menstrual period (Knaus 1934, Ogino 1934, Pryde 1941, Smith 1942).

TUBAL OVA

Several workers have used tubal ova or young intra-uterine embryos to estimate the time of ovulation, and Hamilton et al. (1943) claim that the recovery of tubal ova at a definite period of the menstrual cycle gives the most reliable information concerning the time of ovulation.

The five ova found by Allen et al. (1930) indicated that ovulation took place between the 12th (or 11th) and 14th days of the cycle, although the duration of the cycles is not stated. The ovum recovered by Lewis (1931) indicated that ovulation took place 15 days before the expected onset of the next menses, assuming that the present cycle was one of 35 days, as was the preceding one, although the previous cycles were of 28 days' duration. Of two ova found by Pincus and Saunders (1937) one suggested that ovulation was 12 days before the postulated beginning of the next cycle (28-day cycles), and the other that it took place 9–13 days before the next menstruation (depending on whether the present cycle was of 26 or 30 days' duration). Miller et al. (1938) and Reimann and Miller (1939) concluded that the five ova recovered by them indicated that ovulation took place between the 15th and 17th days before the anticipated onset of the next menses (28-day cycles). Hamilton et al. (1943) discovered two ova, one of which indicated that ovulation took place 14 days before the presumed onset of the next cycle (last cycle 30 days, previously 28 days), and one that it took place 14–15 days before (28-day cycles).

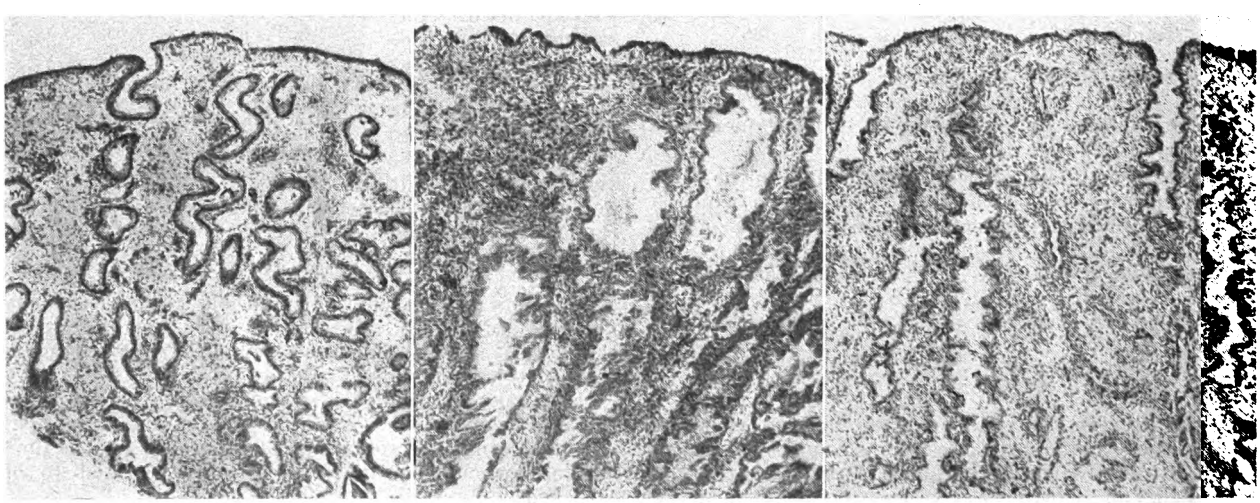
In the cases cited above the writers tacitly assume, for calculating the relation of ovulation to the onset of the next menses, that the present cycle, had it not been interrupted (generally by hysterectomy), would have been of the same length as the immediately preceding one. There is no conclusive evidence that such an assumption is warranted. Rock and Hertig (1944), from a study of three unfertilised tubal ova and eleven young intra-uterine embryos, estimated that the interval between ovulation and the next expected menses in these cases ranged from $11^1/_2$ to 17 days. In the case of the fertilised specimens these figures were obtained by adding the estimated age of each embryo to the estimated interval between operation and the next catamenia, as judged from the condition of the endometrium, although they admit that this last estimation is uncertain. When they computed the lengths of the estimated postovulatory phase in terms of percentages of the estimated lengths of the menstrual cycles, they found that the *average* of these percentages did not deviate from that calculated, by using the theoretical figure of 14 days for ovulation time, sufficiently to interfere with the indication that ovulation took place about 14 days before the onset of the next expected period. But these results relate to the average for the series of cases and mean neither more nor less than that ovulation most often took place about 14 days before the next period but may take place outside this limit, as is indeed revealed by the figures in their individual cases.

ENDOMETRIAL CHANGES

With regard to the changes in the structure of the endometrium during the menstrual cycle, there are notable differences in the results of those who have suggested the division of the cycle into various phases, each of definite duration and with its particular endometrial structure (Schröder 1915, Fraenkel 1924, Shaw 1925, 1941, Markee 1940, Novak 1941, Krafka 1942).

In view of existing uncertainties, some details relating to a very early human embryo described by Davies and Harding (1944) are here reported, since they provide evidence that ovulation can take place early in the menstrual cycle, and that the histological structure of the endometrium on a particular day of the cycle is influenced by the remoteness of that day from the time of ovulation.

The embryo is in a previllous stage of development; it was obtained by hysterectomy from a married woman, aged 26, who had no previous abnormal gynæcological or obstetrical history, and the embryo and the endometrium present no abnormal features. From its histological characters, and by comparison with other previllous embryos both of man and of the macaque monkey,



(a) (b) (c)

Photomicrographs of endometrium (a) on 20th day from a woman with 28-day cycles; (b) on 20th day from the case described in text; (c) on 25th day from a woman with 28-day cycles. (× 50.)

it was estimated to be 9–10 days old. The menstrual and coital histories, obtained at the time from both wife and husband, were clear and definite. The woman insisted that her periods came on regularly every 4 weeks ("every fourth Sunday"); this reply was accepted with full knowledge that variations in the length of the cycle in the same individual are very common. Menstrual bleeding took place during the first 4 days of the present cycle; the first coitus took place on the 10th day; coitus took place also on each of the 11th to 15th days; the uterus was removed on the 20th day. The maximum age of the embryo calculated from the coital history harmonises with the age estimated from the histological examination, and the coitus on the 10th day was concluded to have been the one responsible for fertilisation; from this it was deduced that ovulation took place on the 9th or 10th day. The relation between the coitus and ovulation suggests the possibility that ovulation was induced by this first act of copulation in the cycle (on the 10th day). Postulation that ovulation took place later in the cycle would have led to the unwarranted conclusion that the embryo was younger than is indicated by the stage of development attained by the several embryonic elements.

If ovulation took place on the 9th or 10th day, the resultant corpus luteum would, by its progesterone and œstrogen secretion, begin to induce the secretory phase in the endometrium 4 or 5 days earlier than would have been the case if ovulation had occurred on the 14th day. It is noteworthy that the histological structure of the endometrium on the 20th day of the cycle in the present case is closely similar to that of the endometrium on the 24th or 25th day in several specimens examined from other women with 28-day cycles, and it is certainly much more advanced in the secretory phase than several 20-day specimens from women with 28-day cycles. In these other cases ovulation probably took place nearer the middle of the cycle. The endometrium in specimen *b* (see figure) closely resembles that in *c*, and is more advanced in the secretory phase than that in *a*.

Rock and Hertig (1944) estimate the interval which they would expect to elapse before the onset of the next menses by the stage reached by the endometrium in their specimens. But they admit that this estimated time is uncertain. In the present case the interrupted cycle would in this manner be estimated (in the absence of pregnancy) to terminate in 4 days—that is, the present cycle would be deduced to be one of 24 days (in contrast with the previous regular 28-day cycles), on the ground that the endometrium on the 20th day has reached a stage comparable with that on the 24th or 25th day in specimens from other women with 28-day cycles who probably ovulated near the middle of the cycle. But such a deduction is questionable, since there is no conclusive evidence that the duration of life of the corpus luteum (of menstruation) is rigidly constant; and, while the secretory phase will be *attained* early in the cycle if ovulation is early, this phase will be *maintained* so long as the corpus luteum remains active; the next menses will not ensue until this body ceases its activity. Although, therefore, it may be stated with reasonable certainty that in the present case ovulation took place 9 or 10 days after the onset of menstruation in a patient with hitherto regular 28-day cycles, postulation of the relation of ovulation to the hypothetical next menses cannot be utilised as reliable evidence for estimating the duration of the postovulatory phase of the cycle.

It is concluded that, in the absence of knowledge of the day of ovulation, the structure of the endometrium does not accurately indicate the day of the cycle to which the endometrium belongs. Further, postulation of ovulation time in a given case and deductions based on endometrial structure without knowledge of the ovulation time are concluded to be unsafe indications for use in assessing the age of young embryos.

SUMMARY

The study of a young human embryo and of the maternal menstrual history has provided evidence that ovulation can take place early in the cycle, and that the histological structure of the endometrium on a particular day of the cycle is influenced by the remoteness of that day from the time of ovulation.

Deductions concerning the relation of ovulation to the expected onset of the next menses, based on the study of tubal ova and early embryos, cannot be considered to be conclusive.

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THYROIDECTOMY WITH BLOCK DISSECTION OF THE NECK FOR CARCINOMA OF THE THYROID GLAND

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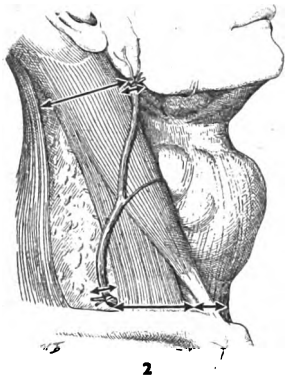
IT is well known that carcinoma of the thyroid gland is apt to recur after partial thyroidectomy. Some patients have survived ten years, during which they have had several recurrences. To prevent such recurrences, especially the sternal, clavicular, and scapular so-called metastases, which are probably due to direct invasion along the muscles and aponeuroses, the need to resect the adjacent veins (Crile 1936) and muscles (Joll 1932, 1941) has been emphasised, and total thyroidectomy with block dissection of the neck has been advocated (Dargent and Bérard 1940, Lahey et al. 1940, Watson and Pool 1940) to ensure that all affected lymph-glands and any aberrant portions of the thyroid gland, which are particularly liable to be the seat of papillary cancer (Crile 1939), are extirpated, and to prevent metastasis through the blood-stream.

Under either local or intratracheal anæsthesia block dissection is done in several steps.

(1) A horizontal incision over the tumour meets an oblique incision along the sternomastoid muscle (fig. 1), and the two flaps are dissected and turned back. The two lobes of the thyroid gland are examined for confirmation of the diagnosis by biopsy if necessary.

I have seen three cases of nodular goitre, in patients aged over 50, which had been wrongly diagnosed as cancer. Other cases wrongly so diagnosed have included,



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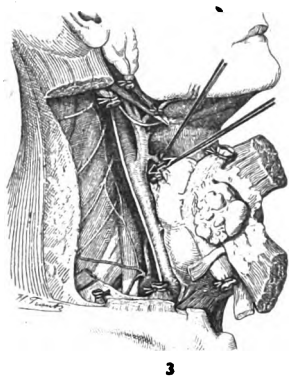

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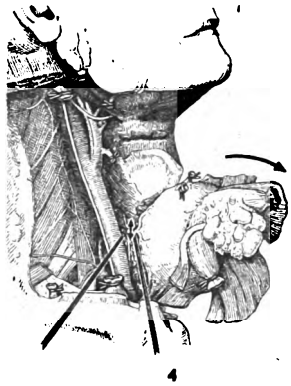

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Fig. 2—Resection of sternomastoid muscle and external jugular vein.
Fig. 3—Resection of facial, lingual, and superior thyroid veins and superior thyroid artery.
Fig. 4—Isolation of recurrent laryngeal nerve, with dissection of its accompanying lymph-glands.
Fig. 5—Isolation of trachea and ligation of thyroid veins. If the other lobe of the thyroid gland is sound, the isthmus is divided. If not, the whole of the thyroid gland is removed, and the parathyroid glands are grafted in the stump of the sternomastoid muscle.

in my experience, hæmatocele of the thyroid gland, and acute congestion of the thyroid gland associated with indurated cervical lymph-glands due to cancer elsewhere (nævocarcinoma of skin, mammary cancer, and cancer of larynx).

(2) The sternomastoid muscle and the external jugular vein thus exposed are divided above and below (fig. 2) and resected, and the inferior belly of the omohyoid muscle is divided to expose the internal jugular vein. If examination of the thyroid gland shows that only one lobe need be extirpated, the internal jugular vein is tied above and below and resected. If, however, total thyroidectomy is to be done, the right and left internal jugular veins are carefully isolated by dissection; and, when the ablated thyroid has been examined, the vein draining the more affected lobe is resected, the other being left.

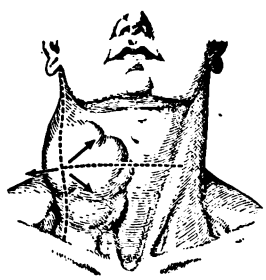

Fig. 1—Incisions for thyroidectomy and block dissection of neck.

(3) The facial and lingual veins are divided, and the superior thyroid vein on the side on which the internal jugular vein is not being resected is tied close to its junction with that vein. The superior thyroid artery can now be exposed and tied as high as possible (fig. 3). Sometimes it is difficult to free the upper pole of a carcinomatous thyroid gland from the thyroid cartilage without considerable oozing from the venules there. In securing hæmostasis care must be taken not to injure the external laryngeal nerve.

(4) After resection of the muscles lying under the thyroid the carcinomatous gland is displaced forwards, the inferior thyroid artery is divided, the recurrent laryngeal nerve is carefully isolated, and the chain of lymph-glands accompanying it is dissected away (fig. 4). Block dissection stops just short of the trachea. If one lobe of the thyroid gland is healthy, the isthmus is divided and its stump is sutured after hæmostasis (fig. 5). If total thyroidectomy is being done, the parathyroid glands are dissected away from the thyroid gland and immediately grafted into the stump of the sternomastoid muscle, and the internal jugular vein on the side of the less affected lobe is not interfered with. If necessary, the extirpation of the second lobe can be deferred to a second stage.

RESULTS

Comparatively few cases are suitable for thyroidectomy with block dissection of the neck. Since 1940 this operation has been done in only 16 of 210 cases seen at the Centre Anticancéreux at Lyons. Of the 210 patients, 34 were not fit for operation; 52 had only enough tissue removed to free the trachea; 33 were treated by radiotherapy alone; 30 underwent subtotal thyroidectomy without block dissection, including 1 who proved at operation to have simple goitre and no cancer; and 45 underwent extracapsular thyroidectomy without block dissection.

Of the 16 cases submitted to thyroidectomy with block dissection of the neck, in 2 the whole of the epitheliomatous thyroid gland was removed, but tetany did not develop, because the parathyroid glands were grafted. Within a year of operation both patients died from metastases already present at the operation. Of the 14 patients subjected to unilateral thyroidectomy and block dissection of the neck, 1 died in hypoglycæmic coma five days after the operation, and 2 patients are still alive, without recurrence, three years after operation not followed by radiotherapy. Of the 11 other patients, all of whom had a postoperative course of radiotherapy, 1 has been lost sight of, 1 died of "Hodgkin's disease" four years later, and the remaining 9 survived 1–8 years. Of these, 1 already had a vertebral metastasis when he was operated on, and he died of complications due to paraplegia five years later. No recurrence or fresh metastasis was found in any of these 9 patients.

One case was complicated by the presence of a bulky calcified carcinomatous thrombus in the internal jugular vein, making resection of the vein difficult owing to the calcareous projections which tended to tear the vein, and owing to bleeding from the thrombus. There were also signs of obliteration of the left innominate vein. The patient's condition made it necessary to defer thyroidectomy to a second stage. The growth in the thyroid gland proved to be a Hürthle-cell carcinoma, and that in the thrombus a vesicular carcinoma. The patient is still alive two years after the operation.

RESULTS OF OTHER TREATMENTS

Freeing of Trachea.—Of the 52 patients in whom only enough tissue was removed to free the trachea, only 2 survived for more than five years (thanks to radiotherapy.)

Radiotherapy.—Of the 33 patients submitted to radiotherapy alone, 2 survived for more than five years, but 6 developed metastases immediately after treatment had ended.

Subtotal Thyroidectomy.—Of the 30 patients submitted to intracapsular subtotal thyroidectomy without block dissection of the neck 1 proved to have a simple goitre. Of the 29 patients with cancer of the thyroid gland 26 were also treated by radiotherapy. Of these, 11 survived for more than five years, but 18 had up to eight postoperative recurrences.

Extracapsular Thyroidectomy.—Of the 45 patients who underwent extracapsular thyroidectomy without block dissection of the neck 28 were also treated by radiotherapy. Of these, 4 survived for more than five years, but 11 developed postoperative recurrences.

INDICATIONS FOR OPERATION

The decision to perform thyroidectomy with block dissection of the neck rests on the diagnosis of cancer of the thyroid gland. The best criteria are the rapidity of growth of the tumour, its hardness, and paralysis of the recurrent laryngeal nerve.

In a series of 131 cases confirmed histologically and including 56 differentiated and 60 undifferentiated carcinomas the incidence of these criteria was as follows: (1) 16 (28·6%) differentiated and 49 (81·7%) undifferentiated carcinomas had taken less than a year to develop; (2) 15 (26·7%) differentiated and 51 (85%) undifferentiated carcinomas were typically hard; and (3) 2 (3·5%) differentiated and 22 (36·6%) undifferentiated carcinomas were associated with paralysis of the recurrent laryngeal nerve.

Precedent goitre, associated thyrotoxicosis, and the presence of nodules in the neck are less characteristic of cancer of the thyroid gland.

Early cancer of the thyroid gland may resemble simple goitre, in which case ordinary subtotal thyroidectomy without block dissection of the neck will probably be performed. Subsequent radiotherapy usually does not prevent recurrence. Therefore, as soon as a recurrence is noted, the operation should be completed by total thyroidectomy with block dissection of the neck.

In the case of a rapid enlargement of the thyroid gland it is advisable to do an exploratory cervicotomy to see whether or not the tumour is due to thyroiditis or to struma lymphatosa, both of which simulate scirrhous carcinoma and should be treated by radiotherapy.

With a slowly growing cancer of the thyroid gland, even if metastases are already present or if the overlying skin has been invaded, thyroidectomy with block dissection of the neck should be performed, because it will prevent further metastases, which otherwise are almost inevitable.

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PENETRATION OF CERVICAL MUCUS BY SPERMATOZOA

A METHOD OF INVESTIGATION

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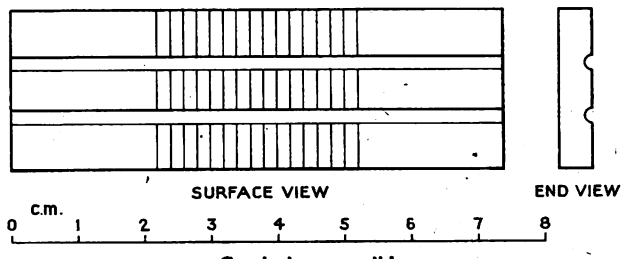
PREVIOUS methods described for investigating the entry of spermatozoa into cervical mucus, such as the capillary-tube method of Lamar et al. (1940) and the coverslip method of Barton and Wiesner (1946), use a system in which mucus and spermatozoa are under considerable stress. The surface tension in mucus held between a slide and coverslip, or in a capillary tube, must be very large relative to the energy of a progressing spermatozoon. Moreover, dead spermatozoa may be drawn across a film of mucus between slide and coverslip by capillarity. Abarbanel (1946), using the capillary-tube method, found "grossly abnormal" spermatozoa invading cervical mucus. This suggests that here also suction is acting, for we have found fewer than 1% of amorphic sperm heads in more than 10,000 spermatozoa examined in stained films of postcoital mucus; and stained films of in-vitro penetration, obtained by the method described below, support the inference that very few abnormal spermatozoa can penetrate mucus.

The present method was devised to reduce interference from surface tension. The special slide used was made to our design by W. Watson and Son Ltd. It is not unlike a Thoma counting slide with the grooves running parallel to the long axis instead of transversely, but the strip between the grooves is at the same level as the rest of the surface. The central region is marked for 3 cm. with transverse etched lines 2 mm. apart.

Mucus used for penetration tests must not contain any spermatozoa at the beginning of the test. If it is desired to test a wife's mucus against her husband's semen, the couple should be asked to avoid intercourse for 8–10 days before the mucus is extracted. All mucus should be examined for the presence of spermatozoa before it is used.



Cervical mucus slide.

METHOD

The mucus is spread over the central strip of the slide, in the region of the etched lines. It should be thin enough for the lines to show as faint shadows when the surface of the mucus is viewed with a $^2/_3$ in. objective, but thick enough not to draw away from the edges of the strip. Too thin a film should not be used.

About 0·05 ml. of semen is placed near one end of the mucus, and the drop is stroked gently with a platinum loop until the mucus is in contact with the semen for the whole width between the grooves. These grooves prevent the seepage of semen round the edges of the mucus, and maintain a standard width of surface between mucus and semen. Some semen seeps over the surface of the mucus but does not usually extend beyond 2–4 mm. It can be minimised by having a rather thick layer of mucus at the junction.

The slide is incubated at 37°C in a petri dish floored with wet filter-paper and sealed with soft paraffin. It is examined under a $^2/_3$ in. objective at any convenient intervals between 30 min. and 3 hours from the beginning of the test. No coverslip is used. In this way capillary forces are avoided except those at the fluid interface and between the mucus and the slide. Another advantage is that the test can be set up in 2 min.

For examination, the slide is placed so that the junction of semen and mucus at the end of the semen overrun is in focus, and the activity of the spermatozoa in the semen drop is noted. The slide is next moved until one of the etched lines has been crossed. (If, owing to opacity of the mucus, the lines are difficult to see, they may be located by examining the uncovered side strip of the slide.) The presence or absence of spermatozoa and their activity between this line and the next are recorded, and the slide is then moved again and the observation repeated for each 2 mm. section until no spermatozoa are found in five microscope fields in each of two adjacent sections. The search is then abandoned, and the slide can be returned to the incubator. In practice we have found that little or no increase in the distance penetrated takes place after one hour. To establish with certainty that spermatozoa are absent from the mucus beyond the last

* Aided by a grant from the Medical Research Council.

point observed with the low power, the mucus can be separated in the following way:

A square coverslip held vertically is placed with one edge pressed firmly on the etched line 4 mm. beyond the last observed spermatozoa. The mucus beyond this is removed with the edge of a second coverslip and placed on an ordinary slide, where it can be covered and examined carefully with a $^1/_6$ in. objective.

APPLICATION

With this special slide different types of penetration can be compared by noting (1) the greatest distance reached by the spermatozoa in a given time, (2) their motility in the mucus, (3) the relative numbers of spermatozoa reaching points at various distances from the semen-mucus junction, and (4) the course of the spermatozoa within the mucus. Lack of homogeneity in the mucus can be detected by the behaviour of the spermatozoa.

The following types of penetration can be recognised, though they grade into one another:

(1) Complete failure of the spermatozoa to enter the mucus, or entry confined to a zone less than 0·2 cm. wide adjacent to the semen-mucus junction.

(2) Spermatozoa enter slowly and travel 0·5–1·5 cm. in an hour, when progress ceases. Usually few spermatozoa go further than 0·5 cm.

(3) Spermatozoa enter rapidly and after an hour's incubation are found active from the edge of the semen overrun to the farther edge of the mucus, a distance of 2·5–3·0 cm., according to the quantity of mucus used. But the numbers in the region farthest from the semen are much fewer, and the activity less, than in the first centimetre.

(4) Entry as in (3) but much more rapid, and complete. Within half an hour, or less, spermatozoa are swarming throughout the mucus.

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PARKINSONISM TREATED WITH PARPANIT

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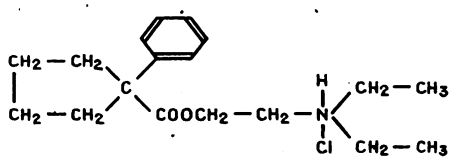
FAVOURABLE reports from Switzerland and other countries on the treatment of parkinsonism with 'Parpanit' led to the trial of this drug at the National Hospital, Queen Square.

Parpanit, a synthetic compound, was found by Grünthal (1946) to cause subjective sensory disturbances when given to healthy people. He thought that the drug might act on the proprioceptive sensory system and therefore might be of some use in the treatment of conditions characterised by muscle rigidity. After clinical trials he concluded that parpanit was of benefit in the treatment of parkinsonism. Later Hartmann (1946, 1947), in a large series of cases, confirmed Grünthal's results. Llavero, in Madrid (unpublished report), and Bickel and Dubois (1947) confirmed Hartmann's findings.

Parpanit, chemically closely related to antispasmodics such as 'Trasentin' and 'Dolantin,' has the following structure:



From the pharmacological studies of Domenjoz (1946) and Heymans and De Vleeschhouwer (1947) it is clear that parpanit has atropine-like activity, but these studies do not explain why it should benefit parkinsonism. (In the case of the solanaceous drugs we are similarly ignorant.)

Tremor and weakness are the commonest symptoms, and tremor and rigidity the most striking signs, of parkinsonism. The patient, or an observer, can readily appreciate any considerable change in the severity of the disability, but, since tremor and rigidity vary from minute to minute, objective assessment of minor changes produced by treatment is difficult. We therefore based our assessments of tremor and facility of movement (under which heading are considered slowness of movement, difficulty in initiating movement, and lack of ability to perform intricate manipulations) on the patients' subjective impressions, obtaining objective confirmation, however, wherever possible. We estimated rigidity in arms and legs by a constant technique in which repeated and irregularly spaced passive movements were performed. Effects on salivation and vision as well as such symptoms as giddiness and paræsthesiæ were recorded as reported by the patient.

In all, 25 patients with parkinsonism were carefully observed. All were moderately severely affected. Post-encephalitic parkinsonism and paralysis agitans were about equally represented. All the patients had been receiving solanaceous drugs in optimal doses for more than a year, and all had been under regular observation as outpatients for at least that period; 4 patients were admitted to hospital for more detailed study. The investigation was conducted in six parts. The results obtained at each stage are described in turn. Their significance and the side-effects observed are discussed subsequently.

METHOD OF ADMINISTRATION AND RESULTS

Part I

In addition to their usual solanaceous medication 8 patients were given inert control tablets.

After a week, no change in their condition was reported or observed.

Part II

To 19 patients, in addition to their usual solanaceous medication, parpanit was given in increasing dosage until disturbing side-effects were observed.

At first, parpanit 0·0125 g. was given thrice daily after food; the morning, then the midday, then the evening doses were then increased on consecutive days by amounts not greater than half the corresponding dose for the preceding day, until unpleasant side-effects precluded further increase. Where benefit was obtained, the interval between doses was decreased and their number increased to obtain as even a level of effect as possible. At this stage a decrease in the size of each dose was sometimes necessary. Though hourly doses (as many as fifteen daily) were given a trial, it was found equally satisfactory to give the doses three-hourly or four-hourly. The optimal individual doses varied from 0·025 to 0·1 g.

On such dosage, 5 patients obtained definite subjective improvement while taking parpanit, and a further 4 reported slight improvement, 7 obtained no benefit, and the remaining 3 felt worse. Of individual signs and symptoms, tremor was reported as reduced in 7, as unaltered in 6, and as increased in 6, though observation revealed no change in any. 10 patients noted improved facility of movement; 9 found no change. In 1 patient side-effects outweighed the improvement in other directions, and in 4 others they were severe enough to be disturbing. The degree of benefit was never great. In only 4 was a slight improvement in gait observed

by us. Greater dexterity with cutlery at meals was claimed by 2 patients and confirmed by their relations. In the 16 patients initially showing rigidity this was decreased in 4, unaltered in 8, and increased in 2. The remaining 2, feeling worse on the treatment, omitted it before examination. In no case was the change pronounced. Patients showing improvement have been treated for as long as thirty weeks without relapse. Of the 8 patients previously given control tablets (part I) 7 were included in this series. Of these, 4 were slightly improved, 2 unchanged, and 1 worse.

Part III

From 17 patients on optimal doses of parpanit with solanaceous drugs the latter were gradually withdrawn.

These patients were the same as those already reported on in part II, except that 2 of the 3 made worse by parpanit were omitted. As compared with their condition on solanaceous drugs alone, 6 patients reported improvement, 2 slight improvement, 5 no change, and 4 deterioration on parpanit. 4 found the tremor reduced, 7 unchanged, and 6 increased. Facility of movement was stated by 7 to be increased, by 6 to be unchanged, and by 4 to be reduced. Rigidity showed an increase in 1 of these patients, was unaltered in 9, and was reduced in 3. 4 showed no rigidity. Further adjustment of the parpanit dosage was without benefit. During eight weeks of this treatment no patient who had improved relapsed. None of these changes were pronounced, with perhaps one exception. One man volunteered that on parpanit he was able to dry himself after a bath, which he had not previously been able to do. This increased facility of movement, however, was not reflected in other activities, such as donning his overcoat and walking.

Part IV

Solanaceous and parpanit tablets were abruptly interchanged in 3 hospital inpatients.

Tablets of the two drugs, identical in appearance, were given to 2 of the patients in this group. The change-over of drugs passed unnoted by 1 patient; in the other the change in side-effects alone caused its recognition. The third patient, who knew of the change in medication, reported slightly improved facility of movement, but, since this persisted when a return to solanaceous drugs was made, this improvement must be considered of doubtful significance. In none of these patients, despite careful observation by medical, nursing, and physiotherapy staffs, was any objective alteration in signs or behaviour noted. These 3 patients were selected for admission to hospital on economic grounds alone. The dosage of both drugs was that which had previously been adjudged optimal.

Part V

Inert tablets were substituted for parpanit when this was being given alone in optimal dosage, the patients being unaware of the alteration (2 patients).

Previously 1 patient in this group had thought parpanit as effective as the solanaceous drugs; the other had thought it more so. On the substitution of inert tablets without the patients' knowledge, so great an exacerbation of their disability was produced that they were almost completely immobilised. (See case-record.)

Part VI

Inert tablets were substituted for parpanit while full doses of solanaceous drugs were also being given (2 patients).

These 2 patients, who had previously benefited somewhat from the addition of parpanit, noted slight increase in their symptoms on its substitution by inert tablets. The tablets were changed in each case without the knowledge of the patient. No objective change was detected.

Side-effects of Parpanit.—The tolerance to parpanit varied from patient to patient, and where benefit was obtained unpleasant side-effects began to intrude. Giddiness, a feeling of weakness, drowsiness, and paræsthesiæ developed in that order of frequency both when parpanit was given alone and when solanaceous drugs were given in addition. Hallucinosis was met with only twice, on both occasions on the combined medication. Increased blurring of vision and dryness of the mouth were complained of by 3 patients, again on combined drugs. Given alone, parpanit produced notable dryness of the mouth twice and blurring of the vision 3 times, but in both instances this was less than that produced by the usual solanaceous medication. In 6 patients hypersalivation, and in 1 rhinorrhœa, developed when the solanaceous drugs were omitted, despite the administration of parpanit. Giddiness, a sensation of weakness, and drowsiness were more common when parpanit was taken on an empty stomach, coming on usually $^1/_4$–$^1/_2$ hr. after a dose and lasting from a few minutes to about an hour. It was during the presence of these side-effects (if these were not too severe) that the maximal benefit was obtained. Throughout, careful sensory testing did not reveal any abnormality, and no changes in the tendon-reflexes were detected.

DISCUSSION

The results of this investigation have confirmed the usefulness of parpanit in parkinsonism. No striking differences in therapeutic activity were seen on replacing solanaceous drugs by parpanit, though minor changes were observed. Sometimes one drug, sometimes the other, seemed more beneficial. In contrast to this, our case-notes show that, in the absence of parpanit, the withdrawal of solanaceous drugs had previously produced a considerable recrudescence of symptoms in 8 of the 14 of our patients in whom this had been tried. As would be expected, there was a similar recrudescence of symptoms when parpanit, given alone to a patient on whom it was therapeutically active, was withdrawn. Some patients derived no benefit from either form of medication. Though as many as 15 doses have been given daily, it was found equally satisfactory to give the doses three-hourly or four-hourly. The optimal individual doses varied from 0·025 to 0·1 g.

Where parpanit was effective it was equally so whether it was added to or took the place of solanaceous drugs; when combined medication was being given, withdrawal of either produced only minor effects.

The side-effects of parpanit were similar to those of the solanaceous drugs, but their relative frequency and intensity were different. Thus, whereas giddiness, a sensation of weakness, dryness of the mouth, and blurring of vision developed with both, the first two predominated with parpanit and the last two with solanaceous medication. This is of some importance, because it is as often upon the nature of the side-effects as upon the degree of the therapeutic effects that the patient may base his choice. In this investigation side-effects were more troublesome on the combined medication.

There seem to have been no criteria by which we could have forecast the therapeutic value of either drug to any individual patient, except that, in general, those who had responded well to the solanaceous drugs responded also to parpanit.

ILLUSTRATIVE CASE-RECORD

A man, aged 68, had had tremor of the left arm for eight years. His chief complaints were unsteadiness in walking, difficulty in rising from a chair, tremor, and increased salivation. Tr. stramonii had been taken in doses of min. 20 thrice daily for four years, larger doses not being tolerated because of dryness of the mouth and blurring of vision. (As a maximal dose this is in our experience unusually small.)

RIGIDITY IN A CASE ON VARIOUS TREATMENTS

Line	Drug and dosage	Wrists		Elbows		Shoulders		Ankles		Knees	
		Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
1	Tr. stramonii min. 20 t.d.s. ..	cw +	cw +	cw +	..	lp +	lp +	..	..	..	..
2	Tr. stramonii min. 20 t.d.s. Inert tablets	lp +	cw +	cw +	lp +	lp +	lp + +	lp +	..	lp + +	lp + +
3	Tr. stramonii min. 20 t.d.s. Parpanit 0·1 g. t.d.s. ..	cw +	cw +	cw +	cw +	..	..	lp +	lp +	lp + + +	lp +
4	Parpanit 0·1 g. t.d.s. ..	..	cw +	cw + +	cw +	..	..	..	..	cw +	..
5	Inert tablets	cw + +	cw +	cw + +	cw +	lp + + +	lp + +	cw + +	cw +	lp + +	lp +
6	Inert tablets	cw + +	cw + +	lp + +	cw +	lp + + +	lp + +	lp + +	cw + +	lp + + +	lp + +
7	Parpanit 0·025 g. six times daily	cw +	cw +	lp +	lp +	lp + +	lp +	..	..	cw + +	cw + +
8	Hyoscine gr. $^1/_{200}$ six times daily	..	..	lp +	lp +	lp +	lp +	..	..	lp + +	lp + +
9	Parpanit 0·025 g. six times daily	cw +	..	lp +	lp +	lp +	lp +	..	..	lp +	lp +
10	Hyoscine gr. $^1/_{200}$ t.d.s. Parpanit 0·025 g. five times daily	..	..	..	..	lp +	lp + +	..	..	..	lp +
11	Tr. stramonii min. 20 t.d.s...	lp +	cw +	cw +	lp +	lp +	lp + +	lp +	..	lp + +	lp + +

lp = "lead-pipe" rigidity. cw = "cog-wheel" rigidity. + = rigidity just detectable. + + = moderate rigidity. + + + = rigidity requiring effort to produce passive movement.

Examination revealed flexed posture and festinant gait, mask-like facies, monotonous weak voice, and tremor of the left arm and of both legs, of moderate severity. Voluntary movements were slow, but muscular power was normal. Rigidity varied from day to day (a representative single finding is shown on line 1 in the accompanying table).

Inert tablets, 2 t.d.s., were administered in addition to the stramonium for a week, with no change in symptoms. Rigidity was of the same order as before (line 2 of table). Parpanit was then given in doses increasing from 0·0125 to 0·1 g. t.d.s. for three weeks, the stramonium being continued. Occasional giddiness was noted, coming on $^1/_4$–$^1/_2$ hr. after the tablets were taken and lasting up to $^1/_2$ hr. Tremor was unaffected, and festination was somewhat increased. A tired feeling in the feet was complained of. Rigidity was of the same order as before (line 3 of table). Stramonium was now reduced, and, after three weeks, omitted. The patient reported increased intermissions in his tremor, and increased ease in rising from a chair. The feet sometimes felt very heavy. Rigidity was again of the same order (line 4 of table). Without the patient's knowledge inactive control tablets of identical appearance were now substituted for the parpanit. Five days later the patient requested a visit, since he could not now attend the outpatient department because of a feeling of weakness and a difficulty in initiating movements. The previous night these had been so pronounced that he had urinated in bed, being unable to climb out. When seen, his face was a more rigid mask, his posture more flexed, and his movements slower. Tremor was notably greater, and rigidity was greater than had been found previously (line 5 of table). The patient was admitted to hospital.

He was observed for a week without any drugs being given. During this period there was no subjective or objective change, rigidity being as shown in line 6 of the table. Parpanit 0·025 g. four times daily, increasing to six times daily, was then given. On this régime, within twenty-four hours, walking became easier, posture showed a slight improvement, and the patient could get in and out of bed without difficulty. Tremor was not appreciably affected, and giddiness recurred. Rigidity decreased (line 7 of table). After parpanit had been given for eighteen days with no further change, tablets of hyoscine gr. $^1/_{200}$ of identical appearance were substituted, being given four times daily. The change was effected without the knowledge of the patient. The mouth became uncomfortably dry, and walking was reported as being somewhat easier, but otherwise no change was noted, rigidity being as shown in line 8 of the table. There was occasional giddiness.

After the patient had been five days on hyoscine, a return to the previous dose of parpanit was made, again without the patient's knowledge. Two days later he was told of the change, and was asked which drug he preferred. He could not decide. No change in his condition had been noted by the medical, nursing, or physiotherapy staffs in attendance; rigidity was as shown in line 9 of the table.

A further reversion to inert control tablets again precipitated a relapse, and the patient was started again on parpanit, with a return to his previous condition on this treatment. He was discharged from hospital, but on his return home he added hyoscine gr. $^1/_{200}$ t.d.s. to the parpanit 0·025 g. five times daily which he had been instructed to take. Next day he called in his neighbours to help him eject imaginary strangers from his room, and the following day he asked his servant, already alarmed at his clumsy manipulation of his cutlery at table, to eject another stranger from his favourite chair. The servant informed us, and on visiting the patient we confirmed his ataxia, and noted unaltered tremor and somewhat reduced rigidity (line 10 of table). Parpanit dosage was halved, and there were no further hallucinations. Giddiness however was troublesome, and after a further fortnight parpanit was omitted, stramonium being given in the original dosage. Giddiness disappeared. The general condition was about the same as it had been on parpanit, on hyoscine, and on stramonium initially. Rigidity a month later was as shown in line 11 of the table.

This patient, then, shows the day-to-day variations of rigidity on constant treatment characteristic of parkinsonism (compare lines 1 and 11 in the table). What were considered significant changes in rigidity were seen only on the omission of all drugs (lines 5 and 6) and on the administration of a combined parpanit and solanaceous dosage which proved toxic (line 10 of table). No objective evidence of difference in type or degree of therapeutic activity between parpanit and solanaceous drugs was shown by this patient, who could not even distinguish between the subjective effects. Either drug, however, could prevent the severe recrudescence of symptoms and signs which arose on the withdrawal of all drugs.

SUMMARY

The therapeutic activity of parpanit has been compared with that of solanaceous drugs in maximal tolerated doses in patients with parkinsonism.

Parpanit appears to have an activity comparable to that of solanaceous drugs.

The side-effects of parpanit differ in relative intensity from those produced by the solanaceous drugs, and

preference for one or other treatment may be determined by this, as much as by the small differences between the therapeutic effects.

We wish to thank Dr. E. Arnold Carmichael, of the National Hospital, Queen Square, for access to the cases treated and for invaluable advice and criticism; Dr. Kurt Hartmann, of Zurich, for advice; and Pharmaceutical Laboratories Geigy and Messrs. H. R. Napp Ltd. for supplying generous amounts of drugs. The investigation was undertaken on behalf of the Medical Research Council.

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FAMILIAL OUTBREAK OF STAPHYLOCOCCAL INFECTION OF BONE AND JOINT

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STAPHYLOCOCCAL infections in a community are sufficiently commonplace to pass without comment, but this familial outbreak is reported because of two unusual features. First, in a family of seven children there were, besides multiple examples of cutaneous infections, three cases of acute infection of bone or of joint. Two children developed acute suppurative arthritis and the third an acute osteomyelitis, and all three patients were in hospital at one time. Secondly, the strain of the causal staphylococcus was found to be the same in each of these major lesions, and the same organism was also recovered from other members of the same family.

The family of nine live under rather crowded conditions in an Oxfordshire village. The following is a summary of the family and their illnesses:

Leslie.—Aged 1 year, had impetigo in January, 1947, which cleared under local penicillin therapy. *Staphylococcus aureus* (phage type 29/31) was recovered from his nasal mucosa in April, 1947.

Christopher.—Aged 3 years, had no known lesion.

Ernest.—Aged 4 years, had impetigo in December, 1946, which cleared under local penicillin therapy. He had a boil over a medial malleolus in March, 1947, and acute septic arthritis of the right knee in April, 1947. *Staph. aureus* (phage type 29/31) was recovered from the knee-joint and blood-culture. A staphylococcus recovered from his nasal mucosa was not typable.

Brian.—Aged 7 years, had impetigo and boils on his heels in January, 1947, which cleared under local penicillin therapy. He had acute osteomyelitis of left pubis and right radius in April, 1947. *Staph. aureus* (phage type 29/31) was recovered from blood-culture.

Eric.—Aged 11 years, had no known lesion.

Mavis.—Aged 12 years, had suppurative arthritis of the right hip in February, 1947. Staphylococcus (phage type 29/31) was recovered from blood-culture and hip-joint, and phage type 47 from nasal mucosa and skin swabs.

Beryl.—Aged 14, had no known lesion, but *Staph. aureus* (phage type 29/31) was recovered from her nasal mucosa.

Mother.—Aged 34, had no known lesion. An untypable staphylococcus was recovered from skin swabs.

Father.—Aged 37, had a chronic discharging ear, but no staphylococci were recovered from the discharge.

TREATMENT AND RESULTS

The three cases of bone and joint involvement were all under the care of Dr. J. Trueta in the Wingfield-Morris Orthopædic Hospital, and were all treated by a similar method.

(1) Penicillin was administered by a continuous intramuscular drip delivering 400,000 units a day as the initial dose, decreasing to 200,000 units a day as progress became satisfactory. In addition, one of the children was given sulphadiazine 14 g. by mouth.

(2) The affected part was immobilised. Ernest, with acute septic arthritis of the knee, was placed in a posterior portion of a split plaster hip spica. Brian, with acute osteomyelitis of the pubis and radius, was placed on a Robert Jones double abduction frame, and a plaster back slab was applied to the affected upper limb. Mavis, with acute septic arthritis of the hip, was placed on a Robert Jones double abduction frame.

(3) When, on the child's admission to hospital, pus was considered to be already present, the lesion was explored with a view to removing it. In Ernest's case, diagnostic aspiration of the knee-joint having yielded pus, under general anæsthesia and a tourniquet an arthrotomy was performed, the pus and fibrin were removed, and the joint was closed. On three subsequent occasions he underwent aspiration of the joint and instillation of penicillin. In Mavis's case, 35 ml. of pus was removed by aspiration from the hip-joint and replaced with penicillin.

(4) When on admission, however, the physical signs and response to treatment suggested that the lesion had not yet progressed to suppuration, conservative measures were found to be adequate. Thus Brian, who had the double bone lesion, recovered completely with penicillin treatment alone.

The results were as follows. Nine months later Ernest's knee was cool and dry, with a full range of active movement, and Brian had full function in his arm and pelvic joints with no residual tenderness. Mavis's arthritis of the hip flared up again five weeks after admission. Eleven months later she has a good gait and function, but radiography suggests some reduction of the joint space in the affected hip, and there is half an inch of real shortening and restriction of full flexion of that joint.

DISCUSSION

In all cases a blood-culture was made before treatment was begun, and any pus recovered from the cases was sent for bacteriological examination. The organisms recovered from all these children were reported as *Staph. aureus*, and all were found to have the same cultural characteristics. A further attempt was made to establish their identity by bacteriophage typing[1] and they were all reported as phage type 29/31. About half of all pathogenic staphylococci cannot be phage typed at all, but of the remainder some fifty different strains can be differentiated by their reactions. The fact, therefore, that these five strains were all of the same phage type seems a reasonable indication that they had originated from a common source.

Despite careful investigation of the home environment no direct source of the organism could be traced, but the close living conditions were almost certainly responsible for the multiplicity and persistence of the infection.

Acute pyogenic infections of bone or joint, though by no means uncommon, are not an everyday occurrence, and the surprise which greeted the arrival in the ward of the second case from the same family grew almost to incredulity when the third child appeared. I have not been able to find any comparable published report.

SUMMARY

In a family of seven children described, there were, besides multiple examples of cutaneous infections, three cases of acute infection of bone or of joint. The infecting organism was a *Staph. aureus*, demonstrated by bacteriophage typing to be the same in all three cases and the same as that recovered from the nasal mucosæ of two of the remaining four children of the family.

I wish to thank Dr. J. Trueta and Mr. J. C. Scott for their kind permission to publish these cases; Dr. J. R. O'Brien for the bacteriological examinations; and Dr. V. D. Allison, of the Staphylococcal Reference Laboratory, Colindale, London, for bacteriophage typing all the organisms.

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CYSTICERCOSIS RESEMBLING MYOPATHY

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THE two cases reported here present features which emphasise MacArthur's (1937) dictum that the different types of cysticercosis described are but isolated phases in the natural history of the disease.

CASE-RECORDS

Case 1.—A Sikh sapper, aged 25, who had been 2½ years in the Army at Poona, and, before that, 7 years huntsman to the Maharaja of Patiala, was admitted to hospital on Feb. 11, 1944, with 4 months' history of weakness, 2½ months' history of bilateral anterior temporal headache of equal intensity day and night but not interfering with sleep nor accompanied by vomiting or any visual or auditory change, and 2 days' history of fever and rigors.

The patient moaned often, gave his history with difficulty, and was uncoöperative. He was right-handed. The only abnormalities found were a palpable spleen, an extensor plantar reflex on both sides, impairment of the sense of position of the right great toe, and a right grasp reflex. Retinæ normal. The psychiatrist reported as follows: "He knows that there is a change in his mind. He says that he understands well enough, and that he knows what he wants to say, but he cannot get it out. His difficulty in speaking is obvious—slow, distinct, delayed. There is ideational retardation, and a tendency in his conversation to wander away from the subject, but he endeavours to return to it."

White-cell count 6800 per c.mm. (polymorphs 70%, lymphocytes 25%, eosinophils 3%, monocytes 2%). Urine: no abnormality. Stools: no ova or cysts. Blood Wassermann reaction and Kahn test negative. On March 25, 1944, lumbar puncture produced clear cerebrospinal fluid (C.S.F.) under normal pressure, containing 1 cell per c.mm., protein 30 mg. per 100 ml., chlorides 750 mg., sugar 150 mg., and urea 38 mg. Encephalogram and radiogram of skull normal.

April 11, 1944: pyrexia and rigor; no malaria parasites found in blood. April 12: white-cell count 8000 per c.mm. (polymorphs 72%, lymphocytes 20%, eosinophils 5%, monocytes 3%). After two months in hospital, all abnormal signs having disappeared and headache having much improved, patient went home on leave. It was felt at that stage that the former provisional diagnosis of a left frontal tumour could not be substantiated.

Readmission.—On Nov. 16, 1944, he was admitted to the psychiatric department, with the diagnosis of anxiety state. He was then complaining of generalised headache and swelling of the body. His face looked bloated; there was a left mastitis, and a small submucous tumour in the upper lip. Other cysts were sought for without result. The only abnormality was a persistent extensor plantar reflex on the right side. Blood-pressure 110/78. White-cell count 6400 per c.mm. (polymorphs 73%, lymphocytes 20%, eosinophils 5%, monocytes 2%). Lumbar puncture produced clear C.S.F. under normal tension, with 6 lymphocytes per c.mm., protein 50 mg. per 100 ml., sugar 45 mg., Wassermann reaction negative. Urine normal; no ova or cysts in stools. Psychiatrist's report: "A cavalier attitude. Emotionally very superficial and apathetic. Conversation tends to be stilted. Appreciable tendency to echo symptoms. Orientation and memory fair. ? visual hallucinations, but very haphazard in answers. No emotional change in his speech or actions. ? commencing behaviour disorder. No ideational disorder, but there is some retardation."

The patient's symptoms much improved and he was discharged on Jan. 7, 1945.

Third Admission.—He was admitted for the third time on Feb. 5, 1945, complaining of weakness and increasing girth of his calf muscles and a constant bilateral frontal headache, worse on the right side. His intelligence was normal, his memory was good, and he gave a connected story, but he was boisterous, childish, and addicted to cracking jokes, and he laughed often without apparent cause. He was the life and soul of the ward. He was docile and he assisted the nurses in their work; he knew the use of objects and could use them, but it was difficult to make him grasp what was necessary. His appetite was now voracious. There was apparent hypertrophy of all muscles of the body, a veritable Hercules, the right calf was 15 in., and the left calf 15½ in. in circumference. (The admitting officer had provisionally diagnosed pseudohypertrophic muscular dystrophy.) There was slight œdema over small of back and over the shins for their whole length. Small subcutaneous nodules, about the size of a pea, were found over the left scapula, mid-sternum, and right forehead. The submucous tumour noticed in the upper lip in the previous November had disappeared. Fundi and visual fields normal. Bilateral extensor plantar reflex. White-cell count 6600 per c.mm. (polymorphs 68%, lymphocytes 18%, eosinophils 10%, monocytes 4%). No ova or cysts in stools.

Cysticercosis was provisionally diagnosed and confirmed by examination of an excised cyst.

C.S.F.: pressure normal (145 mm.), 20 lymphocytes per c.mm., protein 55 mg. per 100 ml., globulin (Nonne-Appelt) increased, Lange 4332000000, Wassermann reaction negative. Blood-cholesterol 150 mg. per 100 c.cm., blood-urea 32 mg. Radiography of a thigh and the skull showed no calcified foci or other abnormality; sella and clinoid processes normal. Treatment with *Filix mas* on two occasions had not produced any tapeworm in stools; and stools were negative for ova in repeated examinations over nearly a year.

Course of Illness.—Feb. 17, 1945: generalised epileptiform fit; no incontinence of urine or tongue-biting, but further details not available. No further fit occurred until 8 months later. March 24: many more cysts palpable, and many seen, in forehead, right cheek, tongue, right anterior cervical region, left suprascapular fossa, left antecubital fossa, anterior and lateral aspects of chest, left infrascapular area, and left lower quadrant of abdomen. All but one of the cysts above horizontal nipple line could be palpated. April 30: more cysts appeared about neck. May 15: C.S.F. contained 18 cells per c.mm. (lymphocytes 88%, polymorphs 12%), protein 70 mg. per 100 ml. Pandy test +, and Nonne-Appelt test negative. May 19: White-cell count 6200 per c.mm. (polymorphs 61%, lymphocytes 27%, eosinophils 9%, monocytes 3%). June 7: white-cell count 6400 per c.mm. (polymorphs 63%, lymphocytes 25%, eosinophils 10%, monocytes 2%). June 11: radiography of calves showed fine diffuse mottling throughout soft tissues but no calcification.

June 17, 1945: right plantar reflex still extensor; right abdominal reflexes less brisk than those on the left. Mental condition had gradually improved. Patient had some headache, relieved by recumbency and not worse on leaning forward. He still complained of tightness of calf muscles, whose circumference and overlying œdema were unchanged. He was quiet and had lost his boisterousness. He was more helpful than ever in the ward. Memory for recent and past events good. He was suffering from insomnia, sleeping only from 5 to 8 A.M. and sometimes during the day. Emotions apparently normal; no hallucinations or delusions. No defects in articulation; no aphasic signs, spoken and written speech being normal. No phenomena associated with aphasia, such as amimia, the inability to understand symbols or to recognise common objects; no apraxia. Cysts more numerous than before; two excised on May 18 were still viable.

Sept. 13: headache and tightness in calves and pectoral muscles only slight. Patient alert and intelligence normal. Girth of all muscles unchanged; slight œdema still present over shins. Liver and spleen just palpable. Blood-pressure 96/66. Cysts unchanged in number and consistency. Plantar reflex still extensor: right abdominal reflexes diminished.

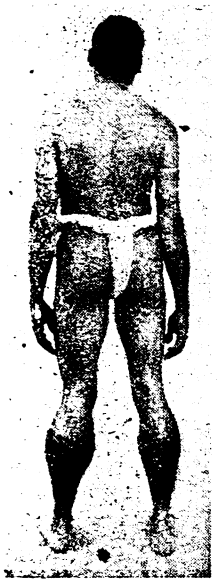
White-cell count 6400 per c.mm. (polymorphs 67%, lymphocytes 24%, eosinophils 7%, monocytes 2%). Urine normal. Erythrocyte-sedimentation rate 35 mm. in 1 hour. Patient was pitifully weak and tired easily.

In October and in November an epileptiform fit was witnessed. In December, his condition unchanged, the patient left on pension for his home in the Punjab.

Case 2.—A Hindu sweeper, aged 20, complained of a year's weakness and swelling of the legs. A year previously while on a long ride, he had been overcome with weakness and fever, and on his return had lain ten days prostrate with fever and limb pains. He then returned to work, but in the subsequent 12 months he noticed that his calves were increasing in size (see figure) and his legs becoming

weak. He also noticed, but did not date, an outcrop of small lumps over his whole body, even in his tongue. There was no history of any such disorder in his family or in his village. His work as a sweeper entailed dealing with refuse and excreta, and as in most Indian villages there were swine rooting about. He had eaten pork.

He was well built and muscular, with remarkable symmetrical hypertrophy of the calves (circumference of right calf 16½ in., left 18 in.). His body was studded with many hundreds of small nodules, chiefly in forehead, chin, neck, upper arms, shoulder girdle, pectorals, thighs, and lower legs. Two translucent nodules in mucosa of tongue. No abnormal signs in cranial nerves or in arms. Calf muscles very weak; and patella and achilles reflexes absent; plantar responses flexor. No sensory change.



Cysticercosis (case 2) showing enlarged calves.

Radiography of skull, muscles, and chest revealed no abnormality. A typical cysticercosal cyst was removed from the chest wall. Incision of calf showed whole substance of muscle superseded by a grape-like mass of many hundreds of cysts. Three were removed and again found to be cysticercosal cysts.

DISCUSSION

Even without the palpation of cysts, this type of cysticercosis may be readily distinguished from muscular dystrophy by several features. Muscular dystrophy develops much earlier in life, and the latissimus dorsi muscle and the lower part of the pectoralis major muscle are not involved in the pseudohypertrophy (Nattrass 1938). In trichiniasis there may be generalised muscular swelling, but the muscles are painful and more obviously œdematous, and the illness is acute.

In case 1 permission to incise the calves was refused, but case 2 is complementary in this respect.

In case 1 the œdema and swelling of the muscles were due probably to the simultaneous growth of many cysts. MacArthur (1937) recognises an occasional localised or generalised œdematous swelling of muscles as a premonitory symptom. In Priest's (1926) case nearly all the muscles were enlarged, especially those of the shoulder girdle, giving the appearance of a powerful man of the Sandow type of development, whereas in reality the muscular power was very feeble. Manson-Bahr (1945) notes that sometimes the localised intramuscular swellings resemble a muscular dystrophy.

The primary undiagnosed fever in each case may represent the period of invasion, comparable with the "sand-fly fever," "headache," "migraine," "P.U.O.," and "clinical malaria" suggested by Dixon and Hargreaves (1944) as prodromata.

Case 1 almost certainly had a cyst in the left frontal area, and the initial provisional diagnosis of frontal tumour, based on headache, changed personality, a right grasp reflex, and a right extensor plantar reflex, had not been far short of the mark. The later development of hilariousness, joking, and almost *Witzelsucht*, with a raised cell count and protein in the C.S.F., makes the similarity closer still.

The eosinophil response has been of little diagnostic value previously (MacArthur 1933–34, 1937, Dixon and Hargreaves 1944), but it was the sudden appearance of moderate eosinophilia coupled with the palpation of three cysts that led to the diagnosis in case 1. Eosinophilia was absent when only one cyst was palpable in November, 1944. The moderate eosinophilia which later developed remained unchanged for more than four months before returning to normal. MacArthur believes that an eosinophilia may develop when the cysts are breaking down and liberating their contents, but the onset of eosinophilia in case 1 coincided approximately with the appearance in the muscles of many viable cysts. Lipscomb's (1935) case showed an eosinophilia of 12%, associated with fever, three other counts in apyrexial periods being normal for eosinophils.

The present two cases also confirm the opinion of Dixon and Smithers (1934) that the palpable subcutaneous cyst may be alive.

Menon and Veliath (1940) found at necropsy that the most notable feature in the histology of the cyst wall in the brain was a plasma-cell reaction in the capsule, and suggested that a cytological study of the C.S.F. for the demonstration of these cells might prove of diagnostic importance. With this in view the fluid was re-examined under the most favourable conditions possible, but no plasma cells were seen after a long search.

At no time in case 1, even when there was well-marked eosinophilia in the blood, were eosinophils seen in the C.S.F., in contradistinction to the case reported by Applebaum and Wexberg (1944) where a normal blood-count was associated with an eosinophilia in the C.S.F.

On the assumption that a single invasion had taken place and that the patient was not harbouring *Tænia solium* and so reinfecting himself, it may be that the tissues were simultaneously involved and that different cysts matured or overcame local resistance at different times. This in no way invalidates the statement in the *British Medical Journal* (1941) that "within one month of the ingestion of ova the parasites begin to develop in favourable sites and that within four months the embryo is fully formed within its cyst." This will explain the appearance of a cyst or cysts in the frontal lobe in January, 1944; another cyst in the lip in November, 1944; three subcutaneous cysts and generalised myositis in February, 1945; and crops of subcutaneous cysts at different times since. This further is in accord with the statements of MacArthur (1937) and Brailsford (1941) that there is a latent period of some years between the ingestion of the ova and the appearance of the nodules. It is also in harmony with Brailsford's belief that auto-infestation is rare, and that most cases are due to ingestion of ova. Moreover, since the worm grows to a normal length of 6–10 ft., it must be almost impossible for proglottides to regurgitate through that length of bowel, and auto-infestation, if it does occur, must occur comparatively early.

Apart from their intrinsic value these cases are of topical interest in that, with the return of so many men from India and the Far East, the incidence of cysticercosis will probably increase in this country.

SUMMARY

Two cases of generalised cysticercosis are described, where the outstanding feature was generalised pseudo-hypertrophy of muscles.

One patient was observed for 18 months, during which he developed an eosinophilia which coincided with the appearance of many viable cysts in the muscles.

It is suggested that in this case generalised muscular infestation occurred on one occasion only, the cysts developing in favourable sites first and in less favourable sites later.

I am indebted to Brigadier J. D. S. Cameron, C.B.E., for his encouragement to publish this paper; Colonel F. M. Lipscomb, O.B.E., for his criticism; Major L. Krainer for his reports on the sections and the C.S.F.; Major A. D. Leigh,

for the notes and photograph of case 2; and the D.M.S., India Command, for permission to publish.

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RECURRENCE OF DUODENAL ULCER SIX MONTHS AFTER ADEQUATE VAGOTOMY

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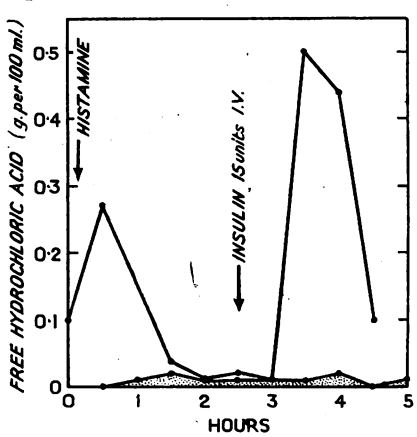
BILATERAL resection of the vagus nerves for peptic ulceration has been performed many times. All published reports list numerous early complications, but recurrence of the initial ulcer symptoms has been uncommon so far, and it has been stated on several occasions that such recurrences have been due to incomplete operation. In the present case recurrence followed an operation which, by the standard of the insulin test, was adequate.

A labourer, aged 40, was admitted to St. Thomas's Hospital in November, 1947, with ten years' history of upper abdominal pain and discomfort typical of chronic duodenal ulceration. He had been invalided out of the Army in 1944 with a duodenal ulcer. He had twice received inpatient treatment, once in the Army and once in St. Thomas's Hospital, but each time his symptoms had disappeared only to recur soon after discharge.

On examination he weighed 147 lb. and, apart from some tenderness to the right of the midline in the epigastrium, no relevant abnormality was noted. A barium meal showed "a normal stomach emptying via a tender and deformed duodenal cap with a basal ulcer—active duodenal ulceration." The gastric acidity after histamine followed by 15 units of insulin is shown in the accompanying figure.



Gastric acidity before and after vagal resection: upper curve, before resection (blood-sugar 52 mg. per 100 ml.); lower curve, twelve days after resection (blood-sugar 48 mg. per 100 ml.). The response six months later, when symptoms had recurred, was no free hydrochloric acid, combined hydrochloric acid 0·03 g. per 100 ml. as highest level after insulin 15 units I.V., and blood-sugar 34 mg. per 100 ml.

Operation.—On Nov. 7, 1947, a resection of the vagus nerves by the transhiatal route was performed, and an active ulcer was noted on the anterior wall of the first part of a scarred and deformed duodenum. There was stenosis.

The postoperative course was uneventful, and the patient was symptom-free and very satisfied on his discharge fourteen days later. A postoperative insulin test was performed before he left hospital and the vagus-nerve resection appeared by this standard to be adequate (see figure).

Recurrence.—The patient remained very satisfied for six months; he gained 6 lb. in weight and even recommended the operation to two of his friends. In May, 1948, however, he reported with a complete recurrence of his symptoms and was of the opinion that his ulcer had recurred because he felt just the same as he had before the operation. A barium meal now showed "a normal orthotonic stomach emptying via a tender and deformed duodenal cap—appearance of activity in a duodenal ulcer." In view of this report a third insulin test was performed. There was no free hydrochloric acid, and only a slight trace (0·5%) of combined acid was present. The blood-sugar level fell to 34 mg. per 100 ml.

COMMENT

By the standard of the insulin test this patient had an adequate resection of the vagal nerve-supply to his stomach, and there is no evidence of regeneration. In spite of this his ulcer symptoms have recurred after six months' complete postoperative freedom.

The barium meal, though not demonstrating a definite ulcer, now shows the appearance of activity in a tender duodenum, and the insulin test performed after the recurrence of symptoms produced no free hydrochloric acid and only a small amount of combined acid.

At St. Thomas's Hospital vagus-nerve resection has been performed on 37 patients for peptic ulcer. The early results in 5 patients with secondary ulceration following gastrectomy or gastro-enterostomy have been very good. In the other 32 patients with duodenal ulcer numerous initial complications have been noted, including temporary severe dysphagia (4 patients); persistent diarrhœa (2 patients); and eructations of foul gas (1 patient); but in no other patients have the ulcer symptoms recurred, though in 4 the operation was by the standard of the insulin test incomplete.

Preliminary Communication

MODE OF ACTION OF HETRAZAN IN FILARIASIS

'HETRAZAN' (1-diethylcarbamyl-4-methyl piperazine hydrochloride) is a new compound which has recently been introduced for the treatment of human filariasis due to *Wüchereria bancrofti*.[1] We report here an investigation carried out on cotton-rat filariasis to study its mode of action.

The cotton-rats used for this work were infected in our laboratory with *Litomosoides carinii*. In this infection the adult worms lie in the pleural cavities and the microfilariæ, which are sheathed and non-periodic, float in the circulating blood. When the infected cotton-rats are treated with hetrazan in doses of 25 mg. per 100 g. of body-weight intraperitoneally, the microfilariæ in the peripheral blood become much fewer.[2]

When 6 mg. per 100 g. is injected intravenously into cotton-rats, the diminution is extremely rapid, 80% of the microfilariæ disappearing in 1 min., and over 90% in 2 min. But even after fairly intensive treatment a few microfilariæ still persist in the circulating blood. Similarly, the pleural cavities still contain many motile and apparently healthy microfilariæ around the adult worms. It seems that these microfilariæ in the pleural cavities form a reservoir from which the supply in the blood is constantly replenished. Hetrazan has only a moderate effect on the adult worms, and our experience confirms the report of Hewitt et al.[2] that prolonged intensive treatment is needed to destroy them; even this sometimes does not kill all the worms.

Microfilariæ of *L. carinii* can be maintained alive for several days at 37°C in a suitable medium—e.g., serum plus Ringer's solution plus glucose. When hetrazan is added to the medium in concentrations up to 100 mg. per 100 ml., the microfilariæ remain actively motile for more than 48 hours, indicating that hetrazan does not

1. Santiago-Stevenson, D., Oliver-González, J., Hewitt, R. I. *J. Amer. med. Ass.* 1947, **135**, 708.
2. Hewitt, R. I., Kushner, S., Stewart, H., White, F., Wallace, W., Subbarow, Y. *J. Lab. clin. Med.* 1947, **32**, 1314.

exert a direct lethal action on them. Similarly, the microfilariæ remain actively motile for more than 48 hours at 37°C in the presence of serum from rats treated with large doses of hetrazan ½–2 hours before bleeding. So it seems that hetrazan is not converted in the body into some other substance which is actively microfilaricidal. This conclusion is further supported by the observation that intrapleural injection of hetrazan does not have any striking action on the microfilariæ in the pleural cavity.

Further studies were made by examining the distribution of microfilariæ in the different organs. Sections were made by the usual histological methods, and the number of microfilariæ per unit area was determined by counting under the microscope. In a typical experiment a piece of liver was removed under anæsthesia from a rat whose blood contained 470 microfilariæ per 10 c.mm.; the section of liver contained 44 microfilariæ per 100 sq. mm. Hetrazan (25 mg. per 100 g.) was then injected intraperitoneally, and an hour later the rat was killed. The number of microfilariæ in the peripheral blood had fallen to 85 per 10 c.mm., and the number in sections of the liver had risen to 193 per 100 sq. mm. In rats killed within an hour of treatment with hetrazan the microfilariæ lay between the liver cells, presumably in collapsed sinusoids. In rats killed 6 hours after treatment many of the microfilariæ were surrounded by phagocytes, which seemed to be attacking them. In most of the other tissues the microfilarial content was lower, relative to the initial blood-count, in treated rats than in untreated controls. The lungs form a special case in cotton-rat filariasis since they are the chief port of entry for the microfilariæ from the extravascular spaces (pleural cavities) into the circulation, and their content of microfilariæ is correspondingly high.

It is concluded from all the above-mentioned observations that hetrazan acts by modifying the microfilariæ in some way so that they are seized by the phagocytes of the reticulo-endothelial system and presumably destroyed; thus its action would resemble that of opsonins. Microfilariæ which are removed from contact with phagocytes—e.g., in vitro, or in the pleural cavity—are not speedily affected by hetrazan.

The chemical and/or physical reactions underlying this "opsonising" effect of hetrazan are unknown. Since the effect is produced so quickly, they must be rapid. Attempts were made to antagonise the action of hetrazan by previous administration to the cotton-rats of substances such as nicotinamide, nikethamide, &c., which have a somewhat similar chemical structure. In some cases the disappearance of microfilariæ caused by hetrazan was less complete than usual, suggesting slight antagonism; but convincing antagonism was not demonstrated. This work will be continued, but various circumstances will prevent its completion and full publication in the next twelve months.

SUMMARY

The action of hetrazan (1-diethylcarbamyl-4-methyl piperazine hydrochloride) on cotton-rat filariasis due to *Litomosoides carinii* has been studied.

This compound acts on the microfilariæ more than on the adult worms.

The compound and its metabolic products do not have a direct lethal action on the microfilariæ, but they seem to modify them in some way (opsonise them) so that they are seized by phagocytes of the tissues and removed from the circulation.

Grateful acknowledgments are due to Mr. D. Garlick and Mr. R. Jones for technical assistance.

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Reviews of Books

Living Anatomy

R. D. LOCKHART, M.D., CH.M., regius professor of anatomy, University of Aberdeen. London: Faber. 1948. Pp. 71. 12*s.* 6*d.*

THIS is an atlas of 149 photographs demonstrating surface contours and the actions of muscles in the living (particularly the male) subject. The purpose of these excellent illustrations is to promote enthusiasm for the examination of muscles in action in the living body. Several photographs are added at the end of the book, affording comparisons between virgin and lactating breasts, and the male and female forms; 6 photographs are also devoted to the surface anatomy of the eye, and 5 to the superficial veins of the forearm. Since at most anatomy schools a knowledge of muscle action is only a part of the knowledge of surface anatomy required of the medical student, this book may perhaps not have much appeal to him; the surface relations of the major arteries and nerves, for example, might be thought of greater importance for the future general practitioner. The atlas should, however, be of considerable use to occupational therapists, masseurs, and teachers of physical training, and also to artists. Since the late Arthur Thomson's *Handbook of Anatomy for Art Students*, now lamentably out of date (although still reprinted), little or no attempt has been made in this country to present surface anatomy to the artist by means of the photography of well-selected models. Here, in Professor Lockhart's atlas, is a series of photographs well suited to this purpose.

Blood Derivatives and Substitutes

C. S. WHITE, M.D., SC.D., formerly professor of surgery, George Washington University; J. J. WEINSTEIN, M.D., associate in surgery at the university. Baltimore: Williams and Wilkins Company. London: Baillière. 1947. Pp. 484. 41*s.*

THE authors say that their book is written "for the purpose of presenting a comprehensive study of plasma, plasma substitutes and by-products from a clinical standpoint," and "the chief emphasis has been placed on the practical and clinical aspects of the various subjects covered, so that it may serve as a reference and guide equally for the surgeon, the internist, pathologist, general practitioner, and student"—a fairly comprehensive field of readers. After a brief survey of the history of transfusion, a chapter describes the physiology and chemistry of the plasma, including a cursory discussion of the blood-groups. Between two-thirds and three-quarters of this chapter are taken up by the details of technical methods for counting blood-cells, the micro-Kjeldahl technique, and the like. The preparation of liquid citrated plasma (assisted by Dr. J. Reichel), the storage of plasma, the preparation, storage, and use of dried plasma (by Dr. E. L. Lozner), and the administration of plasma are then described. Chapters follow on plasma fractionation (by Dr. S. T. Gibson), by-products of plasma preparation, plasma substitutes, human blood-serum, blood preservation, the blood bank (by Dr. R. B. H. Gradwohl), shock, clinical results with human plasma, and reactions with plasma.

The book is of value for two reasons: it is largely an account of the personal experience of the authors in the Gallinger Municipal Hospital, Washington, where a blood-plasma bank has been maintained since 1937, and it presents a general review of work (mainly American) on blood derivatives and substitutes during the war years. It is, however, unequal in its treatment of the various subjects. It seems a pity that a book nominally concerned with blood substitutes does not contain a more complete account of the work done on them: they are dismissed in 28 pages, and no mention is made, for example, of 'Periston,' or the Swedish work on 'Dextran.' Homologous serum jaundice, which must be considered one of the risks of using plasma, is discussed in less than a page, reference being made to only four papers, none of them later than 1944, while the chapter on plasma fractionation and fractions concerns itself almost exclusively with albumin. On the other hand, space has been given to subjects which might well have

been omitted, or treated more briefly. The dilemma which seems to have faced the authors was how to write a book on blood derivatives and substitutes without covering, more or less completely, the whole field of transfusion.

Though not received for review until the middle of 1948, it was published in the United States in 1947. Hence the reader who expects to find references to work later than 1946 will be disappointed.

Education and Health

R. GAMLIN, M.A., M.B. Camb., chief assistant school medical officer, Liverpool. London: J. Nisbet. 1948. Pp. 372. 12*s.* 6*d.*

IT has long been recognised that teachers in training deserve good teaching in the bases of health. This book provides them with a sound complement to the standard works on school hygiene. There are excellent chapters on intelligent thinking, backwardness, scientific estimation of hearing, and immunity. Burt's finding that girls given periods of rest showed greater improvement in arithmetic than those given coaching is instructive; and so is an experiment from Georgia where 18 children picked as likely to fail in their examinations were given complete dental treatment—with the sequel that at the next examination, 17 passed in every subject. In the next edition Dr. Gamlin might mention Bowlby's work on the origin of delinquency, and bring the chapter on dietetics up to date with an account of rationing. The suggestion, recorded as "novel," that children should be taught by "participatory" rather than "rivalry" methods deserves to have as a footnote Dr. Johnson's remark: "By exciting emulation and comparisons of superiority, you lay the foundations of lasting mischief; you make brothers and sisters hate each other."

This book could usefully be read by candidates for the D.C.H.

Oxford Essays on Psychology

WILLIAM BROWN, D.M., D.SC., F.R.C.P., formerly Wilde reader in mental philosophy and director of the Institute of Experimental Psychology, University of Oxford. London: Heinemann Medical Books. 1948. Pp. 148. 10*s.* 6*d.*

IN these lectures to students Dr. William Brown seems to be restraining himself. From time to time, by a particular turn of phrase or concept, the fact that he has made a contribution to psychiatry becomes suddenly evident to the attentive reader. More often, unfortunately, the effect is of an academist presenting his subject to the young. Dr. Brown is too serious and brilliant a student of philosophy, psychology, and human nature to say things that should not be said; moreover, the impression he gives that he is not saying anything new is not entirely true. He is certainly presenting his own standpoint, and it bears the stamp of insight, erudition, and individuality. His views on Nazi Germany, the paranoid tendency, and mental relaxation all strike a note of truth, but the reader seeks in vain for a sense of the immediacy of that truth. Dr. Brown's truth is apposite; it is not insistent.

Le foie vasculaire: angiosclérose hépatique

MAURICE FAVRE, professeur à la Faculté de Médecine de Lyon. Paris: Masson, 1948. Pp. 99. Frs. 220.

THIS monograph is devoted to the morbid anatomy of a peculiar form of hepatic fibrosis of which 50 cases have been studied by the author. The condition is readily distinguishable from Laennec cirrhosis in that the fibrosis is confined to the portal tracts and does not invade the hepatic lobules. No single ætiological agent is held responsible, but the condition is regarded as a standard type of response of the portal connective tissue to injury mediated via the blood-vascular system. The evidence on which this theory is based is tenuous and leads to the remarkable conclusion that the portal fibrosis in congestive cardiac failure is not the result of the failure but is to be attributed to the same factors as are responsible for the cardiac lesions themselves. The anatomical account of the condition is presented in great detail with many clear illustrations. The tissue lesion is remarkable, and it is surprising that it has been overlooked for so long. This may be explained partly, however, by the absence in uncomplicated cases of any symptoms or signs referable to the liver itself. Despite its disappointing discussion on the ætiology, the book is an extremely interesting account of vascular disease of the liver, a subject hitherto much neglected.

Black's Medical Dictionary (19th ed. London: A. & C. Black. 1948. Pp. 995. 25*s.*).—The present edition of the late Dr. J. D. Comrie's justifiably popular work, first published in 1906, has been revised by Dr. W. A. R. Thomson. It is much more than a dictionary, in that it gives not only definitions but also varieties, causes, and treatments of diseases; discusses the disposal of the dead and of refuse and sewage; shows the reader how to change the sheets in a bed occupied by a patient; and contains much other practical information. There are over 500 illustrations in the text and 6 full-page plates, of which 4 are coloured.

Modern Treatment Year Book 1948 (London: The *Medical Press*. 1948. Pp. 338. 15*s.*).—Once again Sir Cecil Wakeley has cast his net wide in his laudable attempt to provide the general practitioner with a concise practical account of modern methods of treatment. The 38 articles in the present volume cover most of the comm ner (and some of the rarer) conditions encountered in practice. It is to be hoped perhaps that practitioners will not follow the advice, in the chapter on pernicious anæmia, not to worry about a complete hæmatological examination in a case of "suspected anæmia" until a few weeks' treatment with iron has failed to produce any improvement; and the chapter on asthma in children suffers from a lack of discrimination. On the whole, however, this is a book which the busy general practitioner will find of value.

Oxidation-Reduction Potentials in Bacteriology and Biochemistry (5th ed. London: Staples Press for the Hospitals and Medical Services Committee of the London County Council. 1948. Pp. 130. 4*s.* 6*d.*).—Since its first publication in 1931 this concise book by Mr. L. F. Hewitt, PH.D., has been in constant demand, as indeed it deserves to be, for it is a plain straightforward account which contrives not to sacrifice accuracy to simplicity. The war has been responsible for a delay of nearly twelve years since the 4th edition, and consequently much new work is summarised here; thus there is a short but useful chapter on polarography, and a brief description of potentiometric work with antibiotics and chemotherapeutic agents. Even in its paper cover, this book provides a welcome example of value for money.

Endocrine Therapy in General Practice (6th ed. Chicago: Year Book Publishers. London: H. K. Lewis. 1948. Pp. 264. 23*s.* 6*d.*).—Dr. E. L. Sevringhaus gives us a short, simple, readable book. Descriptions of the endocrine syndromes are brief, but on the whole clear and up to date, with mention of the latest diagnostic tests. The author is rather optimistic about the efficacy of pituitary extracts, especially the growth factors, and to a lesser degree the gonadotrophins. It is refreshing to find that he devotes a fifth of the book to the therapeutics of diabetes mellitus, which is as yet scarcely regarded as an endocrine problem in this country. He is conservative in his estimate of the rôle of thiouracil in the treatment of thyrotoxicosis, and perhaps a little old-fashioned in his recommendations about deep X-ray therapy to the thyroid gland. Under the heading of the mammary glands, no mention is made of the use of iodinated proteins to stimulate lactation. In a good chapter on the adrenals the complex interrelations of Cushing's syndrome and adrenocortical over-activity are rather summarily dismissed. Gynæcological endocrinology receives too little consideration: such recent therapeutic successes as the control of excessive bleeding with œstrogens and progesterone are not mentioned, and Dr. Sevringhaus deprecates the use of androgens, ignoring their spectacular anabolic effects in the treatment of Simmonds's disease and eunuchoidism. He lays due emphasis on dietary restrictions in the treatment of obesity and provides useful tables showing how to plan 1200-calorie diets. The photographs are excellent, and depict many typical examples of endocrine disorders. References to commercial therapeutic products are based on the American market and may therefore be confusing to the English reader, but the book is a well-balanced exposition of modern endocrine therapy.

THE LANCET

LONDON: SATURDAY, NOV. 6, 1948

Streptomycin in Pulmonary Tuberculosis

Two years ago the Medical Research Council appointed a committee, with Dr. GEOFFREY MARSHALL as chairman, to plan clinical trials of streptomycin in tuberculosis. The committee's first major report, on tuberculous meningitis,[1] confirmed the American experience that in most cases streptomycin would prolong life, that in many it would produce considerable improvement, and that in a few clinical cure was possible—a great advance over the previous hopelessness. The committee's second report,[2] on pulmonary tuberculosis, is also favourable within limits; but whereas the meningitis trials embraced every variety of case, save those in extremis, the pulmonary series was restricted to one category. This category—acute progressive bilateral tuberculosis of recent development in young adults—is usually unsuitable for collapse therapy, but, judging from animal experiments, it is one in which the antibiotic might be expected to have some action. Bearing in mind the shortage of supplies, it was fully justifiable to treat half the patients (S) with streptomycin plus bed-rest and the other half (C) in the ordinary way, by bed-rest alone. The method adopted for assigning patients to streptomycin and control groups, and the precautions taken against bias in the selection of patients, in treatment, and in the analysis of results, have brought this controlled study as near to a laboratory experiment as is practicable and make it unique in the dismal history of tuberculosis chemotherapeutic trials. The 55 S patients received 2 g. of streptomycin daily intramuscularly for four to six months (mostly for four). At the end of six months 4 S patients and 14 of the 52 controls had died, whereas 28 S patients and 4 C patients had considerably improved. Improvement was assessed on X-ray films—viewed independently by two radiologists and a clinician—clinical picture, and tendency to sputum-conversion. The radiological improvement consisted mainly of a clearing of "exudative" lesions; large cavities did not close. In general the results are definite and striking, the comparison with the control group permitting of a numerical assessment capable of statistical test. It is not so much a question of "cure"—none of the treated patients could be said to be clinically cured after six months' or even a year's observation, and not more than 15% had become bacteriologically negative—as of setting the patient on the road to recovery with the aid of his own resistance, or of making the lung condition suitable for collapse measures.

The main value of the trial was to give an unequivocal affirmative to the question: Is streptomycin any good in pulmonary tuberculosis? Since the subacute or acute type of disease investigated is uncommon, the direct application of the favourable conclusion is limited. But since the outstanding effect of the antibiotic was to check, or cause regression in, "infiltrative," "exudative," or "pneumonic" changes in the lung, benefit would be expected in other forms of pulmonary tuberculosis in which such lesions predominate. Thus we can now begin to define the types of pulmonary tuberculosis in which streptomycin can assist the conventional forms of treatment. Two things must be kept in mind. First, though toxicity did not necessitate the cessation of treatment in any case, vestibular damage was frequent (as has been the experience of others); and uncompensated vestibular damage may make a person incapable of driving a car or of walking steadily in the dark. So serious is the prognosis of the category investigated that nobody would hesitate to use the drug on account of this risk (the same is true in meningitis), but the position is different in the types of tuberculosis where the outlook is good without streptomycin. Secondly, the well-known tendency of streptomycin-resistant tubercle bacilli to emerge in the course of treatment was experienced in this trial and may account for the flattening out of the curve of improvement in many cases; improvement was nearly always greatest in the first month or so. Since no recent variation of the scheme of dosage or rhythm of administration of streptomycin has done more than postpone the appearance of drug-resistance, this dialectical phenomenon of nature is with us till further notice. This means that the physician must plan his long-term campaign of treatment on the assumption that probably only one effective course of streptomycin can be given; and if streptomycin is given during a phase of the disease in which good progress would be expected with ordinary management, a critical phase occurring later might find the weapon useless. We can roughly define the field of streptomycin therapy in pulmonary tuberculosis as cases in which the lesions requiring treatment are of recent development, progressive, and unlikely to benefit from ordinary treatment (e.g., bed-rest or collapse measures) alone. This definition would include rapidly advancing disease where pneumothorax is contra-indicated, and acute "spreads"—e.g., after artificial pneumothorax or thoracoplasty (no evidence has yet been produced to show the value of streptomycin in *preventing* spreads after ordinary thoracoplasties); lesions too "hot" for immediate pneumothorax treatment might be made suitable by a course of streptomycin. The definition will exclude old chronic fibroid, or fibrocaseous lesions, or long-standing cavitation—i.e., the commonest type of chronic phthisis. It will exclude terminal conditions, and also minimal early lesions with favourable prognosis. The main reason for excluding the "good chronic" and terminal conditions is that little benefit can be expected, and that a focus of dissemination of streptomycin-resistant bacilli will probably be created. On the other hand, the minimal or early lesion is very likely to benefit, at least temporarily; but this chance has to be balanced against the risks of streptomycin-resistance spoiling the patient's chances in a later recrudescence, and of the occurrence of permanent vestibular symptoms.

1. *Lancet*, 1948, i, 582.
2. *Brit. med. J.* Oct. 30, p. 769.

In the U.S.A. the new hopes for the tuberculous which were based on the first trials in that country, assisted by uncontrolled commercial enterprise and an ever-increasing supply (including eventually sales over the counters of drug stores even without prescription), led to a situation where almost every hospital patient with money, and about 50% of all inpatients, were given the drug at some time—whereas more cautious American physicians estimate that it is medically indicated in about 10%. Indeed it is said in the U.S.A. that if your railway dining-car attendant is unsteady and spills the soup down you, tuberculosis should be suspected! Here a more cautious attitude, together with the dollar shortage, has caused the Government to advance warily. During 1947 and 1948 enough streptomycin was imported for M.R.C. trials, later for official release to hospitals for meningeal or miliary tuberculosis, and still later for ulcerative tuberculosis of the larynx, trachea, and bronchi. Apart from the swelling trickle of individual purchases of American streptomycin, officially tolerated as a safety-valve but of rather doubtful morality, the antibiotic has been unobtainable in this country for pulmonary tuberculosis. Now that home-production has increased substantially, we may expect a wider, though still limited, release from Government internal purchases. Will the wave of indiscriminate use follow the American pattern, or can it be modified by self-discipline? Much will depend on the persuasive guidance given to the doctors entrusted with the drug. It may be wisest to confine distribution to tuberculosis officers and other specialists, with access to laboratory, X-ray, and preferably also hospital facilities; for lack of appreciation of the toxic effects of the drug, failure to test cultures for susceptibility at the beginning, during, and at the end of treatment, and failure to watch progress by X ray under standard conditions, may do harm to the patient besides wasting a valuable drug. No doubt there will be temptation to use streptomycin to treat an early lesion, so as to get the patient back to work quickly; to use it instead of collapse therapy or even bed-rest; and to treat hopeless cases to please relatives. But in the vast majority of cases the physician will have a free hand; he can weigh the advantages and disadvantages of streptomycin and act accordingly. Used with discrimination this remarkable new weapon can successfully supplement the proved methods of attack on a small though important sector of the tuberculosis front. The National Health Service can play its part by seeing that the drug is available at the right place and at the right time.

Epidemiology of Staphylococcal Infections

IF measures of preventing and controlling epidemics are to be logically and successfully applied, the sources and paths of spread of epidemic infection must be exactly known. Such knowledge can only be gained when the infecting organism can be accurately defined and identified. Epidemiological studies of the acute streptococcal infections during the last twenty years have given us a valuable body of new information and are an outstanding example of the incentive to research arising from the definition of serological types within a bacterial species. This has only become possible as a result of the differentiation of some thirty serological types of *Streptococcus pyogenes* by the late FREDERICK GRIFFITH. Another example is the phage typing of *Salmonella typhi*, described by CRAIGIE and YEN, which is now being used every day to trace the sources of epidemics and cases of typhoid. More recently the serological differentiation [1] of types among *Staphylococcus pyogenes* and the development of phage typing [2] of that organism have brought the epidemiology of staphylococcal infections into the limelight. An organism so ubiquitous as the staphylococcus does not readily lend itself to epidemiological studies, but the field has been somewhat narrowed by the recognition that coagulase-production will differentiate pathogenic or potentially pathogenic strains from the rest. Type differentiation by serological and phage methods has therefore been applied only to coagulase-positive strains.

The main application of typing to the study of staphylococcal epidemics has been in institutional outbreaks of pemphigus neonatorum. In one outbreak involving 22 infants, ELLIOTT and others [3] concluded that a nurse who was a nasal carrier of the epidemic strain had been the source and means of spread of infection. ALLISON and HOBBS [4] described three successive outbreaks of pemphigus neonatorum and staphylococcal conjunctivitis involving 132 infants in a large maternity unit, and demonstrated the widespread occurrence of the epidemic strains in the infants' environment; their evidence pointed to the nurses as the source of infection, with the nasal passages as its main reservoir and the hands as the probable vehicle of spread. By phage typing ROUNTREE [5] was able to prove cross-infection with pathogenic staphylococci in 18 out of 82 surgical wounds in a 24-bed surgical ward over a period of seventeen weeks. In a study of penicillin-resistant strains of staphylococci causing infections in a hospital unit, BARBER [6] showed that of 7 strains isolated from patients during a single month, 5 penicillin-resistant strains all belonged to the same phage and serological type while 2 penicillin-sensitive strains belonged to a different type, and she attributed the infections to spread from patient to patient. Similarly in outbreaks of staphylococcal food-poisoning due to enterotoxin, typing of strains of staphylococci isolated from the suspected foodstuff, from the vomit or stools of victims, and from the nose and hands or septic skin lesions of food-handlers has added to our knowledge of the sources and modes of infection. Among the many outbreaks successfully traced to their sources may be mentioned those described by WILLIAMS et al. [7] in which infection of ice-cream was traced to the nose and hands of one of the people who prepared it, and by ODDY and CLEGG,[8] who showed that an outbreak involving 167 miners who had eaten infected pressed-beef sandwiches was caused by staphylococci isolated from the nose and hands of the butcher who prepared the pressed beef.

1. Cowan, S. T. *J. Path. Bact.*, 1939, **48**, 169. Christie, R., Keogh, E. V. *Ibid*, 1940, **51**, 189. Hobbs, B. C. *J. Hyg., Camb.* 1948, **46**, 222.
2. Fisk, R. T. *J. infect. Dis.* 1942, **71**, 153, 161. Wilson, G. S., Atkinson, J. D. *Lancet*, 1945, **i**, 647.
3. Elliott, S. D., Gillespie, E. H., Holland, E. *Ibid*, 1941, **i**, 169.
4. Allison, V. D., Hobbs, B.C. *Brit. med. J.* 1947, **ii**, 1.
5. Rountree, P. M. *Med. J. Aust.* 1947, **i**, 427.
6. Barber, M. *Brit. med. J.* 1947, **ii**, 863.
7. Williams, G. C., Swift, S., Vollum, R. L., Wilson, G. S. *Mon. Bull. Min. Hlth E.P.H.L.S.* 1946, **5**, 17.
8. Oddy, J. G., Clegg, H. W. *Brit. med. J.* 1947, **i**, 442.

When it is realised that about half of all healthy adults harbour coagulase-positive staphylococci in their nose, and that upwards of 20% are hand carriers, there is no need to stress the importance of widening the field of investigation of the epidemiology of staphylococcal infections. The squamous epithelium of the nasal vestibule is considered to be the focus of colonisation [9] of *Staph. pyogenes*, and HOBBS and her colleagues [10] have shown that in sycosis barbæ the infecting type of staphylococcus is regularly present in the nose, where it will provide an autogenous source of reinfection unless the nasal passages are treated at the same time as the lesions. On p. 727 HARRISON records a familial outbreak of staphylococcal infections in which 2 of a family of 7 children developed acute suppurative arthritis, and a third acute osteomyelitis, all within three months. The same phage type of staphylococcus was isolated from the lesions of all 3, and also from the nose of a brother recently recovered from impetigo and from the nose of a sister with no history of acute infection. This is a striking example of the epidemic potentialities of staphylococcal infections in the home, and it makes one wonder whether multiple staphylococcal infections of the skin in a household may not also be due to the spread of a single strain of staphylococcus from person to person. In his daily round the doctor often sees a case of impetigo associated with an earlier or subsequent case of skin infection in one or more members of the family; this may take the form of another case of impetigo, or of boils, styes, acneform pustules, septic fingers, or even sycosis barbæ. The infectivity and contagious nature of staphylococcal infections of the skin are probably not generally realised, and the towel—in particular the roller towel—and other articles of toilet used in common by all the household probably play an important part in their spread.

There is a fruitful field for further investigation into the epidemiology of staphylococcal infections both in the home and in industrial occupations. Some occupations appear to be associated with an unusual prevalence of boils and infected hands; a recent statistical study [11] of the incidence of infections of the skin among workers in three factories has shown a great increase in incidence over four years, the increase being greater in women than in men. It would be interesting to know whether this prevalence is epidemiological or is mainly attributable to contact of the skin with industrial oils, chemical solvents, &c., which lower the natural resistance of the skin to infection with the patient's own skin organisms. In the home only the doctor can assess the part of the staphylococcus in family infections. If it appears to be playing a significant part, then typing of staphylococci isolated from the patient's lesion, nose, and skin, and from the nose and skin of other members of the household, might yield valuable confirmatory information. Meanwhile, it should be recognised that a household in which there is a case of impetigo, boils, or a septic finger should take precautions as least as careful as those recommended in a case of scabies.

9. Moss, M., Squire, J. R., Topley, E. *Lancet*, 1948, i, 320.
10. Hobbs, B. C., Carruthers, H. L., Gough, J. *Ibid*, 1947, ii, 572.
11. Whitwell, G. P. B., Sutherland, I. *Brit. J. industr. Med.* 1948, 5, 88.

The New Zealand Experiment

TEN years after the passing of the Social Security Act, the government and the profession in New Zealand agree that public medical care under the Act requires review, or (as a correspondent on p. 743 puts it) needs a spring-clean. The report lately produced by a joint committee representing the department of health and the British Medical Association reveals shortcomings and suggests some remedies.

Pride of place is given to the general-practitioner service, on which the emphasis has always been placed in developing the system. One of the interesting features of this service is that although the Act allows payment by capitation fee or by salary, nearly all practitioners outside Maori settlements and other under-privileged areas have chosen to be paid on an item-of-service basis, the fee for each item being claimed from the government either by the doctor himself (direct payment) or by the patient (refund system). Each item of service, whether rendered at the doctor's surgery, in the patient's home, or at a private hospital, commands the same fee (7*s*. 6*d*.); but most practitioners have been in the habit of charging additional fees to patients who seemed able to afford them. Obviously, when it can draw on an unlimited State fund this system is open to abuse: the report speaks of "cases where general practitioners were receiving annual sums much in excess of what could be regarded as reasonable and proper remuneration," and it says that "the present invariable practice of obtaining a certificate from the patient, parent, or guardian as to the dates, &c., of attendance has only limited value." Yet, in spite of these shortcomings, the fee-for-service has become so much a part of the New Zealand way of life that the committee does not seriously contemplate any alternative. Of payment by capitation it remarks that "under the existing circumstances in this country a renewed attempt to introduce such a system generally could not succeed," and that capitation "tends to a decline in the high standard of practice." Oddly enough, the few doctors who accept patients under the capitation scheme mostly operate the fee-for-service too. In the absence of safeguards (and none are mentioned) this seems to offer the unscrupulous the best of both worlds—the good lives contributing their regular capitation income, the bad ones the fees for service. The committee understandably recommends that practitioners should not be allowed to practise under both systems at the same time, but should be obliged to choose between them.

Having dismissed salaries and capitation, the committee considers how fee-for-service remuneration can be reformed and simplified. It proposes to abolish the refund system, and require the practitioner to make all the claims for his payment. But to salve the conscience of those who object to being paid directly by the State—lest this destroy their professional freedom and the doctor-patient relationship—a form of words has been devised to make it clear that the doctor is claiming the moneys not on his own behalf but "on behalf of the patients listed in column (3)." So into column 3 of the claim form must go the names of all the patients (or their legal

guardians if they are minors); in column 2 a code letter or letters indicates the service given; column 6 shows the money claimed from the State; while column 5 gives the total amount the doctor intends shall be paid for his services by State and patient combined. To regularise the recovery of fees from the patient the report asks that "every general medical practitioner should have the right to charge and recover a fee additional to that payable from the Fund wherever circumstances, in his opinion, warranted it."

Since the patient is no longer to be asked to sign the claim form, it is recognised that some alternative method of checking the claims made by practitioners is necessary.

> "It is accordingly suggested that the Department devise a system of verification of service as an alternative to the patients' certification, as, for example, postal inquiry from a proportion of the patients of each practitioner. In addition, it is recommended that all practitioners be required to maintain adequate medical records of their patients in support of all claims made, and that these records and daily diary sheets be subject to inspection by medical practitioners duly appointed for that purpose."

But it looks as though the committee doubts whether these methods of sample and scrutiny will be really effective; for later we are told that it

> "discussed the practicability of prescribing limits to the numbers of patients to be seen daily or, alternatively, of prescribing a limit to the amount payable from the Fund to an individual practitioner. It considered that, in view of the wide variation in local conditions, types of patients, and the capacity of practitioners no fixed or arbitrary limits could be prescribed. Nevertheless, there are substantial grounds for believing that an average of, say, thirty attendances [items of service] daily is the maximum number practicable for an efficient and conscientious practitioner, and the Committee considers that Local Investigating Committees [consisting of local doctors with a medical officer of the health department] should be vigilant to investigate cases which habitually exceed the figure mentioned."

As it appears from the other side of the world, this system which our colleagues in New Zealand are arranging for themselves is by no means attractive. If the Minister of Health here were to propose such a combination of snooping and sanctions he would be felt to have exceeded all reasonable bounds. Moreover, the object of the new plan is to support a method of payment which New Zealanders themselves admit does not encourage good medicine. In his presidential address this year Mr. J. A. JENKINS, president of the N.Z. branch of the B.M.A., said: "It is the quality of the medical service that should count, not the quantity. The present system pays premiums for quantity and penalises care, thought, and time spent. This is basically wrong." But even he could see no alternative to the fee-for-service —"the salaried service, the capitation system, in fact anything that departs from what is ingrained in us is bound to fail"—and he based his hopes on placing administration in the hands of a permanent, predominantly medical, corporate body, and on the levying of additional fees for every conceivable item the patient needs. He believed that "if the government . . . placed a small financial barrier between patient and doctor, patient and chemist, and patient and hospital, many of the present abuses would cease at once." Would they? We wonder. But then we have never had quite the same dislike (in principle) of capitation fees, nor the same faith in the fee-for-service. In the next year or two this country will have to find whether a capitation system embracing the whole population is compatible with high standards of practice. Meanwhile, if the New Zealand government accept their committee's recommendations, New Zealand will be ascertaining whether the admittedly unsatisfactory trends of her practitioner service can be reversed by altering the method of claiming fees.

Annotations

THE ACT IN ACTION

UNDER this title we propose to publish a short series of occasional articles on the working of the National Health Service during its first few months. They will describe some of the difficulties encountered and some of the defects observed. Signs of strain can be instructive even when they appear in the less vital parts of an organism, and we shall begin by examining one or two of the most conspicuous. The opening article deals with the supply of spectacles.

HUMIDITY AND INFLUENZA VIRUS

IT is now recognised that the most satisfactory means of preserving most viruses is to dry them in vacuo from the frozen state. By this method the virus is rapidly desiccated past the presumed critical degree of moisture at which its susceptibility to external influences is greatest. Similarly, it has been shown that smallpox virus, in infected crusts or in vesicle fluid dried on glass slides at room temperature (22°C),[1] and foot-and-mouth virus in cattle saliva, will survive and remain infective for periods of several weeks to a year or more (smallpox crusts) under natural conditions. According to Sir Leonard Rogers,[2] these findings support his oft-repeated argument that the spread and prevalence of smallpox is least at periods of high relative humidity of the atmosphere.

In exploring the epidemiology of influenza, a number of attempts have been made to estimate the survival of the virus under more or less natural conditions. For example, Edward[3] showed that when a 5% suspension of infected mouse lung in normal human saliva was allowed to dry on glass slides at room temperature, only 1% of the virus could be recovered when drying was complete. He also found that when pieces of sheet were impregnated with a given quantity of mouse-lung virus, and the virus was allowed to dry under different conditions, much less virus was recovered when drying was slow because the humidity of the atmosphere was high. Loosli et al.,[4] in Chicago, demonstrated that influenza virus dispersed into the air is killed much more swiftly in humid than in dry air, and it has now been shown[5] that when pneumococci type I, suspended in broth, saliva, or 0·5% saliva, are sprayed into the atmosphere, their mortality is very high at relative humidities in the vicinity of 50%. (At humidities above or below this value they survived for long periods.)

Though a similar type of pattern was obtained with staphylococci, the results were not nearly so striking, which makes it probable that the effect of humidity depends on the structure of the micro-organism. From

1. Downie, A. W., Dumbell, K. R. *Lancet*, 1947, i, 550.
2. Rogers, L. *J. Hyg., Camb.* 1948, **46**, 19.
3. Edward, D. G. *Lancet*, 1941, ii, 664.
4. Loosli, C. G., Lemon, H. M., Robertson, C. H., Appel, E. *Proc. Soc. exp. Biol. Med.* 1943, **63**, 205.
5. Dunklin, E. W., Puck, T. T. *J. exp. Med.* 1948, **87**, 87.

what is known of the tubercle bacillus, it is evident that the conditions necessary for its inactivation will differ from those required for the pneumococcus. Certain experiments indicated that the deleterious effect of 50% humidity on the pneumococcus might be due to increased salt concentration, and similar results have been obtained with influenza virus suspended in a broth containing 5 g. of sodium chloride per litre.[6] (Normal human saliva has only about a tenth of the amount of salt that physiological saline contains.) These American experiments, however, did not include tests with influenza virus suspended in human saliva with and without dialysis, which would give crucial information about the rôle of salt. Edward has suggested that the inactivation of the virus in saliva during drying might be caused by the lysozyme-like agent in the saliva, which might well have a maximum effect at a relative humidity of 50%.

It is obvious that many factors besides humidity play a part in producing an epidemic. But it might be useful to ascertain whether maintenance of the relative humidity at a high level will control the spread of influenza in a closed community.

TRACE ELEMENT PIONEERS

In 1937, when Bennetts and Chapman [7] established that copper deficiency was the cause of enzootic ataxia in Western Australia, not much was known about trace elements in nutrition. The subsequent advances in this field must largely be ascribed to the stimulus applied by the successes of these and other pioneers.

In 1928, after a long series of studies, Hart and his colleagues [8] at the University of Wisconsin had shown that copper as well as iron was essential for the formation of hæmoglobin in the rat, but it was not until 1933 that a disease of economic importance was shown to be due to copper deficiency. This was "liksucht," a wasting disease of cattle in Holland which Sjollema [9] cured with copper sulphate. The enzootic ataxia on which Bennetts and his associates did their classic work is a demyelinating disease of the unborn or unweaned lamb, producing a typical degeneration in the spinal cord which is responsible for the ataxia, usually affecting the hind limbs only. Nutritional disturbances as a rule precede and almost invariably accompany the ataxia. From 1932 onwards, on chemical, clinical, and pathological data, Bennetts [10] built up a working hypothesis that the disease was due to lead poisoning. In his first trials, ammonium chloride, as a "deleading" agent, was fed to gestating ewes and gave very satisfactory results. In a later season the results were inconsistent and it was found that a very pure sample of ammonium chloride did not prevent the ataxia. A spectrographic study of the effective and ineffective samples of ammonium chloride and of livers from affected and normal lambs disposed of the lead hypothesis and suggested that copper deficiency was a more probable cause of the disease. In the next lambing season the administration of copper to the gestating ewe was found to prevent ataxia in the lamb. This was a discovery of major importance to the Australian sheep industry, and, coupled with his prevention of "falling disease" in cattle with copper supplements,[11] has earned for Dr. Bennetts and the Western Australian department of agriculture world-wide appreciation.

Another important early success in trace-element therapeutics, also achieved in Australia, was that of E. J. Underwood and J. F. Filmer. They were investigating a fatal disease of sheep and cattle in localised areas of Western Australia, for which Filmer [12] suggested the name "enzootic marasmus," the principal symptoms being progressive emaciation and anæmia. The disease had been prevented by the administration of limonite ($Fe_2O_3H_2O$) and was thought to be due to iron deficiency. Analysis of the pastures and of organs of affected animals, and finally the prevention of the disease with an almost iron-free extract of limonite, showed that this hypothesis was wrong.[13] By a series of fractionations of this extract Filmer and Underwood [14] finally traced the curative property to cobalt, which invariably checked both the wasting and the anæmia. It is interesting to note that Lester Smith and the American group working on the anti-pernicious-anæmia factor of liver agree that the factor contains cobalt.[15]

DETAILS ABOUT ISOTOPE SUPPLIES

In their statement published in our issue of Sept. 18 (p. 469) the Medical Research Council gave details of the conditions under which radioactive isotopes can now be obtained for research and therapy. Radioactive isotopes require very careful handling by special techniques not normally part of laboratory methods, and with these difficulties in mind the M.R.C. pointed out that stable isotopes of some useful elements were available for tracer research which could be used without any of the protective measures needed for radioactive isotopes. But the estimation of stable isotopes has to be done with a mass spectrometer, a complicated instrument costing about £2000 and calling for more technical knowledge than most medical workers possess.

The Ministry of Supply have now circulated some further information about the obtainable radioactive isotopes and also about stable isotopes and their estimation. At present the Atomic Energy Research Establishment at Harwell is working with a low-energy pile whose usefulness, so far as medically interesting isotopes are concerned, is limited. A larger pile is being constructed, and when in operation (no likely date is mentioned) it will produce isotopes of specifications similar to those now provided by the U.S. Atomic Energy Commission. The low-energy pile has been used to produce radiosodium(Na^{24}), radiopotassium(K^{42}), and radiobromine (Br^{82}). These isotopes are useful in biological research, and since they have half-lives of only a few hours they cannot be imported. The low-energy pile has also produced some radiophosphorus(P^{32}) and radio-iodine (I^{131}) pure enough for use in therapy, but the amounts are too small to be of practical value. When the large pile is operating at full power it will provide these and other isotopes in quantities sufficient to meet all expected demands for scientific and industrial, as well as medical, uses. In the meantime isotopes are being imported, mainly from the U.S.A., and supplies are necessarily limited to the longer-lived isotopes like radio-iron (Fe^{59}, half-life 47 days) and radiophosphorus (half-life 14 days).

The stable isotopes now obtainable are those of nitrogen(N^{15}), carbon(C^{13}), and oxygen(O^{18}). The nitrogen and carbon isotopes have been imported from America, but both will soon be manufactured in this country. The Genatosan Co. at Loughborough is making an enriched N^{15} on a commercial scale. At Harwell a plant for the production of C^{13} is nearing completion, and one for the production of O^{18} will be ready in about three months' time. These stable isotopes are therefore likely to be fairly plentiful before long. With regard to estimation, there are two mass spectrometers at the

6. Lester, W. *Ibid*, 1948, **88**, 361.
7. Bennetts, H. W., Chapman, F. E. *Aust. vet. J.* 1937, **13**, 138.
8. Hart, E. B., Steenbock, H., Waddell, J., Elvehjem, E. A. *J. biol. Chem.* 1928, **77**, 797.
9. Sjollema, B. *Biochem. Z.* 1933, **267**, 151.
10. Bennetts, H. W. *Aust. vet. J.* 1932, **8**, 137 and 183; *Ibid*, 1933, **9**, 95; *J. Coun. sci. industr. Res. Aust.* 1935, **8**, 61.
11. Bennetts, H. W., Harley, R., Evans, S. T. *Aust. vet. J.* 1942, **18**, 50.
12. Filmer, J. F. *Ibid*, 1933, **9**, 163.
13. Filmer, J. F., Underwood, E. J. *Ibid*, 1934, **10**, 83; *Ibid*, 1935, **11**, 84.
14. Filmer, J. F., Underwood, E. J. *Ibid*, 1937, **13**, 57.
15. Lester Smith, E. *Nature, Lond.* 1948, **162**, 144.

National Institute for Medical Research, Hampstead, N.W.3, which can be used for assaying samples for research-workers, and the institute will advise on the preparation of samples of blood and other biological materials. Gas samples can be dealt with at Harwell, but so far only to a limited extent.

Some useful addresses are given in the Ministry of Supply's circular. Inquiries about radioactive and stable isotopes should be addressed to the Isotope Information Office, Atomic Energy Research Establishment, Harwell, near Didcot, Berks. Departments and individual research-workers who propose to use either form of isotope for medical research should apply to the secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1. Short-lived isotopes will be distributed direct from Harwell. Isotopes that have to be processed before issue will be sent out from the Radiochemical Centre at Amersham, Bucks.

THE LAW AND INSEMINATION

IN the opinion of Mr. Justice Vaisey and Mr. H. U. Willink, K.C., given in the report of the Archbishop of Canterbury's commission,[1] artificial insemination with donor's semen (A.I.D.) constitutes adultery; and this opinion was shared by eleven out of the twelve members of the commission. Mr. Cecil Binney, addressing the Eugenics Society on Oct. 26, took a different view. The law defines adultery, he said, as any sexual act between any two persons of opposite sexes, one of whom is married. In short, some degree of concupiscence must be present; whereas with A.I.D. concupiscence is wholly absent. He thinks it unlikely in any case that suits dealing with artificial insemination will often appear in the courts. Where the husband's semen is used (A.I.H.) no legal complications arise; and he does not agree that such cases might be affected by the Law of Nullity, since a nullity suit can be successful even where the wife has had a child by the husband. Donor insemination, on the other hand, might conceivably give rise to complications under the Criminal Law, the Law of Divorce, and the Laws of Inheritance. The donor has no reason to fear that his behaviour is illegal, since any man can inseminate the wife of another without committing a legal crime; and though the majority of the Archbishop's commission wished A.I.D. to be made a criminal offence, Mr. Binney thinks it is unlikely that this will be done, since it would encourage perjury and blackmail. He contended that no special provision is needed for the case of the wife who has herself inseminated without her husband's knowledge, since a husband could almost certainly divorce her, if he wished, on grounds of cruelty; while the wicked doctor who inseminates a woman against her will, or the adventuress who has herself inseminated so as to make unjust claims on some man, are figures of fiction rather than ordinary life.

Nevertheless, some possible complications do need study. The child is not the husband's, and strictly speaking the mother ought to register it as illegitimate. In practice, however, Mr. Binney pointed out, a married man can accept as his own any child of his wife's, and can make what provision he likes for it in his will. Troubles are more likely to arise when there are entailed properties or funds in trust. Mr. Binney would meet this objection, given his way, by the abolition of entail and settled funds; but he sees no hope of such a solution.

The danger of incest as a result of two A.I.D. children growing up and marrying he considers small—probably not greater than the danger, always present, of any two unknowingly related people marrying. In village communities, and in small communities of English people living abroad, this is always a possibility, though not one which gives rise to much anxiety. There remains the suggestion that civil proceedings might be taken against the doctor; but this could hardly happen where husband and wife had authorised the operation. If the husband had not been informed, he might, on the curious legal ground that the doctor had interfered with his wife's services to him, take action. This would be akin to a father getting damages when his daughter is seduced. A claim against the doctor could, of course, be made if the operation was unskilfully or negligently done, or if the child turned out to have some hereditary disorder or abnormality; or an awkward situation might arise if a doctor who disbelieved in racial prejudice provided an insular type of woman with a child of a noticeably different race.

Mr. Binney evidently felt that though the subject makes a fascinating playground for lawyers, the practice of artificial insemination—even of A.I.D.—on the existing minute scale is likely to give very little trouble to anyone.

1. Artificial Human Insemination. London, 1948. See *Lancet*, Aug. 21, p. 298, and Sept. 18, p. 463.

THE DONORA DISASTER

DURING the last five days of October a large part of western Pennsylvania was covered by a fog blanket, and at the steel-making town of Donora 18 elderly patients with asthma or with heart disease died in one day, and about 200 persons came under treatment for the alleged effects of "smog" (smoke and fog). The town hospital became overcrowded, and an emergency hospital was set up. A zinc-smelting plant was closed.[1]

The connexion of fog with an increased mortality from respiratory diseases was demonstrated on a statistical basis by Russell, who pointed out that fog alone has apparently no effect; it has to be associated with cold weather to make it lethal.[2] He even claimed that "knowing the temperature and the amount of fog, it is possible to predict the mortality of the succeeding week, but only with a marginal error of roughly 30%."[3] The question how much of this increased mortality is due to fog, and how much to cold has been discussed by Woods.[4] At Donora, however, it is plain that other factors have been at work. We know that fog produced by an earth-bound layer of cold air prevents factory fumes from rising into the upper air, and it was in this sort of weather, at the beginning of December, 1930, that 63 people died of respiratory disease, within a period of little more than twenty-four hours, in the Meuse valley, in an area 25 by 1–2 km., south of Liége.[5] The deaths there were attributed to atmospheric pollution with sulphur dioxide and hydrofluoric acid by zinc and superphosphate factories. So extensive had been this pollution that the soil had been rendered useless for agriculture and spoilt for grazing, and breeders of cattle had obtained damages against the manufacturers. The fact that electric-light bulbs lost their transparency quicker there than elsewhere points to fluorine as the guilty agent. Of the 27 factories 15 used fluorine-containing substances.[6]

The dangers of fluorine have been clearly described,[7] and closure of the zinc-smelting plant at Donora was amply justified by the known facts.

IT was announced at Stockholm on Oct. 28 that the Nobel prize for medicine is to be awarded to Dr. PAUL MOELLER of Basle for "his discovery of the effects as an insecticide of D.D.T."

1. *Times*, Nov. 1, 1948.
2. Russell, W. T. *Lancet*, 1924, ii, 335.
3. Russell, W. T. *Ibid*, 1926, ii, 1128.
4. Woods, H. M. *Ibid*, 1928, i, 539.
5. *Lancet*, 1930, ii, 1305; *Ibid*, 1931, i, 303.
6. *Ibid*, 1946, ii, 835.
7. Kemp, F. H., Murray, M. M., Wilson, D. C. *Ibid*, 1942, ii, 93. Murray, M. M., Wilson, D. C. *Ibid*, 1946, ii, 821.

The Act in Action

1. SPECTACLES

BEFORE the start of the new National Health Service, the output of spectacles from all sources was 4–5 million pairs a year. Representatives of the ophthalmic industry place the present demand at over 650,000 pairs a month (7,800,000 a year). The demand is growing, and the delay in fulfilling orders—which is now from four to eight or more weeks—is also growing, according to the industry, by one week for each week that passes.

The eventual aim is to base all ophthalmic services on hospitals. Meanwhile patients who are not already attending hospital are dealt with under the Supplementary Ophthalmic Services. The original estimate of the cost of these services in England and Wales from July 5 to the end of next March was £2,080,000: the actual amount spent in the 12½ weeks up to Sept. 30 was £981,951. Before having his eyes tested, the applicant must obtain from his own doctor a recommendation for examination, written on a form which he takes either to an "ophthalmic medical practitioner" (who draws £1 11*s.* 6*d.* for testing the vision), or to an ophthalmic optician (who receives 15*s.* 6*d.* for this service). If glasses are necessary, the prescription is sent to the local ophthalmic services committee, which, if it approves, returns the prescription to the patient, who then takes it to an ophthalmic or dispensing optician (to whom a dispensing fee of £1 5*s.* is paid). With the present urgent demand fees are mounting up; and the general practitioner is ruefully comparing the capitation fee he gets for a year's service to a patient with the sum —about double—received by the ophthalmic practitioner for a single test of vision. In the school ophthalmic service, at present administered under the supplementary services, the amount earned on capitation fees has certainly sometimes exceeded reasonable need. Hence the school service is to be placed under the hospital service by the end of next March; and until then payment is to be made on a sessional basis.

The approximate numbers operating the service in England and Wales are as follows [1]: ophthalmic medical practitioners 1126, ophthalmic opticians 5821, and dispensing opticians 620. The patient who applies for examination may find that he has to wait from a week up to a month or longer to have his vision tested by an ophthalmic medical practitioner or optician. To this delay must be added the time taken by the executive council's committee to approve the prescription. This was at first as long as a month in some districts, but it has been reduced, except in one area, to a few days; and it is eliminated altogether by friendly opticians who proceed with the order on the assumption that approval will be given. Thus the time between the date of fixing an appointment and the issue of spectacles is at best about 4 weeks and at worst some 3 months.

PRESENT AND FUTURE

It is easy to understand how the present acute demand originates. First of all, there are those who, though needing spectacles, have never before had them made; some idea of their number is given by the popularity of ready-made spectacles before the war, when a single group of chain stores is reputed to have sold 2 million pairs a year. A second group is composed of people who, having a pair of spectacles, seek a re-test; according to one estimate these form 80% of all applicants. Indeed, at least one ophthalmologist, having entered the service and doubled the time given to refractions, finds that he can see only patients who attended him before July 5. In most cases the claim is reasonable because vision was last tested some years ago. Sometimes less reasonable are the claims of the men and women, from all walks of life, who, ignoring the fact that their actual contribution is never more than 10*d.* a week, announce an intention "to get something back for the £12 a year I pay for medical service." This group seeks a tangible return, often in the form of spectacles, for what is considered an unreasonable outlay. A less querulous section hopes for examination simply because the service is free. Yet by general agreement the proportion of applicants not in need of spectacles is no more than 10%. An optician in East London who surveyed the first few hundred patients examined under the scheme has reported [2] that 19% of these patients were wearing glasses for which they had never been examined; 47%, already with glasses, had not been re-examined during the past 4–10 years; and only 16½% had never worn glasses before.

THE INDUSTRY'S CRITICISMS

The popularity of the new ophthalmic service was partly foreshadowed by a drop in the sale of spectacles from last January onwards; and the ophthalmic industry claims that if, in the months before the service started, it had been given a chance to prepare stocks according to the scales eventually laid down, present difficulties could have been largely avoided. As it was, the scales were made known only in June. The official scales schedule 19 types of frame to be provided under the scheme —10 to be issued free and 9 on payment of a supplement. If an optician stocks a dozen of each type in two sizes, he will have altogether 38 dozen. This, some opticians reason, is extravagantly many; and the range might be reduced. Nevertheless, despite temporary shortages of one or two types, manufacturers' capacity equals the present demand; and no doubt production, especially of the 7 plastic types which are listed, could be stepped up without great delay.

The position with regard to lenses is far less happy, accounting as it does for almost the whole delay in manufacture. Output is restricted both by the number of skilled workers—for lens-making is a craftsman's job —and by the shortage of machinery for grinding; and there can be no substantial increase in less than two years. In the meantime, some manufacturers believe that speedier service could be assured by reducing the types of lenses. Criticism is directed particularly to the issue of toric lenses without charge "for distant and/or constant wear and for reading when prescribed as being necessary," or otherwise on payment of a supplement. It is pointed out that only 4 such lenses can be produced in the time taken to produce 36 flat lenses.

Unfortunately, for present purposes, the industry was geared to increased production of flat lenses in the war, to meet Service orders; in most other countries only toric lenses are now used. The Ministry of Health says that had only "utility" frames been provided the results would have been (1) to cause a great demand for such frames, leading to even greater delay, (2) to make more people get their glasses privately, thus defeating the objects of the service, and (3) to discourage people needing glasses from getting them. The aim has been to set up a good, popular service—"not a utility one to which public opinion would have been justifiably opposed." If the productive capacity for flat lenses was not being fully used, the position with regard to toric lenses, says the Ministry, would be reviewed.

OTHER ASPECTS

Doctors and opticians sometimes argue—in opposition to the spirit of the Act—that if the patient is to value his spectacles, he must pay all or part of their cost. On the other hand, the service is evidently fully appreciated

1. *National Insurance Gaz.* Oct. 14.

2. *Dioptric News*, 1948, 3, 357.

by wives (who may hitherto have unselfishly foregone their claim) and by old people.[3]

Among the wealthier patients a few go to great lengths in trying to obtain through the service spectacles prescribed by a private ophthalmologist of their own choosing. Otherwise there seems to be singularly little abuse by the patient. Indeed, abuse is made very difficult by the triple check enforced by the family doctor, the ophthalmic practitioner or optician, and the executive council's ophthalmic committee. But if there is little abuse, there is equally little inclination to pay for extra service. Among opticians private practice has almost ceased, and now accounts for only about 4% of all work; and an optician in the heart of a very wealthy urban area reports that of 300 people supplied with spectacles under the scheme only 4 have opted for one of the varieties on which a supplement is payable.

There have of course been mistakes and difficulties in administration. Ophthalmologists complain that practitioners sometimes misuse the form recommending test of vision to refer a patient who should properly go to hospital. An ophthalmologist who takes a school clinic is irritated by the experience of being unable to obtain non-splinterable lenses for children at the clinic.

3. *Ibid.* p. 358.

Opticians, for their part, observe with some anxiety that payment is slow in reaching them. These are mostly passing annoyances. The one formidable difficulty is in the supply of lenses.

Doctor, optician, and patient are at one in reasoning that no ophthalmic service can be truly efficient so long as the delay in supply is a month or longer. Among the ways in which delay could possibly be curtailed are these:

1. Eventual increase in production of lenses.
2. Limitation in the types of lenses.
3. Restriction of the service to the patients most urgently needing spectacles—e.g., for work or reading.
4. Propaganda urging temperate use of the service.

None of these courses, except the first and perhaps the last, is likely to find general support. To the crucial question of how soon and at what level demand will settle there is still no firm answer. Mr. G. H. Giles, secretary of the British Optical Association, believes that 40% of the population require an aid to vision; that a fifth of this proportion still have no suitable spectacles; and that the eventual demand from the whole of Great Britain will be in the neighbourhood of 7 million pairs of spectacles a year, costing about £20 million.

Special Articles

A MEDICAL GROUP PRACTICE

Two Years' Experience

A REPORT FROM THE GROUP

THE experiment outlined here is constitutionally English in nature—that is, it has developed freely and naturally in response to local needs without any outside pressure or copying of any model. It is capable of infinite adaptation according to the locality. No attempt has been made to provide a complete medical service. Its function is mainly to complement the medical service in the neighbourhood and to provide treatment, otherwise obtainable only at a distance, in the patient's home town by the doctors who know his particular needs.

The group under consideration was formed in 1945 by the fusion of two old-established medical practices, each previously containing two partners. The motives which led to its formation were:

(*a*) To provide a comprehensive medical service for the patient in his own locality and within his financial means, by increasing the scope of domiciliary and hospital treatment.

(*b*) To increase the scope of each member of the group by providing him with greater experience in his own specialty and thus to increase his competence and skill.

(*c*) To raise the standard of professional skill by mutual consultation.

An illustration will make the first motive clear. A small "group" of two—specialist surgeon and specialist physician—cannot undertake dissection of tonsils without the aid of the special skill of a specially trained anæsthetist. It was therefore necessary to introduce an anæsthetic specialist into the group, and the surgical scope of the practice was thus widened.

The group works in a country town of 10,000 population, the surrounding countryside containing a further 15,000. The area has a radius of 8–10 miles. Two other doctors practise in partnership in the town. The nearest large centre of population is a city 15 miles away. The group is composed of a surgeon-obstetrician (F.R.C.S.E.), a physician (M.D., M.R.C.P.), an anæsthetist (M.B., D.A.), an assistant anæsthetist (M.B.), and a second surgeon (F.R.C.S.E.). The five members of the group all have specialist experience, four out of five having served in the late war as specialists in the Services; four out of five are members of the B.M.A. part-time consultants roll.

All members of the group undertake general practice; all, except the senior partner, undertook N.H.I. work. The physician does no midwifery. Members retain their own patients, but there is close intermingling. Each partner has a recognised deputy, who stands by for him and is introduced to his patients as far as possible. The anæsthetist gives all the surgeon's anæsthetics in the set operating lists, irrespective of the nature of the operation, and either he or the assistant anæsthetist gives anæsthetics for all but minor emergencies. The casual or occasional anæsthetist is thus eliminated. The two surgeons assist each other at all set operations, thus benefiting by each other's experience and shortening the duration of the operation. The second anæsthetist is specially trained in transfusion technique and acts as blood-transfusionist to the team.

The following is an example of the group's coöperation and organisation:

A patient was referred to the surgeon as a hospital out-patient diagnosed as having carcinoma of the cæcum and later admitted to hospital for resection of bowel. He was seen by the group physician for assessment before operation. It having been decided that the procedure was well within the capacity of the group, the operation was performed by the first surgeon, assisted by the second surgeon; the anæsthetic (thiopentone, cyclopropane, and curare) was administered by the first anæsthetist, with the second anæsthetist standing by ready for blood-transfusion if required. Thus all five partners in the group were intimately concerned in the management of one surgical case.

The organisation of the group fits closely into the definition laid down by the American Group Practice Council:

> "In order to be considered a medical group practice unit, an association of physicians of different skills, using medical equipment and nursing, technical and administrative personnel in common, must have a formal pattern of professional collaboration, a definite relationship as a group with a hospital or hospitals in the community and a unified administrative and financial organisation."

Using American terminology, this is a service group, consisting of general-practitioner specialists, with an added "reference" function in which manner it is used by the practitioners of the outlying villages.

ORGANISATION

Income from all sources is pooled and distributed among the partners in accordance with an agreed plan, laid down in the partnership agreement and subject to modification with the passage of time. The division is assessed mainly on two factors: (1) age and seniority in the group; and (2) the recognised higher earning capacity of surgeon-specialists. The government and administration of the group is entirely democratic, decisions being reached either unanimously or by a wise compromise.

The central office of the group is the ground floor of a large residential house, equipped to provide four sets of consulting-rooms, physiotherapy-room and minor-operations' theatre, general waiting-room, dispensary, and offices. There is also a dark-room for eye and ear work. The first floor of the house provides a residential flat for one partner. All the firm's consulting is done from these premises. The property and equipment is owned jointly by the partners. To prevent standardisation, each partner furnishes his own consulting-room and is responsible for its decoration.

Each member of the group is on the honorary medical staff of the local hospital, which has 50 beds and an elected medical staff. The surgeons and physician each hold outpatient clinics at the hospital. The group keep close touch, both in their private and hospital practices. Apart from formal consultations, arranged at the patient's request, members of the group assist each other in cases of difficulty, without additional cost to the patient. Problems of current interest are continually discussed. The group meets regularly to discuss administrative problems, but hitherto pressure of work has made it impossible to arrange clinical discussion on a formal basis.

Non-medical duties are divided between the partners. These include supervision of staff and finance, supervision of dispensary and ordering of drugs, supervision and ordering of instruments, &c., and upkeep of fabric of premises.

The non-medical staff comprises a secretary book-keeper, a part-time shorthand-typist, a dispenser, a receptionist, and a part-time cleaner. The secretary is in a key position, holds great responsibility, and is well paid. The dispenser is "Apothecaries' Hall trained." Wages of the staff amount to £900 p.a., of which the secretary is paid £343 and the dispenser £312. This is not an excessive outlay for a partnership of five doctors. The willingness, interest, keenness, and efficiency of the staff is considered of vital importance. The principle of unloading unskilled work and non-medical administration as far as possible from the partners, as a long-sighted economy, is carefully pursued. Auxiliary help more than pays for itself, by freeing the partners for purely medical work.

DOCTOR-PATIENT RELATIONSHIP

The preservation of the doctor-patient relationship is considered to be an ethical principle of the highest importance to be maintained at all costs. For this purpose, patients are not encouraged to transfer from one partner to another within the group, unless there are special considerations such as transfer of cases from a partner who is so overworked that he cannot cope with his present work, or transfer of a special case to a partner specially experienced in that department—e.g., a difficult diabetic from surgeon to physician, or a difficult surgical case from physician to surgeon.

When another partner treats a patient of a member of the group for a special service, the patient is returned to the original doctor when the service has been completed. If the patient definitely desires to change to another member of the group, he is of course free to do so. No difficulties between partners have arisen for this cause. It has not been found that the service so given has become impersonal, or that the members have sought to pass the responsibility for their patients to the group as a whole. Personal responsibility of one doctor for each patient and free choice of doctor are maintained. When a consultant is required for an opinion or an operation, the patient is free to choose any specialist, inside or outside the group, and no pressure is applied to influence his choice. The group emphasises the place of the family doctor as the key man, directing and coördinating treatment.

SCOPE OF SERVICE OFFERED

The scope of the group is adapted to the needs of the district. It is limited in this area by (1) shortage of hospital-bed accommodation, excluding accommodation for such specialties as ear, nose, and throat work (except tonsil operations) and ophthalmic cases; and (2) the comparatively small size of the area served, which limits the group to the major specialties. The group's service is at present confined to general medical, surgical, gynæcological, and obstetric work, with provision of consultant service in each department, modern anæsthesia for all cases, and facilities for some highly technical procedures which are not always available outside the special departments of big hospitals. Raising the standards of general medical practice within the group is considered as important as providing additional facilities for treatment.

X-ray, pathological, and orthopædic services, as well as the minor specialties, are provided by the local hospital, or by a large non-teaching hospital 15 miles away. No gross inconvenience is caused either to the partners or to patients by the fact that these services are not available within the group.

PHYSIOTHERAPY

Physiotherapy for private patients had been inadequate in the area until the group introduced a physiotherapist. Though the group could finance, accommodate, and use a full-time physiotherapist, it was thought undesirable and unethical to restrict her services to doctors or patients of the group, and she now works in exactly the same way as any other masseuse in private practice, except that she uses the group's clinic for her headquarters and consulting-rooms. To attain close liaison with practitioners outside the group, she is willing to treat patients in other doctors' consulting-rooms, if the necessary apparatus is provided.

In the difficult post-war economic conditions it was clear that no physiotherapist would set up in private practice in this area without being sponsored. That an efficient and keen masseuse is now in active practice in the area is looked on as yet another advantage to the population of the area, whether they are patients of the group or not.

RELATIONS WITH MEDICAL PRACTICE OUTSIDE THE GROUP

The local hospital forms an integral part of the life of the group. Of seven members of the "limited" honorary medical staff five belong to the group. At an early stage it was realised that an efficient hospital was essential to the group (just as the efficiency of the group was essential to the hospital), and later members of the group were chosen with this principle in mind.

The group has two equally important spheres of activity and coöperation—its own consulting-rooms and the hospital. Close contact is maintained between members of the group in their hospital work, surgeons advising on surgical aspects of medical cases, and the physician being available for preoperative examination of operation cases and for advice on postoperative treatment. Without the hospital the group would not have

come into being, and the group is wrapped up with its future.

All routine general surgical and gynæcological operations and abnormal obstetric cases are undertaken, except the more uncommon and the most extensive, which are passed on to specialists with greater experience of these departments. Thoracic and cerebral operations and the more specialised orthopædic procedures are not undertaken, since the function of the group and this hospital is not to compete, but to coöperate, with other hospitals and to do all straightforward operations and investigations sent in by surrounding doctors. The surgeons and physicians hold weekly sessions for outpatients.

Close liaison with the nearest non-teaching hospital is maintained. Members of the group pay weekly or occasional visits to the hospital departments, both inpatient and outpatient. It is hoped that this will develop into their official recognition as clinical assistants to the consultants of the larger hospital. Until recently the principal limiting factor in this advance has been shortage of time of group members.

Many local practitioners refer cases to members of the group for specialist opinions, whether in hospital, at the group consulting-rooms, or at the patient's home. Besides this, two members of the group have been instrumental in forming a medicochirurgical society, of which all doctors in the town and countryside are members. This society has proved of the utmost value professionally, socially, and medicopolitically.

ADVANTAGES OF GROUP PRACTICE

The advantages, to doctors and patients, accruing from any form of medical combine can be divided into those particular to group practice (using the term in the "team" sense) and those common to all forms of medical partnership, including those combines which are financial only. The advantages of the latter include reduction in overhead charges, such as rent and service in joint consulting-rooms, the provision of additional secretarial help (which, perhaps, a practitioner in solitary practice could not afford), and mutual assistance with off-duty and holiday periods, eliminating the need for a locum tenens. These advantages represent a great financial saving to doctors working in partnership.

The advantages obtained from group practice are not, however, of a financial kind. It is doubtful if there is any direct material gain from group practice, except for younger members of the group, who may receive a larger guaranteed income in their earlier years. Other members of the group could earn equal incomes if practising in small partnerships. To quote from the P.E.P. report, *Medical Group Practice in the U.S.*, citing the American Medical Association's questionary:

> "If the physician's ambition is to make all the money possible in the shortest space of time we certainly would not recommend group practice. If his purpose is to have an adequate income with an assurance of its permanency, and under conditions where he can practise his profession under the most ideal conditions, we would recommend group practice beyond any method we know. In other words, if the physician's motive is to render the best possible service for the greatest number of people for a remuneration which is adequate but not extreme, the plan would be by us highly recommended."

This judgment by American group practitioners is heartily endorsed by all members of this group for the following reasons:

(1) The first advantage is raising the standard and broadening the scope of general practice.

(2) Consultant's opinion and treatment can be made available without delay and with the minimum of expense to the patient. This is of particular importance if an acute abdominal case is involved, or as regards the money factor, in less urgent cases, when the consultant has to be summoned from some miles distant.

(3) If a patient has to go to hospital, he is cared for, while an inpatient, by his family doctors throughout his stay, with immense personal advantages, compared with treatment in a hospital remote from his home, where care, though efficient, may be very impersonal. Patients have less dread of illness if they know that they remain throughout under the care of known and trusted doctors. There is no reason why group medicine should lead to an impersonal attitude of doctor to patient.

(4) The combination of general practice with specialisation has a highly beneficial effect on the specialist, making him more practical in his approach to the patient's problems, and making him think in terms of patients and not in terms of diseases. An additional benefit is gained by the specialist in doing more work in his own line (thus maintaining and improving his technique) than would be possible if he worked in the more restricted field of a small partnership.

(5) Additional services can be provided by a group which smaller practices cannot afford. An instance of this is the introduction in this area, within the last two years, of two specialists in anæsthesia, a second surgical specialist, and a physiotherapist, none of whom might have been available if the previous arrangement of individual two-men partnerships had been retained.

(6) The "staggering" of consulting-hours can make one doctor available at the group consulting-rooms throughout almost the entire day. This is convenient for ambulant patients, besides ensuring that one doctor is on call for urgent cases.

(7) Not only can locums be dispensed with but while one doctor is on holiday another doctor who is familiar to the patient and conversant with his case can take his place.

(8) Minor advantages are the sharing of facilities for medical education, given by an efficient practice library, and continual discussion of medical problems with experienced workers, together with the continuous stimulation of enthusiasm which work in a good team provides.

(9) Group practice helps to prevent the staleness and "out-of-dateness" which often afflict the middle-aged general practitioner. This type of practice affords an excellent alternative for the keen well-qualified young doctor, who previously had to choose between general practice and pure specialisation.

(10) Service with an efficient group is an excellent training in domiciliary medicine for young graduates.

No disadvantages have been found by workers in this team, either to patients or to themselves. The dangers of "mass-produced" medicine have been carefully avoided, and any attempt to create a monopoly or to restrict in the slightest degree the patient's free choice of general practitioner inside or outside the group has been rigidly excluded.

ENDURANCE OF A GROUP

The difficulty in personal relationships within the group has been fully realised, and guarded against as far as possible by careful selection of entrants and by an equitable and comprehensive partnership agreement. Agreeable wives are as important to a practice as compatible doctors, and this too has been borne in mind. The endurance of a group largely depends on compatibility of temperament of the partners and the loyalty of their wives. Without such compatibility a group is likely to degenerate into a mere financial partnership or else to break up. The health of this group depends on the enthusiasm and liberty of action of the partners (within the broad limits of the partnership agreement). If a partner proved unsuitable for the practice (or after a satisfactory period became so), and if the other partners could not remove him on grounds of incompatibility, the effect would be very serious.

The success of this group has been built on complete freedom of action as a group, and on the much-discussed personal-profit motive. How greatly it will be affected by restrictions imposed on part-time consultants practising in groups, where some members have G.P. contracts with local executive councils, remains to be seen. Any official attitude which prejudices the free action of the general-practitioner consultant is likely to be fatal to medical group practice.

CONCLUSION

Though reference has been made to the P.E.P. broadsheet *Medical Group Practice in the U.S.*, it should be clearly understood that the conclusions reached by this English group were independent of any outside experience, and that the group developed out of the individual experience of two of its members, without any contact with, or experience of, other such groups in the United Kingdom or abroad. This report was, in fact, prepared before the P.E.P. broadsheet was published, but it was subsequently rewritten to comment on some aspects of group practice emphasised by American exponents, with whose experience this group is in remarkable accord.

SUMMARY

A highly successful experience of two years in group practice is discussed.

The group comprises a physician, two surgeons, a gynæcologist-obstetrician, two anæsthetists, and a physiotherapist.

Each member undertakes general practice as well as his own specialty.

The group works on a basis of planned coöperation, the finances being pooled and distributed on an agreed plan.

The advantages of the group practice as distinct from those of individual practices and financial combines are described.

No disadvantages have been found in this group practice.

NEW ZEALAND MEDICAL SERVICES

FROM A NEW ZEALAND CORRESPONDENT

SELF-CRITICISM is not one of the more obvious qualities of the New Zealander. Indeed a distinguished visitor has recently accused us of smugness. So perhaps as regards the State medical scheme one would not expect the doctors to be very vocal in criticising the goose that lays the golden eggs. After all they are 7*s.* 6*d.* ones, even if it is a goose that lays them. But criticism has been more apparent lately, even to discussion in the House of Representatives; and now we have the report of a committee, consisting of officers of the department of health and representatives of the British Medical Association, set up last October to examine the medical provisions of the Social Security Act and their administration, and to advise what alterations are needed to give effect to the government's policy of making available adequate and proper medical services (general and specialist) free or substantially free of cost.[1]

New Zealand has hitherto had no disciplinary body except the Medical Council, which corresponds to the General Medical Council. There has been nothing analogous to a panel committee, and nothing to maintain ethical standards above the level of "infamous" behaviour. There was indeed provision in the Act and its regulations for the establishment of such committees; but, with the medical profession unwilling partners in the operation of the system, nothing came of them. The new report now agrees to the need for disciplinary bodies, and suggests that they should be set up at two levels. There should be a local investigating committee for each health district to hear complaints against doctors and to investigate allegations of over-prescribing. If it finds that there is a case to answer it is to refer it to a disciplinary committee which would have power to deal with all complaints not serious enough for the Medical Council—presumably on the same basis of fines up to £50 as the original Act provided. There is also to be a General Advisory Committee, recognised by the Minister as the chief consultative body in all matters affecting medical services.

In considering general-practitioner services the committee were satisfied that in some cases doctors were receiving annual sums much in excess of what could be regarded as reasonable remuneration. As a check on this they suggest that 30 patients a day is as much as a doctor can do justice to, and that where he habitually exceeds this number he be invited to meet the local investigating committee. But they do not favour a change from the fee-for-service system, a great merit of which, from the doctor's point of view, is that it leaves him free to accept or refuse a call as he wishes. Some changes are suggested in the payments. An extra 2*s.* 6*d.* is advocated for home visits, so as to discourage large surgery attendances and to bring the system into line with the custom, already common, of making an extra charge for going out. Telephone consultations should be paid for at a rate up to 5*s.* in rural areas approved by the medical officer of health. Where the only service is to repeat a prescription no payment should be made—a recommendation in which the committee show a certain naïveté: what happens if the doctor looks at the patient's tongue? Finally it is suggested that the doctor's right to recover fees at law should be restored, provided that the patient is given a month in which to refer the matter to the local investigating committee.

Hitherto specialist services have not been covered by social security, and the only contribution the patient could get was the 7*s.* 6*d.* standard fee. The committee think that specialists should now be brought into the scheme, and suggest that for their recognition, which would need legislation, there should be four requirements —adequate training, a higher qualification, hospital experience, and recognition by the applicant's colleagues. Most specialists will have to be part-timers, and the committee advocate the system under which hospital staffs are chosen from local doctors, instead of being purely internal, as a means of increasing their number. Many knotty problems are left for future consideration, including most of those concerned with remuneration; but they suggest that the contribution for a consultation, for which the usual fee is £2 2*s.*, should not be more than £1 10*s.* In any case the fund is going to be landed in further heavy commitments, and any decision as to the introduction of specialist benefits must take seriously into account the financial obligations involved.

The heavy, indeed enormous, cost of drugs has long been the subject of apprehension. Something has got to be done about it, and the committee suggest two approaches. The public ought to pay at least a proportion of the cost, except in cases like the supply of insulin; and the doctors should work to a revised formulary, with the possibility of appearing before the local investigating committee as a deterrent against over-prescribing.

Drastic changes are suggested in the method of paying general practitioners from the fund. In the first place it should be for the doctor to make the claim, thus eliminating the present alternative by which the doctor charges his fee and leaves the patient to recover 7*s.* 6*d.* from the fund. Secondly, the individual certificates signed by each patient after he has seen the doctor, which now serve as the authority for payment, should

1. A summary of the report, from our regular New Zealand correspondent, appeared on Oct. 2 (p. 545).

be abolished, and a new form of claim substituted. This would consist of a single sheet giving the date, the name and address of the patient, the type of service rendered, the total fee charged, and the amount claimed from the fund, with a certificate at the bottom, signed by the doctor, that the claim was a true one. There would be two checks on the genuineness of the claims, (1) a scrutiny of the practitioner's records by a medical inspector, and (2) postal inquiries from a proportion of each practitioner's patients. In thus handing out what is to all intents and purposes the equivalent of a blank cheque the authorities may not be as green as they seem at first sight. There have undoubtedly been abuses of the old system, but it has been almost impossible to bring them home, for under the present system there have to be two parties to a fraud, and one of them, the patient who has signed a misleading receipt, is not likely to appear as a witness against a doctor and thereby admit his complicity.

The committee's report consists only of recommendations; and many, if not most, of them are sure to be the subject of controversy. One thing is certain—that the present system, a pioneer in the field of socialised medicine but one that has never been thoroughly overhauled, is in need of a spring-clean.

ORGANISATION OF CANCER SERVICE

WHEN, in July, the governing body of the Liverpool Cancer Control Organisation transferred their responsibilities to other hands, the Organisation had existed for some ten years; and in the light of those years of experience a series of principles has been formulated, and printed in the annual report,[1] for the guidance of those who will now have charge of the service. These principles were laid down when it became clear that, contrary to the Organisation's hopes, the radiotherapeutic centre was not to be an integral part of the teaching hospital.

The first principle laid down is that the respective duties of the regional hospital board and of the board of governors of the teaching hospital in regard to the diagnosis and treatment of cancer are distinguishable but complementary, and that the utmost coöperation is desirable. The regional board's duties should be to provide diagnostic and therapeutic services in all suitable hospitals, including the teaching hospital, and to afford such facilities for teaching as the university may require. For their part, the board of governors should provide, as part of the regional board's service, arrangements for diagnosis and treatment of patients attending the teaching hospital; and they should ensure that these arrangements are sufficient for undergraduate teaching.

Thus the requirements of the regional hospital board comprise: (*a*) from their own resources, a regional team of radiotherapists, medical staff other than radiotherapists employed in regional hospitals, and a headquarters institute for the radiotherapeutic staff; (*b*) from the teaching hospital, medical staff other than radiotherapists employed in the teaching hospital, such treatment facilities as the teaching hospital can provide, and the ancillary services of a general hospital.

The requirements of the board of governors of the teaching hospital comprise: (*a*) from their own resources, medical staff other than radiotherapists, and treatment facilities for complete undergraduate instruction; (*b*) from the regional board, the services of visiting radiotherapists, and access to the radiotherapeutic headquarters institute for such treatment as cannot be provided in the teaching hospital.

The essential condition for an efficient service, says the report, is joint diagnosis and treatment by radiotherapeutic and other medical staff, except where, by full agreement, treatment is conducted solely by one or the other. A cancer diagnostic service staffed by one or other of these two groups alone is thus precluded; and such an arrangement is also ruled out for the reasons that: (1) the volume of cancer cases arises from and is less than the total volume of initially undiagnosed cases attending hospital; (2) diagnostic services being needed in all suitable hospitals, a single hospital is inadequate for the purpose; and (3) from the patient's standpoint the diagnostic services are best located in the normal centres of hospital service and not in a hospital identifiable as a cancer hospital. Furthermore, hospital beds should be allocated to radiotherapeutic and other medical staff according to the proportions in which purely radiotherapeutic and joint treatment are likely to be employed.

The administrative arrangements recommended in the report include the establishment of a cancer services medical advisory committee to assist the regional board.

1. Liverpool Cancer Control Organisation: Annual Report, 1947–48. Issued from 80, Rodney Street, Liverpool.

Disabilities

16. LOSS OF A LEG

AT about midnight 4½ years ago the blast of a German Schu mine took my right leg off. I knew what had happened—it was not necessary to soldier in Italy long to encounter this situation pretty often in others—and my mental condition was not improved by my thinking that I had been blinded, for I could see nothing and could not feel my hands. At that moment I felt so unutterably lonely that my instinct of self-preservation fled entirely, and a vivid memory is of my head falling to the ground in a helpless despair. Then light dawned, in the literal sense, and I found I could see again. It was only tracer shells, but it was vision, and from that moment my efforts at rehabilitation started.

After the usual progress "down the line," with periods of semiconsciousness in which comforting faces made fleeting appearances through mists of sleep, morphine, and pain, I arrived in a general hospital not far from Naples, and when at last it was possible to take an interest in my environment I found myself in a ward full of amputees. True to form—"doctors and nurses never have anything straightforward"—everything went wrong with me, and after a series of operations, reamputations, plasterings, and splintings, I realised that I must face the future with my right leg off below the knee and my other leg ankylosed at the knee with a foot-drop. My arms were still in bandages but they were going to be all right.

I knew that further surgery was pending, so I set myself targets to attain over the next year, which I estimated would be spent in bed in varying degrees of pain. The first target was to get back to England to see my wife, whom I had left 3½ years before; for the thought of seeing her again had borne me up in my worst moments of emotional upset and churlish tantrums. If you can imagine the worst pain you have ever felt concentrated into one small part of your body you will know what it means to have a pyarthrosis of the knee. Even sleep offers no release, for directly the muscles relax the starting pain in the knee comes back and full consciousness is regained with a scream.

This was my life for three months—lying in bed watching other wounded being carried into the ward and seeing them walk out again while I remained static having three-hourly shots of penicillin, watching bottles dripping blood into me, and listening to the rumble of Vesuvius and the guns from Cassino. In the last of these months I realised that a very serious effort would have to be made if I was to get back to England. All the friends I had clung to in the ward were being evacuated, and here I still was. So I embarked on a campaign of saying I felt fine, for by this time my leg was in plaster and the knee becoming less painful. I also forebore to scream

when I was lifted on to the bed-pan and only grunted and swore.

To disguise our emaciated pallor I and some of my immediate neighbours who were in this swindle asked to be carried outside so that we could get sunburnt. At last things seemed to be going well. With the aid of the ward physiotherapist I sat up in bed and tried to bend my right knee on the amputated side over the bed, the other one being in plaster. Here indeed was progress: over the edge of the bed went my amputation, and encouraged by the rest of the ward I bent the knee—or thought I did, but the knee flexed only a matter of 5°. This was stark tragedy. For $2^1/_2$ months I had been planning my life on the lines of one ankylosed knee and one below-knee amputation, and now it looked as though there must be two ankylosed knees and an amputation. A few days later I had to face the fact that all was not well with the amputation, in spite of the most careful surgery and untold mega units of penicillin. The attention of the ward M.O. was drawn to my discovery by the sound of suppressed weeping from behind a screen, for I had found the right tibia making an unexpected appearance through the skin. I had developed a sequestrum. Once again new plans had to be made and another piece of ill fortune digested.

By this time I felt that about everything in the book had happened to me and that all would be plain sailing. Sailing was the operative word, for a few days later three of us were told that there was room for us in a ship sailing next day. This was a real piece of luck. Our hair was cut, we were bathed and changed, and the man in the next bed with a fractured spine somehow packed for me. The last of our carefully hoarded whisky was shared out and swallowed, and with the aid of a hypnotic we settled down for the night with a great confusion of thoughts. Further confusion was added as we went to sleep by the night sister telling us that the ship had been cancelled. Next morning gloom lay in thick dark layers all round the ward. At midday the day sister burst in waving a chit and announced that if we could be ready in an hour we could go. The sun broke through, another bottle of whisky was produced, and another phase was over.

We landed at a West of England port and were delivered via hospital trains to an E.M.S. hospital, where we were handled like fragile porcelain. Here I had a first sight of my wife, and my secret fear that she would be repelled by a limbless man was soon dissipated. Self-confidence began to grow as my family came down from the north to visit me, and when friends made arduous war-time journeys to spend an hour with me. I did not see that pity in their eyes which I had dreaded since I was wounded. I was soon moved to a hospital nearer my home where I could be looked after by my favourite surgeon. A few weeks later it was decided to do a sequestrectomy on my amputation. This went off very well and all appeared to be under control surgically.

A further blow was in store. This time it took the form of a red-tabbed Army colonel who gave me a medical board, announced that I was no further use to the Army, graded me category E, asked what my plans were, and suggested the "psychiatry racket." His idea was that I should be carried in on a stretcher to learn all about it at psychiatry clinics. This was rehabilitation on the grand scale, especially as I had estimated that I would be another year in hospital. Being graded category E was really bad news for it meant that I must henceforth exist on a disability pension. However, with the aid of my friends I was given a respite and my discharge cancelled.

My left knee was still painful, but I no longer needed to sit on an air cushion and I could lie down and sit up at will. Another few weeks and a further reamputation was performed to mobilise an adherent scar. It was done by a personal friend and the anæsthetic was given by an old colleague of mine. The result was a secondary hæmorrhage, and I felt sorrier for them than I did for myself when a few days later a rather exsanguinated amputee had to be whipped down to the theatre to be religatured. Soon after this I could lift my ankylosed leg with the plaster on without too much pain. I went out in a spinal carriage to the cinema and to that mecca of all men in bed—a pub. Shortly afterwards I essayed a wheel-chair, and here at last was true independence. With my leg stuck out in front I could propel myself round the hospital; I could attend the physiotherapy department and have active exercises with my right knee, which was now flexing to 50°. After three months the day came when my calliper was delivered, but after being forced upright on to crutches I found that will-power alone was not sufficient to lift myself long. A month of exercises and it was just possible to make progress.

The next milestone was when I got my artificial limb, and, with a calliper on one side and an artificial limb on the other, I walked. This was the day I had dreamed of. It was an erratic, wavering, shaky walk, but I was proud of it. Several weeks later I was offered a job doing medical boards, when I was out of the Army. Accordingly I travelled to London, was boarded out, shaved off my moustache, and danced at one of the more fashionable hotels. This was a huge success, for I was not the complete social outcast I had anticipated. I started doing medical boards and felt that for the first time for 18 months my existence was justified. I was actually doing something to keep my place in society. Then a post was offered me in a Ministry, and after a London interview I was accepted. By good luck and unremitting endeavour I managed to obtain an unfurnished flat in London and have lived there for the past three years. A year ago I was appointed to the permanent pensionable staff of this Ministry and am working alongside fit men and not in any sense a passenger. In fact, ambition keeps biting me to undertake a job where there is more work and movement. I walk without a stick or calliper and have developed my own mode of life for entertainment purposes. At theatres and cinemas I take a left-hand seat and put my ankylosed leg in the aisle on a small folding stool, where it is not so noticeable as might be expected. The reason I rest my artificial leg on a stool will not be far to seek if any six-footer will try sitting down on a chair with his leg straight, for it either means sitting on the edge of a chair or sitting with the spine extended.

In my usual restaurants I am well known and when I sit down an unobtrusive chair is provided on which to rest my leg. I drive a car, dance occasionally, and go swimming when I can obtain solitude and freedom from curious stares, for my method of entering the water is unorthodox as I cannot hop and do not wear a prosthesis. I am a chronic spectator of all kinds of sport and have stood through two rugby matches one after the other on several occasions.

I still feel sure that had the surgeons yielded to my pleas to amputate this limb, life would have been much more comfortable and I still would have walked without sticks. However, there is still the chance of an arthroplasty when the results are a little better. I have patches of depression and frustration three or four times a year, but fortunately both my wife and I recognise them for what they are and take the necessary steps. Altogether life is a great improvement on what I had anticipated four years ago, but nothing will ever convince me that an ankylosed or arthrodesed knee is a good thing to have. Of the things that irritate me, one is being called a cripple as opposed to disabled, and another is having my amputation referred to as a stump.

In England Now

A Running Commentary by Peripatetic Correspondents

AFTER his talk to the Eugenics Society last week [1] Mr. Cecil Binney should have spent the next evening at the Torch Theatre and blushed for his shortcomings. In Mr. Dan Sutherland's *Breach of Marriage* he would have seen an eminent lawyer who—without any trial run, with no chance to consult a single text or ring up a knowing colleague, and moreover with none of that tiresome legal caution which Mr. Binney displayed—was able to rattle off all the relevant opinions on artificial insemination at a moment's notice; and this, too, when he was rattled himself, having just been told that his coming grandchild was to be what some have called a test-tube baby.

On the whole he took it well; though one of the curious things about this play is that no-one can be sure how anyone is going to take anything. Certainly they have a good deal to take. There is Peter Stuart, the war hero, for example, paralysed "from the waist down" as result of frostbite. This obscure condition does not debar him from having a child, though it requires the intervention of a third party. He is alleged to be going crazy in his desire to achieve this feat; but all the poor fellow betrayed was a very moderate snarkiness with his wife and in-laws—a touch of veteran's rage, perhaps invited by their aggressive forbearance. Well, but then he turns out to have pulmonary tuberculosis, diagnosed in the course of the afternoon by the clever doctor, Erasmus Baring, who happens to know a bit about tuberculosis, he tells us; and so he must, for he spots a minimal lesion without an X ray, and mainly on the basis of a positive Mantoux test. He is weak on modern treatment, though, and shockingly hazy about the dangers of infection for the child. Never mind, the play must go on, rather better than expected. Peter must not be told about his tuberculosis, which (if he were to be the donor himself) might be passed on to the next generation; but at all costs he must be given a child; so the wife plumps for A.I.D. and Peter must never know about that either. But of course he finds out, and like the audience at once engages in the pastime of spotting the donor; as there is only one candidate it doesn't take anybody long. So the war hero, after a last well-ridden row with his wife, wheels himself over the cliff, as we all knew he would the moment we heard there were cliffs in the vicinity.

What, I wonder, was Mr. Sutherland out to say? He gives the doctor every sympathetic consideration and most of the best lines, which suggests a liberal attitude to artificial insemination. On the other hand, the whole affair turned out very badly, and ought to be a lesson to somebody. It is hard to detect exactly whom. But there, as Mr. Binney might say, perhaps it will never happen.

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My peripatetic colleague of Oct. 16 who suffers so severely over his winter pants might obtain the appropriate regulation of clothing without so much heart-searching by the use of an overcoat, and there is a tradition in the Eastern Counties that overcoats should be looked out at the time of Barnet fair. This fair, which is now a ghost of its former self both in size and importance, is held on Sept. 3, 4, and 5, except when one of these days is a Sunday.

* * *

Should a doctor tell? And, if so, how much? The old question came up again the other day. Miss C, a woman of 55, has been under the care of our partnership for 6 years with spasticity due to disseminated sclerosis. We have told her that her trouble is "neuritis" (convenient blanket-word!) and encouraged her to continue at work, and she does quite well with a little morning amphetamine to get her going.

A few weeks ago she was staying in a provincial town and fell sick. On her return she told me that the doctor, a young and enthusiastic physician, examined her thoroughly and warned her that she had a serious disease which would develop over a long period and ultimately paralyse her; it was called Parkinson's disease. I deduced that the doctor had probably diagnosed her correctly but was not quite at home with the nomenclature. Anyway, it gave me a loophole, and I assured her that she had not Parkinson's disease, and that, though we might give her trouble a long latin name, "neuritis" would do quite well, and that she need not worry for the future.

Twenty years ago I might have been less subtle. And then when she heard the name "disseminated sclerosis" she would have looked it up in the *Complete Home Doctor* and become a very unhappy and perhaps needlessly apprehensive woman. I once saw a woman in the fifties who had recently developed a typical spasticity and incoördination having had no symptoms whatever since her original attack of diplopia at the age of 20. That helped to teach me not to darken the lives of my patients with dire prophecies.

It is more difficult to know when to tell in cases of approaching death. I think I should like to know if I had an inoperable cancer or an acute leukæmia, but I don't think this would be true of most people. One gets the "feel" of patients, whether they want the truth or not. Usually it is best to await their approach, and often the form of question helps to determine the answer. One of my best patients and friends—an intelligent, inquisitive, and humorous old man—asked me no single question about his trouble during a long illness with an inoperable bowel cancer. Sometimes the near relatives can help, but usually it has to lie between doctor and patient. A dear old lady of 80 said "Tell me, doctor, I'm not afraid"; and so I told her, and for the many months she lingered on she always had a smile and usually a joke. But for many others the truth would have been mental torture.

And with Pilate one may ask, "What is truth?" At the best we can only tell some of it, for we never know the whole.

* * *

Minor swindles on the Government are the fashion these days, but here is one which I am assured is being perpetrated and must be among the simplest and safest. All you require is a friendly chemist and a busy doctor. The technique is as follows: Go to the doctor's evening surgery; you will probably be one of 100-odd patients there. Complain of a "cough" or a "lump in the throat," or anything which takes your fancy and doesn't sound too alarming. The doctor may or may not examine you but at any rate he will give you a prescription. Take the prescription to your friend the chemist and trade it with him for some toothpaste, hair oil, or cosmetics for your lady friend. If you want some more, simply go on attending the busy evening surgeries. Always say that the last prescription did you good, and you will certainly have it repeated. There's no end to it.

* * *

Your provincial and peripatetic psychiatrist has recently been asking his colleagues in London and in New York: "How do you practise psychiatry in this great wen, this monster, called the Metropolis, anyway? When I see a patient in my home town, I can visualise the street he lives in, the school he went to, the factory he works in. I probably know his family doctor—or his probation officer—personally. A good rapport may exist because I have already treated his cousin or his next-door neighbour. After he goes back to work he can attend as an outpatient shortly after 5 o'clock without any inconvenience to anyone. There's social psychiatry for you." The metropolitan psychiatrists have their answers. They point to their retinues of social workers and their piles of reports from social-service agencies. They too have faithful patients who travel 20 miles to the hospital if they move out to the suburbs. They too can visualise their city districts; even the non-peripatetic reader may understand the connotations of "Lower East Side" and "Harlem" and of "Fifth Avenue" and "Park Avenue."

* * *

We are becoming inured to jargon these days, but I was somewhat startled when my youthful secretary asked me to sign a letter I had dictated to a doctor about a woman patient, recommending ". . . extra rest, absenteeism from intercourse, and careful regulation of the bowels. . . ."

[1] See p. 738.

Letters to the Editor

THE FULL-TIME SPECIALIST

SIR,—At the last meeting of the Leeds Regional Consultants and Specialists Committee, following a discussion upon domiciliary visiting by full-time specialists, it was decided that no full-time specialists should be allowed to take part in the scheme for domiciliary visits with or without pay; that any such visit would impinge upon the prerogative of those specialists working part-time in hospitals; and that, as the profession was solidly against a salaried service, specialists should be discouraged in every possible way from remaining full-time and should be encouraged by these financial penalties to take up part-time work.

In this region most of the consultants I know are employed the maximum of eight sessions per week in hospital. With the weighting already given, and domiciliary visiting, they will be receiving, for about 26 hours a week, the remuneration of the full-time specialists, who have no time-limit to the hours worked and who are in many cases now doing 40–50 hours a week.

Is it the opinion of the profession that specialists are to be discouraged from working full-time? That they are to be prevented from indulging in professional activities outside their hospital work? That appointments under the boards are to be limited as far as possible to part-time specialists, and full-time appointments are not going to be made except in very special circumstances?

Incidentally, the Leeds regional committee is in my opinion an illegally constituted body. Its constitution was decided upon at a meeting of a committee representing the non-teaching voluntary hospitals, who arbitrarily decided to exclude hospital areas from participation where the hospitals were mental, fever, or tuberculosis.

Halifax. H. I. DEITCH.

LOCAL INFECTIONS TREATED WITH DIBROMPROPAMIDINE

SIR,—Lest the article by Kohn and Cross, in your issue of Oct, 23, engender false optimism, we feel it necessary to record briefly our experience of local chemotherapy with dibrompropamidine isethionate ('M. & B. 1270'). Using a 1·5% cream in the carbowax base recommended, we have now treated 8 inpatients (6 burns, 2 dermatitis) suffering from surface infections with *Pseudomonas pyocyanea*. The cream was applied for periods of four or more days. In 4 of the cases it was applied daily, and was combined with perfect dressing cover which minimised the possibility of added infection. In no case was appreciable clinical or bacteriological improvement noted. All the strains of *Ps. pyocyanea* isolated were inhibited in vitro by 1 : 1000 dibrompropamidine.

On the other hand, our results confirm the effectiveness of dibrompropamidine in treating surface infections due to *Streptococcus pyogenes* and *Staphylococcus aureus* (including penicillin-resistant organisms). The bacteriological findings have been clear-cut, and the clinical results good. We would recommend the use of the drug where penicillin-resistant organisms are found, and in patients previously sensitised to penicillin. Controlled trials are now commencing, and it is possible that for these organisms a less concentrated preparation will suffice and be less likely to have undesirable side-effects (e.g., toxicity to leucocytes). It is also hoped to investigate the use of the drug as a prophylactic against *Ps. pyocyanea* infection of burns, for it is not impossible that a drug might pass this test in spite of its failure as a therapeutic agent.

J. P. BULL
W. P. DALLAS ROSS
J. R. SQUIRE
ELIZABETH TOPLEY.

M.R.C. Industrial Medicine and Burns Research Units, Birmingham Accident Hospital.

TREATMENT OF BURNS

SIR,—With fashion rooting about in the past for something to whet our jaded appetites, may I make a plea for the resurrection of tannic-acid jelly? I have used this agent for many years and still believe it to be the best of all protectives for severe burns.

The excellent article by Dr. Colebrook and Dr. Hood (Oct. 30) suggests to me that results, when it is properly used, are consistently good because a thin film of it approximates to the ideal flexible membrane postulated as a necessary guard against "infection through soaked dressings."

Dr. Gissane, as I found on a visit to the Birmingham Accident Hospital during the war, certainly picked a winner in 'Cetavlon' as an initial cleansing agent. After using this I apply a thin coat of tannic-acid jelly and a single layer of gauze. This is allowed to dry as far as possible before packing with cotton-wool. On subsequent days more jelly is added to repair sodden areas until a firm dry scab of gauze and jelly covers the burnt area. Healing is usually rapid, and the artificial scab flakes off or can be removed like autumn leaves.

Naturally, with advance of knowledge we have added sulphonamide and penicillin to the local and general treatment. This diminishes unpleasantness, as the method has something in common with the Winnett Orr plaster for osteomyelitis and external appearances are far from elegant. My last case was a large second and third degree burn of the buttocks and anus in a child of 3. It required some fortitude to persevere with the outwardly dismal dressing. But the boy was discharged healed without a scar.

There is one considerable word of warning: *never encircle a limb or finger with a gauze dressing.* If the burns involve the fingers, make a series of half-hoops back and front till the swelling subsides. With this precaution one can even treat third-degree burns in babies. A recent case of palmar burns down to the flexor tendons in a child of 2 who grasped the element of an electric fire gave us complete healing and function in two months.

Lastly, since using this method I have not had to resort to skin grafting. But there is no reason why in a sufficiently extensive raw area both methods should not be combined. I do not think the skin graft would mind.

Walmer. JAMES S. HALL.

APPLICATION FOR HOSPITAL POST

SIR,—It is in the backwash of an emotion compounded of anger and confusion that I address this letter of inquiry to you. What is the policy adopted in the selection of candidates for interview and eventually for appointment to a post advertised in this journal?

I applied two weeks ago for such a post at a well-known hospital near one of our university towns. I received no acknowledgment of my application, and it was only from a chance remark of a friend that I learned that the interview was today. Having made an exhaustive search to find a mislaid letter, I went to the trouble and expense of telephoning the hospital. Believe it or not, the secretary was angry with *me* for inquiring about my application, and quite furious when I asked him how candidates were selected for interview, telling me that it was none of my business and a hospital affair. May I register my protest here? It is my business, and should be a public affair. He finally apologised for not sending a letter of acknowledgment. This was due to an oversight, though it leaves me in some doubt whether my application ever received any attention. It would seem that more tact and consideration are applied in obtaining the services of a cook than those of a doctor.

To most of your readers, this issue is one which they have forgotten, though at some time most of them must have had some similar experience. Heaven knows how much preselection and wire-pulling contribute to an eventual appointment; it was ever so, and I suppose always will be. But is it not farcical widely to advertise a post when the record of appointments to a hospital shows that those chosen are almost always students from the nearby university town?

Furthermore, what is meant by the phrase "Required —house-physician, A or B2"? Does it mean that this is a first appointment open to newly qualified practitioners, unless an ex-Serviceman or registrar with an M.R.C.P. cares to apply? Or, more charitably, does it mean that a post normally of B2 status is found difficult to fill and offered to A practitioners?

To many, I said, this issue is dead. To me, and to many other newly qualified men, it is very much alive.

A. B.

BLOOD FOR TRANSFUSION

SIR,—In view of the recent correspondence and last week's leading article on this subject, I think it is worth recording that recently we obtained 30 pints of group-O blood from the North London Blood Transfusion Depot for the purpose of exsanguination transfusion. We are particularly indebted to the director of this unit for his help in supplying this large quantity at short notice.

St. Bartholomew's Hospital, London, E.C.1. I. P. MACDOUGALL Chief Assistant.

NITROUS OXIDE SUPPLIED BY PRACTITIONERS IN MIDWIFERY SERVICE

SIR,—There appears to be confusion about the supply to general practitioners of cylinders of nitrous-oxide gas for analgesic purposes in maternity cases under the National Health Service. As the National Birthday Trust is particularly interested in the provision of analgesia to women confined in their own homes, approach was made to the Ministry of Health for guidance in the matter; and the following is from the Ministry's reply:

"The position is that if a doctor is engaged by the patient to give maternity medical service under part IV of the Act, he is in the same position as any doctor giving general medical service under part IV. He may write prescriptions or may himself supply any drug 'personally administered'—e.g., nitrous oxide. For drugs so supplied he will receive payment from the executive council on presentation of a claim on E.C.10 to the executive council.

"If the doctor is called in by a midwife in emergency, he is not giving maternity medical service under part IV of the National Health Service Act but is giving services under the Midwives Act, 1918. He receives a fee which includes the supply of necessary drugs and dressings, except that he gets extra payment for certain expensive drugs named in part 2 of the schedule to S.I. 1453 of 1948. In such cases, the patient would have a midwife in attendance and, as you know, midwives are supplied by the local health authority with cylinders of nitrous oxide. Many, but not all, doctors have cylinders but some may not have realised that when giving maternity service under part IV they can be paid for any nitrous oxide they supply themselves."

57, Lower Belgrave Street, London, S.W.1. D. V. RIDDICK Secretary, National Birthday Trust Fund.

MEDICAL RESEARCH IN AFRICA

SIR,—I am very glad that your correspondent of Oct. 16 (p. 624) has called attention to the attitude (or lack of it) of the Colonial Office to the immense medical problems of Africa. I note that he makes no reference to venereal diseases, but in this respect the official attitude seems to be much the same as in others.

During 1944 and 1945, as Command venereologist and dermatologist to the British Army in East Africa, I devoted fifteen months to the study of the special problems of venereal diseases in these territories. The war saw an enormous increase in the incidence of venereal diseases in East Africa, and at the same time provided means by which that increase was likely to go on. In this respect the V.D. problem has an urgency not presented by such a condition as malnutrition, which was presumably not changed very much in recent years. It is also comparatively remediable; yaws has been virtually "stamped out" in many districts, and comparable medical "campaigns" on a larger scale would do much to control the spread of venereal diseases.

Three times since the end of the war have I tried to induce the Colonial Office to show an interest in the problem. I have submitted a survey of some 3000 words, called twice at the Colonial Office, and written letters; but I have never detected any spark of real interest. My correspondents in Kenya are still unable to tell me of any material steps which have been taken to cope with the situation in that country.

No doubt, as your correspondent says, there is a shortage of personnel to do the work; but I am not satisfied that this is the reason why so little has been done. The official mind does not seem to be appalled at so many tasks and so few people to carry them out; its attitude more resembles indifference, which can only result from a lack of appreciation of the importance of the work or from apathy. So long, of course, as this is the attitude of Whitehall the field workers of the Colonial Medical Service will be frustrated in their work; and, if they are good doctors, many of them will leave the service as soon as they can.

Meanwhile, what of our trusteeship of the Africans?

London, W.1. F. R. BETTLEY.

UNDER TENSION

SIR,—In his letter on Oct. 23, Dr. West insinuates that because I admit the obvious fact that the Muscovite rulers wish to destroy non-Communist States, I must therefore be a warmonger intent on a preventive war against the U.S.S.R. This is a very serious charge, which I deny. In everyday life, a man who is threatened by a homicidal paranoiac neither reflects, while awaiting the mortal stroke, that it takes all sorts to make a world, nor decides to murder him first. He does the common-sense thing. If he lives in an ordered and policed State, he calls on the police to protect him, and he no doubt hopes that psychiatrists will cure the paranoiac of his mental aberration in due course. If, on the other hand, he lives in a State without police, law-courts, or psychiatrists, he collects trusted friends and fortifies his house.

This is my logical counter to Muscovite threats. I am fortunately able to answer Dr. West's whimsical question about what voices are to be heard in the U.S.S.R. In the Stalin-Tito exchanges, Stalin writes that the idea that there can be "peaceful development of capitalist elements alongside Socialism is a rotten and opportunist theory." Stalin also said, in the same Tito-Cominform controversy: "Communist parties can live and develop only in open warfare against the enemies of Communism." Dr. West's counter to these bloodthirsty threats seems to be that no-one is really to blame and that it will all be the same in 40 years. Very whimsical, very. A mighty droll and fantastical fellow, 'pon my word.

Bridlington. P. D. H. CHAPMAN.

STAPHYLOCOCCAL ENTERITIS DURING STREPTOMYCIN THERAPY

SIR,—At the end of the case-report admirably presented by Mr. Kramer on Oct. 23, I was surprised to find in the summary the suggestion that "the *Staph. aureus*, already present elsewhere in the body, was rendered streptomycin-resistant by the small amount of the drug absorbed from the gut."

In the absence of proven facts the subject is one for speculation; but it is of great clinical importance. My experience is limited to penicillin, about which similar suggestions are frequently made. I find regularly after giving normal dosage of penicillin for 2 or 3 days in proper cases and failing to obtain improvement, that a characteristic defervescence by crisis is obtained by doubling or quadrupling the dose. I would submit that clinical experience in this and other ways is against the theory of education of a bacterial strain to immunity to penicillin.

By an interesting coincidence, in the same number of THE LANCET Dr. Barber and Dr. Rozwadowska-Dowzenko find "that it has not so far been possible to train a staphylococcus in vitro to destroy penicillin." Furthermore, in Mr. Kramer's case, the staphylococcus causing conjunctivitis was present on the face and was therefore being ingested before penicillin or streptomycin was administered. Why then did it not cause the fatal enteritis at that stage? Is it suggested that small doses of streptomycin not only produced insensitivity to the drug but enhanced the virulence?

I believe Mr. Kramer's second suggestion to be nearer the truth—"that elimination of the normal intestinal flora may have contributed to the establishment of the staphylo-

coccus there." Such elimination was in fact proved. It is accepted that the normal intestinal flora is essential to health; and this flora is profoundly disturbed under the influence of chemotherapy and antibiotics. Intestinal disturbances, sometimes serious in children, often seem to occur during the period of relative sterility of the canal. Research on this problem might well lead to interesting and clinically useful conclusions.

Royal Infirmary, Sunderland. D. ASTLEY SANFORD.

DENTURES AND ANÆSTHESIA

SIR,—Are there not two simple ways of obtaining airtight fit for edentulous patients, which do not require special apparatus or expose dentures to risk of fracture? A swab of normal theatre size packed into each cheek around the airway or tube (unless the nasal air passage is ensured) will bring the face to a good round contour, over which a face mask fits well. A really large face-piece of the old conical, unmoulded type will "sit" so far out on the face that the edentulous collapse is usually avoided, and a good fit is far more likely than with any of the patterns of small mask. Unfortunately these large masks are now difficult to buy. The principle of fitting the bony margin of the face is the same as Mr. Phillips is applying with his inhaler.

London, E.11. J. BARNARD.

CRISIS ON QUALIFICATION

SIR,—The annotation entitled The Prentice Practitioner in your issue of Oct. 23 has aroused considerable interest among some who hope shortly to be the object of the arrangements proposed by the Minister of Health. The writers of this letter are students of a London hospital who have had their medical studies interrupted by six or more years of war service and feel considerable concern over that part of their training which will begin as soon as they qualify.

In the next twelve months a considerable number of ex-Service students will be finishing their undergraduate courses at the various medical schools and colleges; and the following year this class of students will amount to about half the total qualifying. Still another year later the proportion will be even higher. The average age of ex-Service students on qualification is, or will be, about 30. It is realised that in a few years, although a small ex-Service element may remain because of conscription, the age will be considerably less. Owing to their age, this present group (a result of the recent war) has certain problems which deserve consideration when such schemes as the present one are worked out.

Many of these students are married and have children; and, although the Ministry of Education is paying maintenance grants to most of them, nearly all of them are suffering real financial hardship, as their gratuities and savings are soon exhausted. On qualification these grants cease abruptly, so that, unless some measures are instigated in the immediate future, very few will be able to apply for house-appointments, which are a necessary part of medical training. The present rate of pay for house-appointments will almost entirely preclude those who have a family to feed, clothe, and educate from applying for such appointments. By the simple consideration of averages, the ex-Service group must contain a number of men of ability. Many, too, were trained for, and held positions of, considerable responsibility in various arms of the Services. Surely any such ability, training, and experience will have its uses in the profession. It will be regrettable if a certain number of men from sheer necessity short-circuit some aspects of their training and offer their services to the highest bidder.

We feel most strongly that the salary for house-appointments should be uniform throughout the country and that there should be a definite scale, taking into consideration such factors as age, and number of dependants. The Minister of Education has adopted a scale for students' maintenance on these lines, and the Services, too, pay their personnel in a similar manner.

After house-appointments, those of us entering general practice will welcome the latest suggestion for further training under experienced general practitioners. With regard to the salary mentioned by you and to which the Insurance Acts Committee has objected, we feel that this is not, in all conscience, too liberal. The principal will have, as you point out, fully qualified, enthusiastic assistance and all that this means to someone who must be feeling the effects of a life of unstinted labour. From the assistant's point of view, he will almost certainly have to take temporary furnished accommodation for his family, which alone will cost him at least five guineas a week. (We know, we have had to pay it.)

These are hard facts and not flights of fancy which we have put in this letter. We appreciate that it is easy to criticise and difficult to construct, but we hope that by raising these problems we may enable the highest standards in medicine to be maintained by ensuring that the newest members of the profession may follow the excellent paths which have been, and are being, laid down for them.

J. M. BROWN
W. A. BULLEN
G. DOUGAN
I. F. G. MCLANNAHAN
J. F. TRUNCHION.

RETURN TO PHILANTHROPY

SIR,—In last week's leading article, is the sharp antithesis between "the enthusiastic gatherings of the hospital contributory schemes of a decade ago" and the meetings of a regional board quite justified by the structure of the new organisation? The contact with the people is through the management committees rather than the regional board.

Camberwell provides an example. Ten days ago the mayor presided over a large and representative gathering of voluntary workers in, and friends of, the three hospitals (formerly L.C.C.) of Dulwich, St. Francis, and St. Giles. Mr. Lesser, chairman of the Hospital Saving Association, accompanied by many of the local group secretaries, spoke in advocacy of the formation of the Camberwell Hospitals Fellowship, which was constituted by those present. The fellowship will be formed by various groups and friends of the hospitals. Patients will be the first group, under the guidance of the Vicar of Camberwell, who has been a patient. Librarians, who are already doing excellent work for the patients and other voluntary workers in various capacities, will elect their representatives to form, with representatives of the patients, the governing council of the fellowship. Thus there will be a representative organisation to which the management committee can render an account of their stewardship annually. As patients will have a preponderant voice it will represent the "consumer interest" which can only be found with much difficulty in other public-service undertakings.

C. E. A. BEDWELL
Chairman,
Camberwell Hospitals Management Committee.
Dulwich Hospital, London, S.E.22.

Public Health

Mobile Dental and Medical Units

PROMPTED by the unsuitability of some of the existing temporary dental clinics, Kent County Council's primary-education and welfare subcommittee has recommended that a mobile clinic should be provided for the school health service in country districts. The units, of which there are likely to be three, will be drawn in turn by a single "mechanical horse." The trailer portion will contain a waiting-room, surgery, and recovery room, and will have its own X-ray apparatus and electrical system. Where a mains supply is unobtainable, water will be drawn from built-in tanks.

The *Empire News* (Oct. 24) reports that a travelling surgery will soon be operating in the rural district of New Earswick, Yorkshire. A caravan, drawn by a shooting-brake, will be partitioned into a reception room, a consulting-room, and two small dressing-rooms. The surgery is being sent out by the Rowntree Village Trust with the backing of the Ministry of Health; and if it is successful further units of the same sort may be introduced.

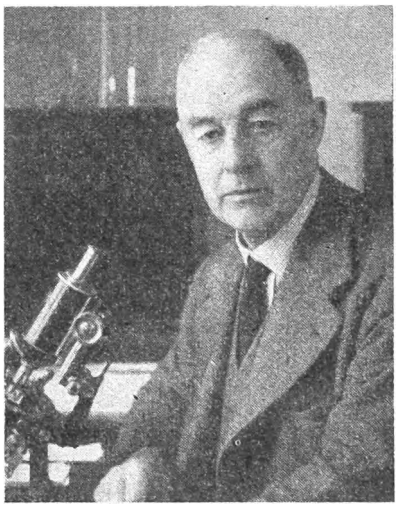
Obituary

CHARLES MORLEY WENYON

C.M.G., C.B.E., M.B., B.SC. LOND., F.R.S.

Dr. C. M. Wenyon, who died in London on Oct. 24, was one of the greatest authorities on medical protozoology. He was born at Liverpool on March 24, 1878, but spent most of his childhood in China, where his father, Charles Wenyon, was a pioneer medical missionary. At the age of 14 he was sent back to England to be educated at Kingswood School, Bath. Later he went to Leeds University, and then to London where he studied at University College and Guy's Hospital, graduating as B.SC., with protozoology as a special subject, in 1901, and M.B. in 1904.

In 1905 he was appointed to the first post of lecturer in protozoology at the London School of Tropical Medicine, where he worked under Patrick Manson. In the years that followed he continued his studies in protozoology at Munich and in Paris, and collaborated with the late Sir Andrew Balfour at the Wellcome Tropical Laboratories in Khartoum. He also undertook a number of scientific expeditions to Africa and the Near East: working in a floating laboratory on the Nile, he investigated protozoal diseases in the Sudan, and later he studied leishmaniasis in Bagdad, Aleppo, and Malta. On his return to England in 1914, he was appointed director of research in the tropics to the Wellcome Bureau of Scientific Research. During the war of 1914–18 he conducted classes in protozoology for Army medical officers, and as a member of the Medical Advisory Committee in the Near East visited Egypt, India, and Mesopotamia, where he worked on amœbic dysentery and other protozoal infections. He was subsequently appointed consultant in malaria with the British Salonika Force, and after the war became consulting pathologist to the Army of the Black Sea. He came back to England in 1920, and in 1924 succeeded Sir Andrew Balfour as director-in-chief of the Wellcome Bureau of Scientific Research, later becoming director of research in the Wellcome Foundation—a post which he held until 1944. On retiring from the directorate he maintained his connexion with the foundation as consultant in tropical medicine.



Wenyon's scientific activities, lasting half a century, were not restricted to the purely medical sphere. In fact his name has left an imprint on our knowledge of every group of parasitic protozoa in man and the lower animals. Before the first world war medical protozoology hardly existed, but at the beginning of the second war the relative medical importance of the different human protozoal parasites was fully established. This achievement was due largely to the pioneer work of Wenyon. In Egypt he examined the incidence of amœbiasis and other intestinal protozoal infections, with special reference to carriers of *Entamœba histolytica* and the epidemiology of amœbiasis. Much of our understanding of the intestinal flagellates and their relation to man is due to his investigations. Of the five species now known to parasitise man, two (embadomonas and chilomastix) were discovered by him. These investigations were brought together by Wenyon and O'Connor in a book on *Human Intestinal Protozoa in the Near East* (1917). Wenyon was the first to describe the exogenous development of the human coccidium, which he named *Isospora belli*, and his subsequent researches on the coccidia of dogs and cats brought order out of our confused knowledge of these parasites. He was the first to establish the coprozoic nature of certain amœbæ and flagellates found in human stools and often mistaken for genuine human parasites. He made important contributions to our knowledge of the leishmanias and trypanosomes and the diseases caused by them. He revised the classification of the Trypanosomidæ and described their cytology, while his work in the Mediterranean area served to elucidate the epidemiology, course of infection, and diagnosis of the leishmaniases; he was the first to find leptomonad flagellates in the sandfly. While working in Macedonia, he made valuable investigations on malaria, dealing with its epidemiology, transmission, and treatment, and with mosquito suppression. His experimental studies on the development of malaria parasites in mosquitoes at low temperatures served to elucidate the behaviour of the parasite in the hibernating vector and to account for the occurrence of outbreaks of malaria in the spring.

The most important single work published by Wenyon is his *Protozoology*—a treatise of two volumes, profusely illustrated, which appeared in 1926. This work gives the most complete account of all parasitic protozoa of medical, veterinary, and general parasitological importance. Unlike most textbooks, it synthesises knowledge of the subject and reflects the author's erudition and vast practical experience.

Not the least of Wenyon's achievements was the development of the Wellcome Bureau of Scientific Research (now the Wellcome Laboratories of Tropical Medicine) from a modest information centre to a scientific institute with an international reputation, in which fundamental research in parasitology and tropical medicine is carried out.

As editor of the *Kala-Azar Bulletin*, and subsequently sectional editor of the *Tropical Diseases Bulletin*, during the last 36 years Wenyon contributed authoritative critical reviews of world literature on leishmaniasis and other protozoal diseases. He was hon. secretary of the Royal Society of Tropical Medicine and Hygiene from 1920 till his election as president in 1945. For a quarter of a century he was the guiding spirit of the society, which has risen to its present position largely through his energy and perseverance. He was also instrumental in making the society's *Transactions* an important medical journal of international standing. As a person, he was ever ready to help others with his advice, which was sought by workers all over the world. He was essentially modest and tolerant, and to colleagues under him he was *primus inter pares*.

Wenyon's work was recognised by many awards and honours. For his services in the first world war he was appointed C.M.G. and C.B.E.; in 1927 he was elected a fellow of the Royal Society; in 1933 he became officier de la Légion d'Honneur; in 1945 he was elected hon. life member of the New York Academy of Sciences; in 1946 he was awarded the Theobald Smith gold medal of the American Academy of Tropical Medicine; and last year he was elected hon. fellow of the Royal Society of Medicine and was awarded the Manson medal of the Royal Society of Tropical Medicine and Hygiene.

C.A.H.

To his colleagues Wenyon was more than a protozoologist; he was a great leader in the affairs of men, and there are many who relied upon his sane pronouncements and his wisdom. It was a sad day when, some 34 years ago, he decided to leave the London School of Tropical Medicine with which he had been connected for the 10 previous years. In that comparatively short time he had established his department on a firm basis and had contributed very substantially to the fame and prestige of this school. In my judgment his most solid contribution was to the Royal Society of Tropical Medicine; he founded Manson House as the home of what he forged as a great society. Wenyon will always be remembered as its architect. His management of the society's *Transactions* made of them a journal of the highest order.

No-one could have preserved a more friendly outlook to his colleagues and to those around him, however humble. He refused to be led into intrigues or entangled in quarrels. He was a very brave man. The qualities of courage and endurance he showed on many occasions during the first world war, and in a high measure during the long and painful years which preceded his death.

P. M.-B.

The obscurities of protozoal life-cycles produced a considerable literature of controversy and some false starts. Dr. Wenyon was indefatigable in his endeavours to keep the main path open, and he entered the polemic arena with a conscientious gusto reminiscent of his missionary origin. If one told him that these confusions would settle themselves in the course of time he would stoutly maintain that error was dangerous and should not be allowed to go uncorrected. He had an obstinate sense that things should not be let go by default. There was something realistic and practical in his approach to the scientific problems that occupied him and his contemporaries, and he did not take much interest in what he considered to be theoretical hair-splitting and vague or doctrinaire speculation. Indeed sometimes he seemed to inhibit his own advance by this sceptical turn of his mind. He was a generous and encouraging fellow-worker, and had a robust and unspectacular friendliness that endeared him to those who knew him well.

M. R.

Wenyon had a great personality. He was entirely unaffected and utterly honest, without a trace of cant or intellectual snobbery. Even the chance encounter with him never failed to warm and illuminate the day; maybe he would be jauntily swinging along the street, often with an old walking-stick; maybe he would be in his laboratory or at some meeting or social function; but always he could make time for a few moments' chat to relate some experience or to make some shrewd comment that sent one on one's way refreshed, stimulated, and informed. Always was he willing to discuss problems, to examine specimens or material, and help any who sought his never-failing aid; but much of his help was not fully realised even by those who benefited most from it. For example, he gave untold hours to reading, correcting, and polishing manuscripts submitted by less experienced and meticulous authors to the *Transactions* of the Royal Society of Tropical Medicine and Hygiene, and other journals with which he was concerned; and many writers and countless readers owe more than they know to his advice and labour.

I have never heard a single person make an unkind comment concerning him—a measure of affection and a testimony to real greatness.

F. M.

ALBERT EDWIN HAYWARD PINCH

M.D. BRIST., F.R.C.S., M.R.C.P., D.M.R.E.

Mr. Hayward Pinch, who died at Bideford on Oct. 14 at the age of 81, was the first medical superintendent of the Radium Institute, London, a post which he held for 21 years.

He received his medical education at Bristol and St. Bartholomew's Hospital, taking the Conjoint qualification in 1894. At Bristol he had been first entrance scholar and he also held the Suple and Clarke scholarships, and he later became an assistant lecturer in physiology at Bristol University College. At the Army Medical College, to which he went after receiving a commission in the Indian Medical Service, he continued to carry off awards and received in turn the Fayrer, De Chaumont, and Montefiore prizes, and the Herbert scholarship. In 1896 he took his F.R.C.S., and he served for a period as a surgeon specialist in Bengal. After returning to this country he held the posts of superintendent and lecturer in pathology at the London Medical Graduate College and Polyclinic and pathologist to the Alexandra Hospital for Children with Hip Disease. But he became more and more interested in the new specialty of radiotherapy, and Sir Frederick Treves, who was the first president of the Radium Institute, persuaded him to accept the appointment of medical superintendent there in 1909. Thus he became the first whole-time research clinician in the specialty. His annual reports of the work of the institute were more than records of successful achievement; they were also guides in brief to contemporary advances in the treatment of disease with radioactive matter. Cautious in his assessment of results and alive to the dangers of the new technique, he characteristically ended an address to the Medical Society of London with Talleyrand's words: *Pas trop de zèle.* His *Clinical Index of Radium Therapy* appeared in 1925 and *Superficial Radium Therapy* two years later. He was also the author of a *Manual of Technique in Radium Therapy.*

When the work of the institute was reorganised in 1930 on its affiliation with the Mount Vernon Hospital, Mr. Pinch, whose health was poor, felt unable to undertake the additional burden. The committee appointed him consulting surgeon to the institute in appreciation of his services during his long tenure of office. He spent his retirement happily in his native West Country, and a colleague writes: "He was full of abounding vitality, and despite exalted Harley Street prognosis, the invalid survived for 18 years. Kind and generous, he was a sound clinician, especially good on eyes. Golf was one of his enthusiasms, and he was also a keen salmon fisher and a lover of Deeside where he spent a month every year."

THE LATE SIR BRUCE BRUCE-PORTER

L. K. writes: "As perhaps his oldest friend I may be allowed to mourn, with many hundreds, the passing of B.-P. His vital principle was his vivid and brilliant enthusiasm for that which he believed to be right, thus he harnessed his dream of helping others to the chariot of practical endeavour. His chief characteristics were his wholehearted devotion to his patients, regardless of all personal consideration of leisure or fatigue, and his contagious optimism. Never idle, he was always willing to help anyone over a stile and to take infinite trouble in so doing. He bore the last six months of suffering with fortitude and grace, until 'out of the stress of the doing, he has passed into the peace of the done.'"

Births, Marriages, and Deaths

BIRTHS

BLANSHARD.—On Oct. 24, in London, the wife of Dr. Paul Blanshard—a son.

BRAINES.—On Oct. 28, in Jersey, the wife of Dr. F. M. Braines—a son.

BRAND.—On Oct. 22, at Vellore, India, the wife of Mr. Paul Brand, F.R.C.S.—a daughter.

ELLIOTT.—On Oct. 24, at Reading, to Dr. Katherine Elliott, wife of Mr. A. M. Elliott—a daughter.

HOLMES.—On Oct. 25, at Edgware, the wife of Dr. S. W. Holmes—a son.

JONES.—On Oct. 29, at Morden, the wife of Dr. G. Lewis Jones—a daughter.

KELLY.—On Oct. 28, at Cheam, the wife of Mr. Patrick Kelly, F.R.C.S.—a daughter.

LOGIE.—On Oct. 26, at Aberdeen, the wife of Mr. N. J. Logie, F.R.C.S.—a daughter.

LOW.—On Oct. 26, the wife of Dr. M. G. Low—a son.

MASON.—On Oct. 13, the wife of Dr. H. A. C. Mason—a daughter.

NICHOLSON.—On Oct. 30, at Harrogate, the wife of Dr. B. Clive Nicholson—a son.

RICHARDS.—On Oct. 20, at Tripoli, the wife of Major H. J. A. Richards, R.A.M.C.—a daughter.

SCOTT.—On Oct. 25, in London, the wife of Dr. Oliver Scott—a daughter.

WHITTAKER.—On Oct. 24, to Dr. Margaret Morgans, wife of Dr. Norman Whittaker—a son.

MARRIAGES

FAIRBURN—NICHOLSON.—On Oct. 23, at Bangor, co. Down, Ernest Alfred Fairburn, M.D., to Margret Isabel Nicholson.

HUNT—HALEY.—On Oct. 29, at Hampton, Middlesex, Jack Naylor Hunt, M.B., to Anne-Claire Haley.

DEATHS

BREWS.—On Oct. 28, in London, Richard Vincent Brews, J.P., L.R.C.P.I.

BRIND.—On Oct. 23, at Gorran Haven, Cornwall, Harry Hanslow Brind, M.R.C.S., D.P.H.

BULLMORE.—On Oct. 29, in London, Edward Augustus Bullmore, F.R.C.S.E., aged 73.

GROSSART.—On Oct. 23, Robert Kerr Grossart, M.B. Glasg., D.P.M.

MACKINNON.—On Oct. 25, in London, Donald Mackinnon, M.B. Glasg.

MITCHELL.—On Oct. 26, at Bexhill, Ernest John Drum Mitchell, M.A., M.B. Camb.

PATERSON.—On Oct. 22, at Millbrook, near Plymouth, Alexander Cowie Paterson, M.B. Aberd., D.P.H.

WENYON.—On Oct. 24, 1948, in London, Charles Morley Wenyon, C.M.G., C.B.E., M.B., B.SC. Lond., F.R.S.

Parliament

The New Session

ON Oct. 26 the King opened the new session with the full splendour of ceremonial which has been in abeyance since 1938. The main legislative proposal mentioned in the Gracious Speech was, of course, the controversial Bill to nationalise sections of the iron and steel industry, but other useful and important measures foreshadowed included a Bill to establish national parks, and improvement of the law relating to footpaths and access to the countryside as well as the better conservation of wild life. A housing Bill will provide for the improvement of existing dwellings by local authorities or private owners.

No mention was made of the promised Bill to amend the National Health Service Act to meet points raised by the medical profession, but it is expected that this matter will also be dealt with during the current session. Legislation is promised modifying the constitution and powers of the General Nursing Council and to provide for the better training of nurses. This measure will follow the recommendations of the Working Party's majority report that nurses in training should have full student status, a shorter but wider training, and a 40-hour five-day training week, and that the council should be reconstituted.

To secure the supply of safer milk a Bill will be introduced compelling retailers in certain areas to sell milk of a required quality; but the pace at which this measure can be implemented will depend on how soon pasteurisation plant can be provided.

Debate on the Address

In the debate on the Address in the House of Lords on Oct. 27 Viscount SAMUEL hoped that the Government would give speedy attention to Lord Beveridge's recent report on voluntary agencies, and Viscount HALL, on behalf of the Government, agreed that this report was well worth examining. Reviewing the legislative programme of the past three years, the noble Viscount said that the new social insurance schemes were well on their way, and benefits were beginning to be realised by the people. The same thing might be said of the Health Service, for already there was abundant evidence that the scheme was working smoothly. The many prophecies of its breakdown had proved to be wrong, for over 90% of the population had chosen doctors, and doctors had agreed to accept them.

Lord ELTON, supporting the plea for national unity in view of the international situation, suggested that a Government might shrink from some unpopular course if the consequent odium was likely to fall on it alone, and a Government which faced difficulties realistically might well be compelled to consider not "guns before butter," but at least "guns before orange juice and free spectacles." When that time came it might be easier for Ministers to take the steps which they themselves judged necessary, not by way of conflict but by way of national coöperation.

QUESTION TIME

Spectacles and Prescriptions (Cost)

Sir ERNEST GRAHAM-LITTLE asked the Minister of Health what was the cost to date of the provision of spectacles and pharmaceutical benefits, including medical prescriptions, and dental services, including the supply of dentures, under the National Health Service Act, 1946.—Mr. ANEURIN BEVAN replied: The actual payments for the provision of spectacles, including fees paid for sight-testing, and for pharmaceutical benefits including medical prescriptions, up to Sept. 30, amounted to £981,951 and £1,905,447 respectively. These figures do not include the provision of spectacles or medicines through the hospital service. The payments for dental treatment amounted to £1,232,057. This figure does not include the cost of dental treatment provided through the hospital service.

Notes and News

SOCIAL AND ECONOMIC RESEARCH

NEARLY two years ago a standing Interdepartmental Committee on Social and Economic Research was established. Mr. George North, LL.D., the Registrar-General, is the chairman, and the members, who include Prof. G. A. Clark, M.D., are drawn from the academic staffs of the universities and from Government departments.

In their first report [1] the committee point out that, as Governments become increasingly involved in social and economic questions, the administrator within departments has a greater need of the knowledge which social and economic research supplies. Conversely, as the area of Government activity expands, the outside research-worker becomes increasingly dependent upon the factual raw material which departments collect for their own purposes. The committee are therefore examining the material which departments collect, the extent to which it is or can be made available, and whether there are any fields of statistical or other information in which a change in present methods of collection or treatment might benefit departmental or other research-workers. Subjects on which they give their views include the preservation of documents (and making their existence known) and the confidentiality of Government information: they believe that information of general social utility should not be kept confidential unless there is some good reason. They are already taking steps to make available to research libraries papers which, though not confidential, are too detailed or too limited in interest to justify publication. One of their principal functions, they feel, is to stimulate all forms of collaboration, whether formal or informal, between the departments and research institutions.

CHRISTMAS SEALS

A HALFPENNY doesn't seem much; yet, by means of halfpence the National Association for the Prevention of Tuberculosis has carried on its work for nearly 50 years. The attractive Christmas seals with the double-barred Red Cross which are seen on so many letters and parcels at Christmas time have provided most of the association's funds, and about a quarter of a million pounds has been raised in 10 years. The money is used to carry on education in the prevention of tuberculosis, research, and social welfare work. In 3 years over a million booklets on such subjects as mass radiography, childhood tuberculosis, rehabilitation, and tuberculosis nursing have been distributed. Nearly 138,000 copies of the *NAPT Bulletin*, and more than 58,000 copies of their magazine, *Health Horizon*, have been issued. Refresher courses for doctors and social workers have also been arranged. The seals for Christmas 1948 are now on sale and can be obtained for 4*s*. per 100 from the Duchess of Portland, chairman, N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.

University of London

Prof. R. W. Scarff has been appointed to the Bland-Sutton chair of pathology at the Middlesex Hospital medical school from Oct. 1. He became reader in morbid anatomy and histology at the school in 1933 and the title of professor was conferred upon him in respect of his post in 1946.

The title of professor emeritus has been conferred on Sir Alexander Fleming, F.R.S., professor of bacteriology at St. Mary's Hospital since 1928, and on Sir Francis Fraser, professor of medicine at St. Bartholomew's Hospital (1920–34) and at the Postgraduate Medical School of London (1934–46).

Royal Society of Medicine

At a joint meeting with the Scientific Film Association to be held at 1, Wimpole Street, London, W.1, on Monday, Nov. 15, at 8 P.M., Dr. Pedro Belou, professor of anatomy in the faculty of medical sciences, Buenos Aires, will show his films on the Neuraxis.

London School of Hygiene

The following awards have been made to students of the 1947–48 course at the school for the academic diploma in public health:

Chadwick prize, Dr. P. M. Elliott; Hecht prize, Dr. G. Ladkin and Dr. N. S. Hepburn; Industrial Medical Officers' prize, Dr. P. M. Elliott and Dr. D. F. Eastcott.

The Duncan medal in the course for the diploma in tropical medicine and hygiene was awarded to Dr. Hing-Yui Mok.

1. Cmd. 7537. H.M. Stationery Office. Pp. 15. 4*d*.

Royal College of Physicians of London

At a comitia of the college held on Oct. 28, with Lord Moran, the president, in the chair, Dr. J. H. Sheldon, Dr. J. M. H. Campbell, Dr. E. R. Cullinan, and Sir Weldon Dalrymple-Champneys were elected councillors. Sir Weldon Dalrymple-Champneys was appointed Milroy lecturer for 1950, his subject being Undulant Fever, a Neglected Problem.

The following, having satisfied the censors' board, were elected to the membership:

Ian Anderson, M.B. Sheff., M. W. Arthurton, M.B. Lond., H. S. Baar, M.D. Birm., M.D. Vienna, D. W. Barritt, M.B. Lond., R. E. Beamish, M.D. Manitoba, A. C. Blandy, M.B. Camb., H. J. Boutourline-Young, M.D. Lond., R. J. K. Brown, M.B. Camb., J. A. Campbell, M.B. Camb., C. O. Carter, B.M. Oxfd, F. B. E. Charatan, M.B. Lond., J. A. H. Collyns, M.B. Camb., E. G. Cook, M.B. Lond., R. I. G. Coupland, M.B. Camb., R. H. Cutforth, M.B. Lond., D. F. Davies, M.B. Birm., D. M. Davies, M.D. Leeds, P. D. B. Davies, M.B. Camb., Walter Dickson, M.B. Manc., Alphonsus Dolphin, M.D. Dubl., B. V. Earle, M.B. Dubl., J. R. D. Eaton, M.B. N.Z., Ali El-Sayed Eissa, M.B. Cairo, H. L. Ellis, M.D. Camb., C. C. Ewart, M.B. Sydney, A. N. Exton-Smith, M.B. Camb., Walter Fabisch, M.D. Berlin, M.D. Palermo, D. A. Ferguson, M.D. Lond., H. V. L. Finlay, M.B. Edin., P. B. Fox, M.B. N.Z., T. T. Fulton, M.D. Cincinnati, M.B. Belf., Irving Gilbert, M.B. Lond., Shivapuje Veerabadra Setty Govinda Setty, M.B. Mysore, M. J. Greenberg, M.B. Camb., Christopher Gresson, M.B. N.Z., J. R. Harries, M.B. Lond., R. V. Johnston, M.B. Durh., E. C. B. S. Keat, M.B. Lond., J. O. Laws, M.B. Camb., A. G. Leishman, M.B. Camb., I. C. Lewis, M.B. Edin., G. H. T. Lloyd, M.B. Lond., Josephine M. Lord, M.B. Lond., L. C. Lum, M.B. Adelaide, R. H. G. Lyne-Pirkis, M.B. Camb., A. R. Lyons, M.D. Belf., R. K. MacCuish, M.B. Aberd., A. C. Macdonald, M.B. Glasg., George Macdonald, M.D. Lpool, L. E. McGee, M.B. Camb., J. K. Martin, M.B. Lond., Harold Miller, M.B. Lond., Irving Miller, M.D. Manitoba, E. H. Minors, M.B. Edin., Behman Sorab Moos, M.D. Bombay, A. A. Morgan, M.B. Lond., John Nash, M.D. Dubl., Siva Rama Krishna Padmavati, M.B. Rangoon, I. C. L. Patch, M.B. Lond., Somabhai Hirabhai Patel, M.B. Bombay, M. B. Pemberton, M.B. Witw'rsrand, Abdur Rahim Piracha, M.B. Punjab, E. MacL. Poulton, B.M. Oxfd, F. I. Rackow, M.B. Lond., D. H. Reilly, M.D. McGill, P. K. Renshaw, M.B. Camb., P. L. Robinson, M.B. Lpool, R. S. Savidge, M.B. Lond., Joseph Shein, M.B. Witw'rsrand, George Skinner, L.R.C.P., A. W. Sloan, M.B. Glasg., W. H. Smith, M.D. Melb., W. G. Spector, M.B. Camb., M. P. Spence, M.B. Camb., J. W. Stephens, L.R.C.P., J. P. P. Stock, M.D. Brist., D. H. P. Streeten, M.B. Witw'rsrand, J. L. Taylor, M.B. Manc., R. W. Temple, M.B. Dubl., H. R. Thomson, M.B. Lond., P. A. Thorn, M.D. Lond., Eric Waddington, M.B. Lond., D. C. Watson, M.B. Lpool, S. P. B. Way, M.B. Lond., William Whitaker, M.D. Leeds, J. B. Wild, M.B. Lond., H. B. L. Williams, L.R.C.P., I. G. Williams, M.B. Lond., F. B. M. Woodhouse, M.B. N.Z., D. G. Wraith, M.B. Camb., G. A. Wright, M.B. Wales, M.B. Lond.

Licences to practise were conferred upon the following 146 candidates (113 men and 33 women) who have passed the final examination of the Conjoint Board and have complied with the by-laws of the college:

M. S. M. Adams, Maureen B. Adams, D. A. Ager, D. D. Alexander, H. D. Alexander, J. D. Arneaud, N. O. Ascroft, K. A. Baker, K. L. Batten, D. F. Bedford, D. P. Belgrave, Silvio Benaim, G. R. Benett, Elizabeth Bennett, J. M. Bernstein, A. I. Berwitz, T. B. Binns, J. A. L. Bonnell, P. H. Bracewell, A. T. Broadbridge, Ena K. Bruck, R. J. Carey, J. K. Carter, W. I. Carter, J. A. Cheese, Ellen M. Chippindale, Montague Cohen, W. W. H. Colmer, Elizabeth D. Connan, W. E. Cooper, A. A. Craigen, Phyllis A. M. Crozier, D. A. Davey, D. H. Davies, G. J. Davies, Gwenhwyfar Davies, V. J. E. Davies, Nuala M. Dowdall, R. W. Doy, Shirley R. Drake, B. H. du Heaume, Gwenllian Edwards, A. A. Eley, Mary G. Ellis, H. B. F. Fairley, Jack Fine, C. A. Foster, Lois Gardiner, Robert Gardner, G. M. Gould, A. A. Graham, Edwina E Green, H. J. A. Hahn, D. C. Hall, J. A. H. Hancock, D. F. N. Harrison, J. M. Haughton, G. E. Haward, R. B. Heisch, A. A. Hobbs, P. H. Holden, C. I. Hood, J. C. Humber, K. M. S. Hume, Marjorie J. Ion, T. E. Jeffreys, Beryl M. Joles, C. R. Jolly, D. H. Jones, Miriam Kahn, M. A. Kalina, A. J. Karlish, Mohan Singh Kataria, Hari Ratan Ker, Eric Killey, G. S. Laing, Percy Lancer, B. H. Lawrence, Gerda Lewin, E. A. C. Lloyd, V. A. Lloyd, Mary Lloyd-Evans, F. A. H. Logie, R. H. Longton, J. A. Ludwig, Bernard Lytton, Elizabeth G. S. McDowall, Meherbanoo Hormasji Masina, Leela Menon, John Monckton, D. K. Morgan, D. McK. K. Muir, J. G. Neville, W. T. Newman, Anne Nunan, H. M. C. O'Driscoll, Jean M. Ottaway, K. L. Owen, J. J. Owies, Owen Parry-Jones, Jacqueline I. C. Payne, G. W. Pearce, M. C. Peterside, E. M. Poulton, D. G. Price, Margaret D. E. Quinet, B. W. Richards, D. F. Richards, J. L. Richards, W. R. Riley, I. R. L. Rose, Marian W. Ruscoe, D. G. Rushton, J. M. S. St. John, E. R. J. Sarfati, Habib Janmahomed Sayani, W. K. Schnarr, D. N. M. Scott Warren, R. G. Seager Thomas, S. A. V. Serviss, Pauline M. Seymour-Cole, P. W. Shillito, D. W. Smith, R. S. Sneath, D. H. K. Soltau, Margaret Speight, G. D. Starte, G. A. Steele, Mildred A. R. Stilson, Mary C. Sumption, R. L. H. Tasker, D. G. Taylor, Margery W. Taylor, Jindrich Tintner, D. A. T. Tizard, Jean M. Tomlinson, J. T. Trencham, S. E. Trickey, P. G. Tuffnell, R. J. Vale, Jehangir Sohrab Vazifdar, Tom Wade-Evans, P. R. Wagner, Norma M. Whalley, F. R. H. Wrigley, J. R. W. Wynne.

Diplomas were conferred on those named in the report of the meeting of the Royal College of Surgeons in THE LANCET of Oct. 23 (p. 673). The following diplomas were also conferred:

D.O.M.S.—J. S. McKenty.
D.C.H.—M. F. Moses.
D.Phys.Med.—G. H. Dobney, D. M. L. Doran, Joan M. Gold, George Gregg, J. B. M. Milne, K. W. N. Palmer, J. D. Thompson, M. E. Wigfield, R. W. Windle.

Royal College of Surgeons of Edinburgh

At a meeting of the college held on Oct. 27, the following office-bearers were elected for the ensuing year: president, Mr. Frank Jardine; vice-president, Mr. J. M. Graham; secretary and treasurer, Mr. K. Paterson Brown; councillors, Dr. G. Ewart Martin, Mr. W. Quarry Wood, Mr. Walter Mercer, Prof. J. R. Learmonth, Dr. W. F. Theodore Haultain, Mr. R. L. Stewart; representative on the General Medical Council, Sir Henry Wade; conservator of museum, Mr. J. N. J. Hartley; convener of museum committee, Mr. W. Quarry Wood; librarian, Dr. Douglas Guthrie.

The following were admitted to the fellowship:

Alexander Adam, Ghanim Yacoub Akrawi, J. L. Anderson, J. H. H. Balmer, Narendra Chandra Banerjee, Aubrey Beiles, Solomon Bender, J. A. Bentham, T. A. Berry, Kalindi Ganesh Bhate, J. G. Bickerton, O. M. Brewster, D. T. A. Brown, J. C. McC. Browne, P. L. Brunnen, Samuel Burke, A. E. Burton, R. W. Busschau, T. S. Chalmers, HHimangsu Sekhar Chaudhuri, Kahan Chand Chopra, Daphne Wai Chan Chun, G. L. Clark, Harry Colman, P. U. Creighton, Kandarpa Tuljashanker Dholakia, W. A. J. Donald, J. W. Eadie, C. O. Easmon, Ahmed Fattouh Abdel Fattah, R. J. A. Fraser, J. R. Frylinck, Yogendra Lakshmidas Ganjawala, C. C. Gardner, Surajit Prosad Ghosh, I. E. W. Gilmour, M. A. Goodwin, Don F. de S. Goonawardena, Alexander Gonski, Walter Gordon, A. A. Haig, R. L. Hartley, F. J. Hedden, O. K. Hjertaas, A. R. Hodgson, J. M. Hoffman, D. W. Huish, Margaret A. Ingram, F. L. F. Innes, L. A. Jacobs, H. V. Jones, J. D. Joubert, C. V. Jumeaux, Rasiklal Mohanlal Kamdar, S. K. Kay, H. H. Kennedy, H. I. Le Brun, R. B. Lynn, Girija Shankar Das Mahapatra, C. B. R. Mann, W. B. Martin, Annamma Mathan, N. D. Matson, G. E. Mavor, Khushru Mancherji Mehta, B. F. Miller, R. J. V. Milner, G. P. Mitchell, Philip Moore, Salathiel Morgan, Ernest Morrison, E. L. F. McConnachie, Alasdair MacKellar, R. G. MacLeod, R. A. M. McVicker, J. D. O'Flynn, W. J. O. Page, A. T. S. Paul, A. M. Porter, Henry Proctor, Alexander Raxlen, Frank Riggall, E. L. S. Robertson, A. P. Sandrasagra, P. P. H. Schmidt, N. C. Scott, El Sayed Abdel Khalek Himmat Abou Shabanah, William Sillar, Appacutty Sinnatamby, E. W. O. Skinner, Arthur Skowron, H. A. Smith, W. F. Smyth, Ralph Spencer, H. M. Stevenson, W. B. Stirling, Bahman Sohrabji Surti, Geoffrey Sutherland, J. W. Sutherland, K. G. Symonds, L. R. Taylor, M. N. Teubes, L. W. Warcup, C. C. Wark, Samir Riad Wassef, Arthur Webb-Jones, W. F. White, A. E. Wilkinson, D. G. Wright, S. P. Wrightson.

Physiology of Vision

Prof. H. Hartridge, F.R.S., will give four lectures on this subject at Gresham College, Basinghall Street, London, E.C.2, on Monday, Wednesday, Thursday, and Friday, Nov. 8, 10, 11, and 12, at 5.30 P.M.

South East Metropolitan Regional Tuberculosis Society

The inaugural meeting of this society will be held at the County Hospital, Sevenoaks Road, Orpington, Kent, on Saturday, Nov. 13, at 11 A.M. Brigadier H. L. Glyn Hughes, senior administrative medical officer of the region, will speak, and all interested doctors in the region and particularly those engaged in chest work are invited to attend.

Retirement of Dr. Fairfield

Dr. Letitia Fairfield, whose retirement is announced, was a senior medical officer in the L.C.C. service, which she entered in 1912.

For some years, Dr. Fairfield, who is also a barrister-at-law, worked in the council's school medical service, first as assistant and later as divisional medical officer. In 1930 she was promoted to senior medical officer—the first woman to hold this rank—and since then she has been engaged mainly in the hospital and ancillary services. During the first world war she became woman medical director, Royal Air Force; and in 1919 she was appointed C.B.E. In the late war she was chief medical officer of the A.T.S. until 1942, when she reached the age-limit for this appointment.

Faculty of Ophthalmologists

On Oct. 8 the council considered the question of fees for ophthalmic examination of school-children. When it was discovered that extremely high figures were being claimed in fees for this work, the Ministry of Health, after communication with the hon. secretary of the faculty and the British Medical Association, issued a circular postponing all payments until a figure had been agreed. At a meeting of the ophthalmic subcommittee of the Negotiating Committee with the Ministry of Health it was agreed that the school medical service should come under the hospital service by March 31, 1949, and that in the meantime a fee of £6 6*s*. per session should be paid, subject to Treasury approval. In spite of the strong recommendations of the delegates at this meeting, the Minister remained adamant that glasses prescribed privately should not be obtained free within the service.

It has been agreed that opticians working under the Supplementary Ophthalmic Service should refer to ophthalmic surgeons all patients who do not achieve a visual acuity of 6/6.

Medical and Dental Defence Union of Scotland

In this union's report for the year ended Aug. 8, the membership is given as 6096—an increase of 191 over last year's total. Assets amount to over £37,000, representing a reserve per member of £6 2*s*. 4*d*.; and the cost per member during the year was 15*s*. 10¾*d*., leaving a balance, out of each £1 subscription, of 4*s*. 1¼*d*.

Manchester Regional Hospital Board

On Oct. 26 the board, as reported in the *Manchester Guardian* of Oct. 27, decided to submit for the approval of the Minister of Health estimates of expenditure for 1949–50 amounting to £12,906,248. Of this sum £696,258 represents capital expenditure. Under the heading of maintenance account, the cost of the board's central administration is put at £61,500; and other direct expenditure at £784,500. Costs of central administration of hospital management committees are estimated at £235,240, and of their general maintenance at £11,128,750.

London Hospital Dinner

Presiding over the old students' dinner in London on Oct. 28, Mr. Robert Milne welcomed back the women students who had "come to the rescue" in the 1914 war, and who now attended the gathering for the first time. In a chronicle of events since the last dinner he spoke of losses to the hospital by the death of Cecil Wall, George Riddoch, and G. T. Western, and by the retirement of W. S. Herm n, Arthur Burrows, Charles Goulden, John Parkinson, H. S. Souttar, and Ashley Daly. Of retirement he remarked that when for many years one has spent three or four half-days (not "sessions") at hospital, and then stops, one can find life very pleasant. Among new appointments, he mentioned especially the return of Victor Dix to be professor of surgery, and Dorothy Russell's appointment to the chair of pathology—in succession to a man who was consecutively known as H. M. Turnbull, Dr. Turnbull, Professor Turnbull, and The Chief, and was entitled to all four names because he did four men's work. Permitting himself a single reminiscence, Mr. Milne then described a night in 1903 when Warner and Dawson's house-physician was operated on for appendicitis (he has lately written to say that he can still run after a bus) and soon afterwards a burglar had a stab wound of the heart sutured (he has lately written to say that he can still run after a bus, *and* catch it and has led a respectable life). People had the idea that hospitals are places to which patients go for perhaps four weeks, and then pass on; to which students go for perhaps four years, and then leave forever; a place where ships pass in the night. But this was not true: a hospital was a place of continuing friendships and lasting memories—memories of chiefs who bullied you when you were a house-man, and of housemen who bullied you when you were a chief. The London Hospital, for all its internal changes, still stood exactly where it did: and on emerging from Whitechapel station one could still detect the faint smell of coffee and human unwashedness described by Henry Bashford 38 years ago. The hospital's ambition was to produce a thoroughly sound doctor, to be depended on in emergency, who would do the right thing even if he didn't quite know why. It had produced great men of science, like Henry Head and Hughlings Jackson, but also men of great service like Barnardo and Grenfell. He had a faint fear that in the new system unselfishness and the spirit of service might be snowed under, but he asked his hearers to drink the hospital's health in the hope that they would continue.

Mr. Souttar proposed The Chairman, whom he praised as an example of something now lost—the general surgeon who has made a brilliant success as a specialist. He also mentioned qualities of character, familiar to all Mr. Milne's students, which made the response to this toast particularly warm.

Dr. R. J. Peters, deputy chief medical officer of the Department of Health for Scotland, has left for the United States where he is to attend the annual conference of the American Public Health Association. Dr. Peters will also attend, along with Dr. A. H. Gale of the Ministry of Health, a sub-committee on the control of infectious diseases set up by the committee on research and standards of the association.

CORRIGENDUM: *Dentures and Anæsthesia.*—As printed, the reference to acrylic resin in Mr. Phillips's letter last week (p. 708) was incorrect. His point was that acrylic resin is *not* opaque to X rays.

Appointments

BLAKE, H. E., M.A., B.CHIR. Camb., F.R.C.S., F.R.C.S.E.: plastic surgeon, St. George's Hospital, London.
WAMBEEK, W. G. L., M.R.C.S.: airport M.O., Middlesex County Council.

Guy's Hospital, London:
BEYNON, D. W., M.B. Lond., M.R.C.P., D.C.H.: assistant to director of department of pædiatrics.
HAFFNER, C. E. L., M.B. Edin., D.P.M.: registrar in department of psychological medicine.
REDMAN, E. G., M.B. Dubl., D.M.R.: registrar in department of diagnostic radiology.

St. Andrew's Hospital, London:
BOLGER, J. T., M.B. N.I.U.: asst. M.O., class I.
HAMILTON, J., M.B., D.A.: senior resident anæsthetist.

Diary of the Week

NOV. 7 TO 13

Monday, 8th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Mr. R. M. B. MacKenna: Dermatology in its Relation to General Medicine. (Part I.)
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. G. A. Mitchell: Autonomic Nervous System.
5 P.M. Mr. R. J. Ludford, D.SC.: Malignant Growths in Tissue Culture.
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8 P.M. Pathological meeting.

Tuesday, 9th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. J. Purdon Martin: Local Lesions of the Spinal Cord. (Part I.)
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. John Kirk: Topographical Anatomy of the Thorax.
5 P.M. Dr. J. E. Cates: Renal Function.
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. Harold Corsi: Scars.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.2
11.30 A.M. Dr. T. S. Littler: Physical Principles of Audiometry and Hearing-aids.
2.15 P.M. Dr. E. H. R. Harries: Respiratory Tract in Infectious Diseases.
CHELSEA CLINICAL SOCIETY
7.30 P.M. (South Kensington Hotel, 47, Queen's Gate Terrace, S.W.7.) Mr. John Hanby, F.I.S.CH.: Value of Chiropody in Foot Disabilities.

Wednesday, 10th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. W. D. W. Brooks: Recent Advances in the Treatment of Pulmonary Tuberculosis. (Part I.)
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. Cates: Renal Function.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. N. L. Lloyd: Placing the Impaired Worker in Industry.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow
5 P.M. Prof. D. M. Dunlop: Clinical Use of the Anti-histamine Drugs. (Finlayson lecture.)

Thursday, 11th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. W. H. Sheldon: Tuberculosis in Childhood.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Professor Kirk: Anterior and Posterior Abdominal Walls.
5 P.M. Mr. L. E. C. Norbury: Proctology Throughout the Ages. (Bradshaw lecture.)
INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5 P.M. Prof. W. E. Le Gros Clark, F.R.S.: Olfactory System and the So-called Rhinencephalon.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. L. Forman: Pruritus.
HONYMAN GILLESPIE LECTURE
5 P.M. Dr. T. A. H. Munro: Diagnosis and Treatment of Depression. (Edinburgh Royal Infirmary.)

Friday, 12th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Purdon Martin: Local Lesions of the Spinal Cord. (Part II.)
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. H. G. Hanley: Micturition.
5 P.M. Dr. H. F. Brewer: Blood Transfusion.
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION
2.15 P.M. (26, Portland Place, W.1.) Mr. Claud Mullins, J.P.: Psychiatry in the Criminal Courts. (Maudsley lecture.)
LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. R. Sleigh Johnson: Acute Respiratory Infections.

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CONTENTS

THE PERIOD OF TRANSMISSION IN CERTAIN EPIDEMIC DISEASES

AN OBSERVATIONAL METHOD FOR ITS DISCOVERY

R. E. HOPE SIMPSON
M.R.C.S.

From the Epidemiological Research Unit (M.R.C.), Cirencester, Glos

FOR the effective practice of public-health measures it is important to discover (1) when and for how long in any case of infection a communicable disease may be naturally transmitted to other persons; (2) the range of variability of this infective period; and (3) the maximal error of the method used.

A single over all measurement including all three factors is required, and this paper seeks to show how the simple observational methods practised by Budd and by Panum and Manicus in the nineteenth century, and by Pickles and others more recently, can provide this information for certain sorts of epidemic disease.

The method is based on the information derived from two types of measurement: (1) the time elapsing between receipt of infection and manifestations of illness—the incubation period—and (2) the time between the illness of one patient and the illness of those he has infected —the serial interval.

A hundred years ago Panum [1] stated clearly the simplest relationship of these two measurements—that, where they are equal, transmission is taking place at the time of the manifestations of illness.

"If it is now regarded as a rule that the contagion of measles requires between thirteen and fourteen days after its reception into the organism to develop the exanthem" —i.e., the incubation period=13–14 days—"and, as numerous experiences show, that there are usually thirteen or fourteen days between the time at which the exanthem appears on the patient and that at which it breaks out on his infected associates"—i.e., the serial interval=13–14 days —"it is then clear that the persons who are infected by him receive the contagion into their organisms at precisely the time when the exanthem is breaking out on him."

Panum does not pursue the significance of the relationship where the measurements are not equal, and at times appears to confuse the two, an easy enough confusion which the literature of epidemiology shows to be still not uncommon. Later records do not altogether support his observation of the identity of the incubation period and the serial interval in measles, and it is a study of the differences between the two which can reveal the position, duration, and variability of the period of transmission.

The underlying principle is simple. The serial interval in a disease with direct case-to-case transmission represents the interval from receipt of infection in one patient to the transmission of infection to others. The incubation period is the interval from receipt of infection to development of the symptoms of illness. The relationship between the two therefore fixes the time of transference of the infection in relation to the symptoms of illness of the first patient.

An illness may last a long time, and for the sake of precision some particular manifestation of the disease must be selected for the purposes of measurement, and there is an obvious advantage in measuring both the incubation period and the serial interval from the same manifestation. In this way, where one person has infected another, three points of time only will be involved:

A, receipt of infection by case 1
B, transmission of infection from case 1 and receipt of infection by case 2
C, the manifestation used as a measurement.

1. Panum, P. L. Observations made during the epidemic of measles on the Faroe Islands in the year 1846. New York, 1940.

The serial interval (indirectly) measures AB. The incubation period measures AC. It is simple to subtract the incubation period from the serial interval and so find BC, the interval between the chosen manifestation and the transference of the disease. It is well at the outset to be rid of any preconceptions about where, in relation to the clinical illness, the period of transmission will be discovered.

A very variable incubation period will introduce a factor which might well dwarf the period of transmission and stultify the practical utility of the method. The constancy of the incubation period depends on the stability in the cycle of the illness of the manifestation chosen for measurement, and the methods of making a wise choice are fully discussed below. Those acute exanthems which appear in successive crops of cases at a more or less constant interval clearly possess relatively small variability of their incubation period, and form suitable subjects for study by the present method. Nevertheless some symptoms in measles, for example, are far more variable in the time of their appearance than are others, and Panum commented on the stability of the time of appearance of the rash compared with that of the first onset of illness, and he chose the time of emergence of the exanthem as the manifestation for measurement of the incubation period and the serial interval.

NOMENCLATURE AND SYMBOLS

Epidemiological studies are often difficult to compare, even when they are similar, because of differing interpretations of the technical terms in use. For precision and comparability it has been thought necessary to define certain terms used here. The definitions are not claimed as final or universally applicable. The want of a nomenclature agreed by epidemiologists is, however, so pressing that it is to be hoped that one will not be long in appearing.

Study of the principle outlined above leads to a recognition of certain relationships which can most clearly and briefly be represented symbolically and mathematically. The following symbols will therefore be used:

d, point of measurement for a case
D, point of measurement for a group of related cases
K, serial interval
K′, median of individual values of K
k, range of variation of K
X, incubation period
X′, median of individual values of X
x, range of variation of X
Y, time elapsing between receipt of infection in receptor case and point of measurement d in donor case
Y′, interval between mid-point of period of transmission and measuring-point d
y, duration of period of transmission.

For comparison with other work, synonyms taken from epidemiological literature are supplied, and the reason is sometimes given for the choice of the preferred name. Inappropriate terms, if much used, have been included as "synonyms" of the correct term, with a note of the error.

A communicable disease is an example of host-parasite relationship and, from the viewpoint of the invading organism, is a part of the cycle of parasitism.

Cycle of parasitism (cycle of the infection): the natural history of an infecting organism, including means of access to and entrance into the human host, migrations, abodes, and morphological changes in the host tissues, means of egress, and transmission directly or indirectly to other human hosts, the biology of any intermediate stages, and the behaviour and destiny of any of the organisms remaining in the host after the period of transmission.

The necessities of reproduction and species-survival are closely linked with the phenomena of human illness,

individual or communal, especially perhaps in infection by obligate parasites. Hence it is wise continually to attempt a mental picture of the correlation between the cycle of parasitism and the human aspect of the relationship with which the remaining definitions are chiefly concerned.

Cycle of illness (disease cycle): the effects on the human host of parasitism by a particular species of organism or complex of organisms, including disturbances to health, periods during which he is infectious to others directly or through intermediate agencies, complications, sequelæ, any resulting change in resistance to the causal or to other species of organism, the duration and temporal relationships of these episodes, and their correlation with the cycle of parasitism.

The synonym "disease cycle" is rejected because it has also been used for the next conception.

Cycle of the epidemic (disease cycle): the course of an outbreak of infectious disease in a community.

Waves (epidemic waves; waves of the disease; waves of the infection): fluctuations in the morbidity due to a communicable infection in a community.

The following definitions relate particularly to the present method of intimate epidemiology:

Day of measurement for a case (symbol d−1): the day of occurrence of the sign chosen for epidemiological measurement. The day of measurement for a series of cases (d−1 in the initial case) is symbolised D−1.

Hitherto most analyses have been related to the day of measurement itself, sometimes written d_o. This is confusing in that the "measuring-point" occupies 24 hours, a disadvantage also found in block charts. When accurate dates can be secured with certainty, it is better to fix an arbitrary zero point from which to measure forwards and backwards serially, those days preceding the point being distinguished by a minus sign. The least disturbance to current methods is caused by selecting midnight after the manifestation chosen for measurement.

Point of measurement d *for a case* (zero point): midnight (24.00 hr.) on the day of measurement.

The *days of the disease* are then enumerated not from the usually unknown receipt of the infection but from d.

Point of measurement D *for a series of cases* is the zero point of the initial case, and the *days of the epidemic* are enumerated therefrom. Reference to the charts will make the system clear.

Attempts are often made to study infectiousness by the effect on small communities, such as households, of the occurrence of the first case of a disease, usually termed primary. Subsequent cases, if they fall about the expected interval from the primary case have been termed secondary, whether or no there is evidence that they were due to the first case. A modification of this usage is proposed here as follows:

Primary case: in respect of a single case, a group, or a series of cases of any size, the case giving rise to them.

Secondary case: a case arising directly from a known primary case.

Tertiary case: a case arising from a primary case through the mediation of a secondary case.

Quaternary case: a case arising from a known primary case through a secondary and a tertiary case.

The series continues indefinitely. For present purposes the problems of the carrier and of the inapparent infection are ignored. They will be dealt with when the principle of this work has been clearly established.

These more precise definitions are useful where access to the basic data is sufficiently intimate to make them workable, and they may reveal information concealed by including intervals between cases not causally connected. For remote work, based for instance on notifications, such terms as "first cases" and "second-group cases" might be substituted.

The word "wave" is often used to describe the successive crops of cases occurring, for instance, in measles, but is here reserved for those larger fluctuations of a disease where precision about case-relationships is impossible. In small epidemics it is usually possible to be definite that each crop forms a fresh "generation" of the infecting organism.

Second generation (secondary wave): the total crop of secondary cases derived from a primary case.

Third generation (tertiary wave): the total crop of tertiary cases derived from a primary case.

The series continues indefinitely. Each case is recorded at the point of measurement, and the time from the zero point of the first case of the crop to that of the last case is the duration of the generation. It will be shown below that this is an important measurement.

Serial interval K (transmission interval, incubation interval, case interval, wrongly incubation period): the interval between the measuring-points in a primary case and its secondary case.

The serial interval for a disease, an epidemic, or a group of cases is collectively described by $K' \pm \frac{1}{2}k$, where K′ is the median value, and k the range of variation of the individual serial intervals K. A second generation offers a direct measurement of $K' \pm \frac{1}{2}k$ from the primary case.

Incubation period X: the interval between receipt of infection and point of measurement d.

The incubation period in a disease or group of cases of any size is collectively described by $X' \pm \frac{1}{2}x$, where X′ is the median value, and x the range of variation of individual incubation periods X.

Period of infectivity (period of infectiousness or of transmissibility): the days of the cycle of illness during which the disease is naturally transmissible.

Period of transmission y: that portion of the period of infectivity during which transference of infection actually takes place in any case or group of cases.

The time elapsing between a single transmission of infection and the point of measurement d in any case is denoted Y. When it is possible to determine the duration of a period of transmission y, it is described in relation to the point of measurement by the formula $Y' \pm \frac{1}{2}y$, Y′ being the median of the individual values of Y—i.e., that measured from the mid-point of y.

The limits of the period of infectivity are difficult to ascertain, depending on correlation of the periods of transmission with the times at which exposed susceptibles consistently do not take the disease. The period of transmission usually does not represent the whole period of infectivity, for such reasons as (1) high infectivity exhausting the supply of susceptibles; and (2) severe illness removing cases from effective contact with susceptibles.

The study of the variability of these epidemiological measurements is of great importance, and the variation may be usefully divided into two groups:

Extraneous variability not attributable to the behaviour of the disease—e.g., that due to faulty memory, witnessing, observation, &c.

Inherent variability attributable to the disease—e.g., that due to variation in the incubation period.

In some diseases the extraneous variability can with care be reduced nearly to nil. The variation of the serial interval k will then be entirely inherent and will depend on two components only: (1) the variability x of the incubation period X; and (2) the duration of the period of transmission y. Thus:

$$y + x = k \quad \ldots \quad \ldots \quad \ldots \quad \text{I}$$

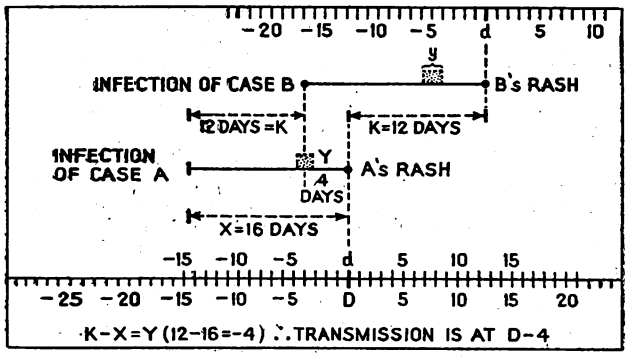

Fig. 1—Case A infects case B. Diagram shows that the serial interval K equals the time from receipt of infection by case A to transmission to case B. Use of formula K − X = Y gives day of transmission in relation to point of measurement d, X being the incubation period, Y the time between the transference of infection to case B, and d in case A.

It will be of interest ultimately to determine y separately from x. This will be part of the fruit of the painstaking collection of data giving direct knowledge of the variability of the incubation period and the whole duration of infectivity, and will perhaps be of most importance in the study of the biology of the infecting organism.

For duration of isolation or quarantine the total value of k—i.e., x + y—gives the requisite information, and for purposes of deliberate exposure to infection the mean figure K′ − X′ will serve until days of differing degrees of infectiousness have been decided precisely.

SIGNIFICANCE OF THE SERIAL INTERVAL: K

The serial interval K between the zero points in two cases, if the incubation period is the same in both, gives a precise indirect measurement of the time elapsing between receipt of the infection in the first case and receipt of infection in the second. If transference is direct from case to case; it therefore gives a measure of the time between receipt and transmission of infection in the first case (see fig. 1). The serial interval gives no information about the duration of the incubation period. Moreover, the time of transmission that it reveals is related to an unknown point—the receipt of infection. To be of practical use the information must be anchored to the known point, the point of measurement d, by the discovery of the incubation period X. Then K − X will describe Y, the point of transmission in relation to d:

$$Y = K - X \quad .. \quad .. \quad .. \quad II$$

The quotation from Panum might be summarised as follows:

$$Y = K - X = 13 - 13 = 0$$

i.e., transmission is taking place at d, the point chosen for measurement. If the incubation period had been found to be 4 days longer than the serial interval, clearly transmission would have been occurring 4 days before the point of measurement—i.e., on d − 4. Thus:

$$Y = K - X = 13 - 17 = -4.$$

If the incubation period was 10 days shorter than the serial interval, then

$$Y = K - X = 15 - 5 = 10$$

and transmission would be occurring on d 10—ten days after the zero point.

Simple as is this relationship, experience shows that it is wise to emphasise it clearly. The incubation period accurately and frequently determined could by itself provide the necessary information, but the incubation period is difficult to determine, and discovery depends on the relatively rare observation of "brief and only possible exposures," experimental infection, and correlation of numbers of longer exposures to find the common agreement between them. X is fairly readily determined for a few cases, but to find x (the range of variation) in a reliably large series is a formidable undertaking.

The serial interval K, on the other hand, is readily available and relatively easy to determine accurately. The range of variation x of the incubation period is less than that of the serial interval k because, as shown above, k = y + x. The period of transmission, y, will usually have a perceptible duration, and x must be smaller than k. In this way determinations of the serial interval can give some idea of the degree of variability of the incubation period; and, if k is small, x will be even smaller, and may in some circumstances be negligible.

CHOICE OF MOST SUITABLE MANIFESTATION FOR MEASUREMENT

To approximate as nearly as possible to a true value of y, it is important to have the minimal variability x of the incubation period, and the value of x depends entirely on the stability in the cycle of illness of the manifestation chosen for the purposes of epidemiological measurement. The selection is therefore a nice matter and deserves more attention than it has received.

The requirements are: (1) obtrusiveness and memorability, to reduce extraneous variability; (2) stability in the cycle, to reduce inherent variability; and (3) constancy of presence, to avoid "missed cases." Investigations with different objectives will lay differing emphasis on the relative importance of each factor. Obtrusiveness and memorability can be decided by common sense, and constancy by experience. Stability is tested by the value given by k. It is well to test all the possible manifestations, as follows:

Measles

Sign	*Median serial interval* K	*Variability* k
(1) Onset of illness	13 days ..	10 days
(2) Onset of rash	10½ days ..	5 days
(3) Fullest rash	10 days ..	4 days
(4) Onset of conjunctivitis ..	9 days ..	5 days

24.00 hr. on the day of the fullest development of the rash is chosen as d.

Infective Hepatitis

Sign	*Median serial interval* K	*Variability* k
(1) Onset of illness	28½ days ..	29 days
(2) Onset of jaundice	28 days ..	14 days

The onset of the jaundice is the better choice. Unfortunately it is possible that in some epidemics anicteric cases are not uncommon. The first appearance of unusual pigmentation of the urine might merit consideration in this way. (For details see table I.)

TABLE I—SERIAL INTERVALS K IN INFECTIVE HEPATITIS TO SHOW EFFECT ON VARIABILITY k OF CHOICE OF POINT OF MEASUREMENT

Case-interval no.	Points of measurement		Case-interval no.	Points of measurement	
	Onset of illness (days)	Onset of jaundice (days)		Onset of illness (days)	Onset of jaundice (days)
1	14	28	10	31	29
2	16	25	11	31	35
3	17	21	12	34	31
4	21	24	13	39	32
5	21	26	14	39	35
6	24	24	15	40	32
7	25	25	16	43	35
8	26	31			
9	28	23	—	k = 29 days	k = 14 days

These examples are purely illustrative of the principles and importance of the choice and, though taken from actual epidemics, are too few to make the result final. To emphasise the difference made by the choice, it is instructive to give an arbitrary value to y, say 7 days, in infective hepatitis. Then:

By choice (1), $x = k - y = 29 - 7 = 22$ days
,, ,, (2), $x = k - y = 14 - 7 = 7$ days

In words, if the infectivity lasts a week, the incubation period is three times as variable when measured to the onset of illness as it is when measured to the onset of jaundice.

Whatever manifestation is chosen for measurement should be stated precisely to make work generally comparable, and the opportunity should be given of testing the stability of the selected measuring-point against measurements made from other manifestations. It is advisable to determine the reliability of the different measuring-points in the same cases, and not to compare the stability of one point in one series of cases with that of another point in another series, at least until the stabilities have been determined for a very large number of cases.

SUCCESSIVE GENERATIONS OF AN EPIDEMIC

It is convenient at this point to turn from considering the incubation period and the serial interval as isolated measurements to interpret the behaviour of outbreaks of such diseases as measles in the light of the conceptions outlined above.

Primary Generation.—An outbreak usually begins with a single case, the primary.

Second Generation.—Each secondary case will fall at a serial interval K from the primary. The range of variation between these intervals gives a direct measure of k. $K' \pm {}^1/_2k$ is therefore determined directly. In an ideal epidemic with susceptibles inexhaustibly and effectively exhibited the period of transmission y would be maximal and would represent the whole period of infectivity.

Third Generation.—The third generation in such a "saturated" epidemic would erupt during precisely twice the duration of the second and therefore occupy 2k or 2 (x + y) days, however great the pool of susceptibles.

Fourth Generation.—This similarly can occupy no more than 3 (x + y) or 3k days.

The K : k *Ratio*

The erupting-time can only increase by one maximal value of k in each successive generation regardless of the abundance and temporal and geographical presentation of susceptibles. Therefore the number of successive generations which can appear without overlapping can be ascertained by the ratio between the (minimal) serial interval K and its inherent variability k. $K = nk$ where n gives the number of generations which will appear without overlapping.

The reason for this is that K : k also expresses the ratio between the time K taken to develop infectivity and its duration y and variability x; $K = n\ (x + y)$. If n is 1 or less, only the primary case will be distinct; if n is between 1 and 2, the second generation; if n is between 2 and 3, the third generation; if n is between 3 and 4, the quaternaries; and so on.

A comparison of the epidemic pattern predicted from the ascertained values of K : k with that actually observed is a useful indication of the completeness of the observations presented by an outbreak, and of the degree of "saturation"—i.e., the extent to which susceptibles have been infected throughout the period of infectivity. It is one of the methods of studying the degree of "infectiousness" of a disease and provides suggestive evidence of possible methods of transmission.

If several distinct generations of a disease appear, it may be said in broad terms that the incubation period is not very variable and the period of transmission short in comparison with the development of infectivity. The actual duration of the incubation period does not affect the phenomenon. If no clear serial pattern is perceptible, either the variability of the incubation period or the period of transmission or both are so great that their combined values equal or exceed the time taken to develop infectivity, or else the spread of the disease is not due to direct case-to-case transmission.

Geographical Synthesis.—Even after temporal overlapping of generations has happened it is sometimes possible, especially in a country district, to continue analysis of the separate generations by taking advantage of the spatial scatter of the cases that usually occurs. For example, a tertiary case in area 1 may become the primary case for area 2. The secondaries to which this tertiary case gives rise are the whole second generation for area 2, but are also a part of the quaternary crop of the epidemic arising in area 1. By recording on parallel charts it is simple to combine related cases from widely different areas into a geographical synthesis of the true extent of the later generations. The method demands intimate and comprehensive acquaintance with the conditions in the whole area if mistakes are to be avoided.

Evidence on K *and* k *Provided by Each Generation*

The second generation gives a direct expression of $K' \pm {}^1/_2k$.

For subsequent generations it should be ruled that no serial intervals may be directly inferred, even where serial infections appear to have taken place in households, except where the possibility of another source of infection can be certainly excluded. Measles, for example, is so infectious that it is usually unwise to be dogmatic about

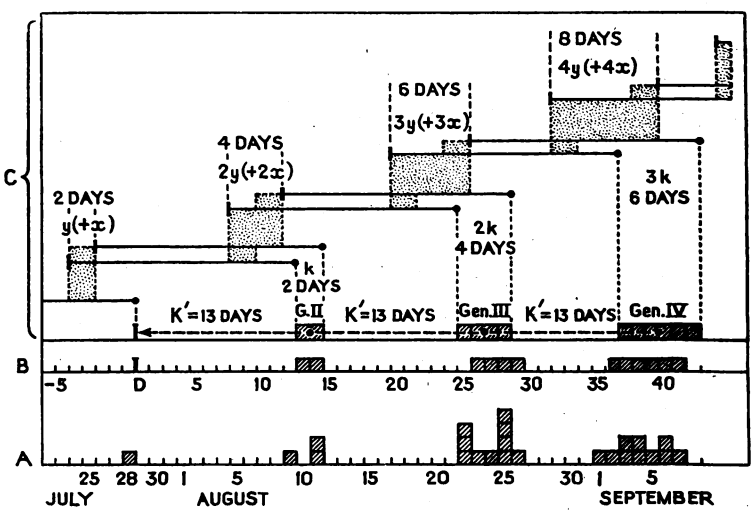

Fig. 2—A, block chart of epidemic (1947 M1) described in text; B, proposed method of charting same epidemic, using midnight on day of measurement; C, "model epidemic" illustrating temporal relationships described in text. Data were provided by epidemic illustrated in A and B; hence calculated epidemic blocked on lower line of C is comparable with actual epidemic in B.

Data: Incubation period X = 17 days
Variability of incubation period x = 0 days
Period of transmission y = 2 days
Median point of transmission Y' = d − 4 days.

Method is to draw first and last possible cases that could be infected from primary case—horizontal lines running from receipt of infection to d in each case—and to chart second generation therefrom. Process is repeated for each generation. Time during which each generation is transmitting organisms is shown by stippling. Duration of appearances of d in each generation is shown by shading on lower line.

TABLE II—SERIAL INTERVALS K AND THEIR VARIABILITIES k OBTAINED DIRECTLY (GENERATION 2) COMPARED WITH THOSE OBTAINED BY AVERAGING COMPONENT INTERVALS IN LATER GENERATIONS (SEE FIG. 2)

Generation 2	Generation 3		Generation 4	
Serial interval K (days)	D→d = 2K (days)	2K ÷ 2 (days)	D→d = 3K (days)	3K ÷ 3 (days)
12	25	12½	35	12
14	25	12½	36	12
14	25	12½	37	12⅓
Other direct values of K	26	13	37	12⅓
12	27	13½	39	13
13	28	14	40	13⅓
14	28	14	40	13⅓
14	28	14	41	13⅔
..	28	14	..	..
..	29	14½	..	..
k = 2 days	2k ÷ 2 = 2 days		3k ÷ 3 = 2 days	

which case in a preceding generation has infected a particular person. Experience will furnish a criterion of strictness with which to apply the rule in different diseases. Its intelligent application gives great value to any exceptions which may be allowable.

The weakness of basing conclusions on secondary cases in households without strong evidence that the patients were infected by the first case in the house can be understood by considering the steady expansion of the appearance-time of successive generations. In the first three generations such conclusions are not likely to be very misleading. Later in the epidemic, on the other hand, it is clear that two members of the same household might well both have been infected in the previous generation, and yet the first might develop the disease a fortnight before the second (see fig. 2).

Nor is it just to argue that the secondary cases in a household would have more early opportunity to contract the disease from another member of the household. This may be true of the first few generations, but later in the epidemic of a highly infectious disease like measles, if the first case in the household occurred late in a generation, the other members of the household might have been at risk for many days outside the household from those forming the earlier part of the generation.

Conclusions about times and methods of transmission, based solely on the occurrence of "secondary" cases in households are thus liable to grave error, and the more protracted the epidemic, the larger the possibility and degree of error.

There is, however, valuable evidence on K to be obtained from the tertiaries, because each, through one of the secondaries, is remote from the primary by the sum of two serial intervals. It has been said that the span of the generation should be 2k; hence the position and duration of the generation may be considered from D as $2K' \pm \frac{1}{2}(2k)$, and the fourth generation is $3K' \pm \frac{1}{2}(3k)$ in days from D. Numerous average values for K and k may thus be obtained for comparison with those observed directly. Some are shown in table II.

APPLICATION OF THE PRINCIPLE

At the beginning it was stated that this paper would describe an observational method of obtaining the dates and duration of infectivity, the variability of the infective period, and the maximal error of the method used. These desiderata have been symbolised as follows: median day of infectivity $d - Y'$; and duration of transmission y.

The error of the method is the same as the instability of the manifestation chosen for measurement, which is identical with the variability of the incubation period x. The variability of the infective period is contained partly in x and partly in y.

The over-all information that is sought may therefore be expressed symbolically as $Y' \pm \frac{1}{2}(y - x)$. It has already been shown that $y + x = k$, and that $Y' = K' - X'$. Hence the unknown position, duration, and variability of the period of transmission, and the error of the method, may be discovered from the observed serial interval and incubation period:

$$Y' \pm \tfrac{1}{2}(y + x) = K' - X' \pm \tfrac{1}{2}k \quad .. \quad \text{III}$$

The validity of the principle is self-evident. It remains to discover if any infectious diseases present a sufficiently large K : k ratio to make the methods fruitful in practice.

EXAMPLES

An analysis of a small epidemic of measles is given as a demonstration. No final conclusions about the limits and significance of any of the figures ought to be drawn until they have been correlated with large numbers of other outbreaks observed under similar conditions.

(I) *Epidemic (1947 M1)*

Primary case: on July 24, 1947, the schools being closed for the summer holidays, a girl, aged 4 years, incubating measles, probably taken from a contact 13 days before, came twenty miles to spend the holidays with a friend in a small village which had escaped measles for ten years, and which contained on that date only 29 persons, all children, not known to have had the disease. On arrival she showed signs of illness, but was not kept in bed until her rash appeared on July 27. The rash was fully developed next day; so midnight (24.00 hr.) on July 28 is d in this case and D for the epidemic.

Second generation: her friend and two little girls who played with her on July 25 and 26 are the only known susceptibles to have been at risk; d for her friend occurred on Aug. 9 and for the other two on Aug. 11. There are therefore 3 cases from D 12 to D 14:

$$K' \pm \tfrac{1}{2}k = 13 \pm 1$$

Third generation: 10 cases recorded from D 25 to D 29:

$$2K' \pm \tfrac{1}{2}(2k) = 27 \pm 2 \text{ (observed values)}$$

Fourth generation: 10 cases from D 35 to D 41:

$$3K' \pm \tfrac{1}{2}(3k) = 38 \pm 3 \text{ (observed values)}$$

Two of the susceptibles moved to another village, where they developed the disease. For simplicity they are excluded. Four of the presumed susceptibles were spared. No other cases derived from this epidemic occurred anywhere. The attack-rate of all susceptibles was 86%.

Fig. 2A shows the usual block chart of the epidemic with the method of measurement suggested in this paper superposed (fig. 2B).

Calculation: table II shows the serial interval as derived from the various generations and gives the figures for K and k. The accord is truly remarkable. The suggested incubation period of the primary case is accepted as valid for the present purpose of demonstration. The girl was infected 13 days before July 24—i.e., 17 days before d (July 28):

d is midnight (24.00 hr.) on day of fullest development of rash. Then $K' = 13$ days; $X = 17$ days; and $k = 2$ days.

$$Y' \pm \tfrac{1}{2}(y + x) = K' - X \pm \tfrac{1}{2}k = 13 - 17 \pm 1 = -4 \pm 1$$

Therefore $x + y = 2$ and Y' is at d − 4.

Therefore throughout this epidemic the measles was being transmitted from the fifth to the third day before midnight on the day of fullest development of the rash, d − 5 to d − 3.

It is instructive to take theoretical values of Y', X, and y and to construct charts of epidemics for comparison with those found by observation. In this way it was found that y of 3 days gave too big a value for each generation. A very close fit with the observed facts is obtained by the values

$Y' = 4$ days; $X = 17$ days; and $y = 2$ days (note that x is ignored). This model is fully set out in fig. 2c. The relationships illustrated should help to elucidate the definitions, formulæ, and statements in the text of the paper.

(II) *A Wensleydale Epidemic*

Dr. W. N. Pickles has kindly allowed me to use an epidemic recorded in his book [2] to show to what extent the method is applicable to precise records not specially collected for this type of analysis.

Second generation: 24 cases D 12 to D 15

$$K' \pm {}^1/_2k = 13^1/_2 \pm 1^1/_2 \text{ days.}$$

Third generation: 11 cases D 22 to D 27

$$2K' \pm {}^1/_2(2k) = 24^1/_2 \pm 2^1/_2 \text{ days.}$$

From data supplied: d is midnight (24.00 hr.) on first day of rash; $X = 16$ days; $K' = 13$ days (average value); and $k = 3$ days (average value)

$$K - X \pm {}^1/_2k = -3 \pm 1^1/_2.$$

Therefore the disease was being transmitted during a period extending from d $- 4^1/_2$ to d $- 1^1/_2$.

An approximate comparison with the other epidemic (1947 M1) is made by adjusting for the measuring-point d, giving an incubation period 24 hours longer. This gives the period of transmission from d $- 5^1/_2$ to d $- 2^1/_2$, strikingly similar to the other, with differences readily accountable to the use of a slightly less stable symptom for measurement. Too much importance ought not to be attached to the coincidence of results.

K : k *Ratios*

Epidemic 1947 M1:

$$K = nk$$
$$n = K \div k = 12 \div 2 = 6.$$

Had the epidemic continued, generation 6 might have been distinct.

Epidemic Wensleydale:

$$n = K \div k = 11^1/_2 \div 3 = \text{less than } 4.$$

By the method of measurement used it is doubtful if generation 4 would have been distinct from generation 5.

SUMMARY

A simple method of obtaining the date of infection in cases of some communicable diseases is provided by the serial interval and the incubation period.

The method can be extended to discover the period of transmission and its vagaries by a study of the inherent variability of the serial interval.

The importance of the measuring-point, and the principles guiding its wise selection are discussed and illustrated.

The relationships determining epidemic pattern are analysed, and a demonstration is given of the use of model charts of ideal epidemics.

The principles discussed are illustrated by the analysis of two small epidemics of measles.

I wish to thank the numerous people who have helped, especially my staff, my colleagues, and our patients, and Dr. Robert Knox and his colleagues, and Dr. Allan McFarlan, Prof. Major Greenwood, and Prof. G. S. Wilson, for much valuable criticism and encouragement. I am indebted to the Medical Research Council for financial and other assistance.

2. Pickles, W. N. (1939) Epidemiology in Country Practice. Bristol.

"... In exploring the world of medicine the student should be guided in methods of map reading, but his knowledge of detail should lean to the three-miles-to-the-inch scale rather than a mile to the inch. There must be left to postgraduate study and training the preparation of the doctor for his special vocation in medicine. Above all, since medical knowledge is ever expanding, the undergraduate curriculum must favour the acquisition of enduring habits of work and thought and of enthusiasm for study."—Prof. HENRY COHEN, at King's College Hospital. (*Medical Press*, Oct. 27, p. 360.)

RAPID DISINFECTION OF CLEAN UNWASHED SKIN

FURTHER EXPERIMENTS

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THE rapid disinfection of unwashed skin, experimentally infected with bacteria, has been investigated in a previous inquiry, which showed that 2% iodine in 70% alcohol disinfected more rapidly than any of the other substances tested (Gardner and Seddon 1946). Further experiments on the same lines are described here.

EXPERIMENTAL METHODS

About a dozen circular areas 1 in. in diameter on the shaven but not specially washed skin of the forearm are successively infected and disinfected. The area is first swabbed with a bacterial suspension of known density, and when dry it is treated with the disinfectant for a given time either by swab-application, if a very short action is proposed, or with discs of sterile lint soaked in the disinfectant. In the latter case the time of exposure of the bacteria to the disinfectant is reckoned as the time of application of the disc plus the time taken for the skin to dry after removal of the disc. In the case of swab-application the time is reckoned from the first wetting of the whole area to the moment when the area looks dry. A sterile swab moistened with sterile broth is then rubbed all over the area and immediately streaked over the surface of an agar plate.

A control area, treated with bacteria but not with disinfectant, is included in the experiment; and, when strongly "bacteriostatic" substances are being used, a combined control for bacteriostatis is used: an uninoculated area is treated with the disinfectant; and, when the area has dried, a moist swab is rubbed over it and then streaked on the surface of an agar plate. Another area, treated with bacteria only and then dried, is swabbed, and the swab is streaked all over the surface of the same agar plate. If full growth takes place on incubation, it is clear that the amount of disinfectant transferred by the swab to the agar is insufficient to prevent free development of the bacteria.

The aim being practical rather than theoretical, the effect looked for is the virtually complete killing of the bacteria, or "virtual" disinfection. The controls must give a semi-confluent growth, or at least densely set colonies assessable at 50,000 or more; and a test plate is recorded as "virtually disinfected" when it shows less than 6 colonies of the test microbe. Colonies of contaminating organisms or of sporing bacilli from the skin are disregarded. "Virtual disinfection" therefore allows the survival of not more than 1 in 10,000 of the microbes applied to the skin. But, since the final examination is of a sample, not of the whole, and can only be applied to the whole with reservations, a higher standard—i.e., no colonies at all on the great majority of plates and only one or two on any plate—was demanded in the chief final experiments.

In the great majority of the experiments *Ps. pyocyanea* was used in place of the epidermal white cocci mostly employed in the previous work. To the rapid action of strong disinfectants *Ps. pyocyanea* is at least as resistant as cocci, whereas to the slow action (bacteriostatic or slowly bactericidal) of low concentrations it is much more resistant, and it is therefore far less likely to be inhibited on the test platings by traces of disinfectant carried over on the swabs.

IODINE IN ETHYL ALCOHOL

Continuation of our previous work (Gardner and Seddon 1946) has confirmed that alcoholic solutions of iodine are an extremely rapid means of disinfecting skin areas for surgical incisions or punctures. The skin need not—indeed should not—be previously washed.

The method was recommended by Grossich in 1908 and gained rapid support on all sides (Waterhouse and Fenwick 1910, Kolle et al. 1931). It was the routine method at least in some of the great London hospitals by 1911, though it was usually preceded by scrubbing

TABLE I—DESTRUCTION OF *Ps. pyocyanea* ON SKIN BY IODINE IN 70% ETHYL ALCOHOL

Iodine % (in 70% ethyl alcohol)	Length of application											
	15–20 sec.			30 sec.			1 min.			2 min.		
	No. of tests	Virtually disinfected*		No. of tests	Virtually disinfected*		No. of tests	Virtually disinfected*		No. of tests	Virtually disinfected*	
		No.	Per 10		No.	Per 10		No.	Per 10		No.	Per 10
2·0	20	20	*10·0*	..	..	..	..	..	..	..	..	..
1·0	30	30	*10·0*	30	30	*10·0*	..	..	..	..	..	..
0·5	30	15	*5·0*	30	30	*10·0*	..	..	..	..	..	..
0·35	..	..	..	30	23	*7·7*	..	..	..	..	..	..
0·25	..	..	..	30	24	*8·0*	..	..	..	..	..	..
0·125	..	..	..	30	10	*3·3*	..	..	..	..	..	..
0·0	..	..	..	30	10	*3·3*	20	8	*4·0*	20	20	*10·0*

* > 99·9% killed.

Note.—Applied wet on lint for all times over 15–20 sec.—e.g., for 30 sec. thus: 10 sec. application on lint + 20 sec. to dry.

with soap and water, a procedure discountenanced by Grossich as reducing the effectiveness of the disinfectant. No more than occasional and mild trouble from iodine-sensitiveness seems to have been encountered.

The present experiments (table I) show that 1% iodine in 70% ethyl alcohol is effective in the least time taken for the disinfectant to dry on the skin—i.e., 15–20 sec. If the solution is allowed to act in the wet state for 30 sec., 0·5% iodine is sufficient. If the time can be extended to 2 min., no iodine is needed, since 70% alcohol alone gives disinfection in that time.

ZEPHIRAN

This kationic detergent solution of high-molecular alkyl-dimethyl-benzyl-ammonium chlorides, introduced by Domagk (1935) and Hornung (1935), is a pleasant-smelling fluid which makes clear solutions in water and does not irritate the skin.

In our previous work (Gardner and Seddon 1946) a few tests indicated that at 25–100% concentration in water 'Zephiran' disinfected skin areas, previously infected with *Ps. pyocyanea*, within 1½ min., which is the least time it generally takes for such concentrated solutions to dry on the skin. Shorter exposures could therefore not be tested; and consequently great rapidity cannot be claimed for aqueous solutions. In the present investigations concentrations lower than 25% proved ineffective in 1½ min. By prolonging the exposure to 5 min. disinfection was obtained with a 10% solution.

Since zephiran and similar substances act more rapidly and intensely on gram-positive cocci than on gram-negative rods, the table of actions of both aqueous and alcoholic solutions on *Ps. pyocyanea* may be taken as guaranteeing at least as effective action on other non-sporing bacteria (contrast the action of ether below).

ZEPHIRAN IN 70% ETHYL ALCOHOL

Starting from the bottom of the right half of table II one sees again that 70% ethyl alcohol alone was effective in 2 min., and that the addition of zephiran up to 10% increased the proportion of areas disinfected in a given time but did not give complete virtual disinfection in less than 2 min.

When, however, the zephiran concentration was increased to 30% (note that zephiran is itself an approximately 10% watery solution and the solids in the final solution are consequently only 3%), virtual disinfection was achieved in about ½ min. in 28 out of 30 tests. The 2 failures showed a dozen colonies and about 150 colonies of *Ps. pyocyanea*. But, since of the remaining 28 plates only 2 showed a single colony each and the rest none, it is highly probable that the 2 failures were of the nature

TABLE II—DESTRUCTION OF BACTERIA ON SKIN BY ZEPHIRAN

Zephiran %	Aqueous solutions												In 70% ethyl alcohol								
	Length of application (min.)												Length of application (min.)								
	1·5			2·0			5·0			6·5			0·5			1·0			2·0		
	No. of tests	Virtually disinfected		No. of tests	Virtually disinfected		No. of tests	Virtually disinfected		No. of tests	Virtually disinfected		No. of tests	Virtually disinfected		No. of tests	Virtually disinfected		No. of tests	Virtually disinfected	
		No.	Per 10		No.	Per 10		No.	Per 10		No.	Per 10		No.	Per 10		No.	Per 10		No.	Per 10
100	6	6	*10·0*	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
30	..	..	..	..	..	..	..	..	..	..	..	..	30	28	*9·3*	..	..	..	..	..	..
25	6	6	*10·0*	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
10	10*	0	*0·0*	10	9	*9·0*	(12*)	(12)	(*10·0*)	..	..	..	50	28	*5·6*	30	27	*9·0*	10	10	*10·0*
5	..	..	..	10	3	*3·0*	1*	1	..	20	10	*5·0*	39	27	*6·9*	..	..	..	..	..	..
2	..	..	..	..	..	..	1*	1	..	..	..	..	20	9	*4·5*	..	..	..	..	..	..
1	..	..	..	..	..	..	..	..	..	..	..	..	10	4	*4·0*	..	..	..	..	..	..
0	..	..	..	..	..	..	..	..	..	..	..	..	30	10	*3·3*	20	8	*4·0*	20	20	*10·0*

* = Test done with epidermal coccus. All the others done with *Ps. pyocyanea*.
( ) = Tests possibly unreliable, since the controls showed some bacteriostasis.

TABLE III—DESTRUCTION OF *Ps. pyocyanea* ON SKIN BY MIXTURES OF DI-ETHYL-ETHER AND ETHYL ALCOHOL

Mixture %			Length of application					
			20 sec.			30 sec.		
Ether	Alcohol	Water	No. of tests	Virtually disinfected		No. of tests	Virtually disinfected	
				No.	Per 10		No.	Per 10
100	0	0	17	17	*10·0*	23	23	*10·0*
30	70	0	..	..	..	30	29	*9·7*
20	80	0	20	7	*3·5*	30	30	*10·0*
10	90	0	..	..	..	30	30	*10·0*
15	70	15	30	8	*4·0*	30	28	*9·3*

Note.—The normal cocci of the skin survived in many cases (see text).

of technical errors, and that the whole result can be taken as satisfactory. It is to be noted that the quantity of the disinfectant applied by swabbing with a tiny moistened swab is very small. A more liberal application and a slight prolongation of the time of action to 45 sec. should ensure regular virtual disinfection.

We may take it, then, that the rapidity of the action of 30% alcoholic zephiran is little less than that of 0·5–2·0% iodine in 70% alcohol, and therefore we have in this solution a feasible substitute for iodine, to which a few people are hypersensitive.

CETRIMIDE (C.T.A.B. OR CETAVLON)

We showed earlier (Gardner and Seddon 1946) that aqueous solutions of cetrimide ('Cetavlon') at 5% and 2·5% were incompletely disinfectant in 1½ min. to areas treated with *Ps. pyocyanea*. After verifying the inadequacy of 5% aqueous solutions, which in this experiment disinfected 8 of the 10 areas tested, and represent the strongest concentration easily procurable in water, solutions in 70% and 97% ethyl alcohol were examined for their rapid disinfecting power (30 sec.). It should be mentioned that there is no appreciable difference in the antibacterial actions on the skin of 70% and 97% alcohol containing nothing in solution.

In alcohol a 10% solution of (solid) cetrimide can easily be made, and it was found that such a solution in 97% alcohol disinfected in 30 sec. all of 24 areas infected with *Ps. pyocyanea*, and in 70% alcohol 23 out of 24, the single failure being probably attributable to a technical error.

It may therefore be considered that 10% cetrimide in 70% alcohol, as a rapid disinfectant, nearly equals the performance of alcoholic iodine.

Similar experiments with a 5% solution of cetrimide in 70% alcohol showed a partial disinfection, only 8 out of 20 areas being virtually disinfected in 30 sec. Likewise the effect of 2% solutions in the same time was incomplete.

DI-ETHYL-ETHER

The destruction of *Ps. pyocyanea* on the skin by ether and by mixtures of ether and alcohol is shown in table III. Ether alone was successful in 20 sec., but neither of the two alcohol-ether mixtures tried for this time gave satisfactory results. In ½ min., however, two of the mixtures gave complete disinfection, whereas the other two gave only a very small proportion of failures, which might well have been due to technical errors.

It was noted, however, that on the platings from skin areas treated with ether or with the mixtures, unexpected crops of white colonies of staphylococcus developed, which seemed to show that the normal cocci of the skin were surviving a treatment that eliminated *Ps. pyocyanea*. To investigate this possibly selective action of ether, bactericidal tests were performed in vitro, the results of which are shown in table IV. From these it is clear that the two gram-negative microbes are killed more rapidly than staphylococci.

As regards the epidermal coccus used in the bactericidal tests it was not realised at the time how slowly it grows in blood-broth (the test medium), and there may possibly have been a minimal growth, invisible to the naked eye, in some of the test cultures recorded as 0. With the other three organisms any growth that occurred was clear enough to simple inspection; hence the records of experiments with them are reliable.

To sum up: in the in-vitro bactericidal test pure ether does not kill even small doses of cocci in 30 sec., nor large ones in 4 min., whereas it kills large doses of *Ps. pyocyanea* and *Bact. coli* in a minute and small doses in ½ min. It follows that the skin-disinfecting action on *Ps. pyocyanea* shown in table III must not be interpreted in general terms. Cocci would almost certainly take longer to kill; and, if many were present the time might be impracticably prolonged.

MERCURY PREPARATIONS

Mercuric chloride at 1 in 1000 in water acting for 1½ min. (the least time it took to dry on the skin) failed to achieve virtual disinfection in 8 out of 10 skin areas infected with *Ps. pyocyanea*.

'*Merthiolate*' *tincture* (Lilly no. 99), containing 1·0% merthiolate, 0·1% monoethanolamine, 50% ethyl alcohol, and a trace of eosin, did not, in 30 sec., virtually disinfect any of 10 areas infected with a white epidermal coccus. With *Ps. pyocyanea* as the test organism only 2 out of 10 areas showed virtual disinfection in 30 sec.; but in 1 min. 11 out of 20, and in 2 min. all of 20, were disinfected. It is, however, to be remembered that 70% alcohol disinfects in 2 min., and that 50% alcohol may be expected to have almost as strong an action.

Merthiolate solution (Lilly no. 45), a 0·1% solution in water with 0·1% monoethanolamine, entirely failed to disinfect *Ps. pyocyanea* on the skin in 1½ min., and only disinfected 7 out of 20 areas in 5 min.

In all experiments with mercury preparations the test platings were done on agar containing 0·1% sodium thioglycollate to neutralise traces of the mercurial substance carried over with the sample inoculum. It is evident, as might have been expected from our knowledge of the very slow bactericidal action of mercurials in vitro, that a rapid skin-disinfectant is not to be found among them. It does not seem, therefore, that any mercurial is as useful for our purpose as most of the other substances whose actions are described here.

TABLE IV—THE BACTERIAL ACTION IN VITRO OF DI-ETHYL-ETHER

Time (min.)	Approximate no. of bacterial cells put into 5 ml. of ether											
	3 × 10³				3 × 10⁶				3 × 10⁹			
	Ps. pyocyanea	*Bact. coli*	*Staph. aureus*	Skin coccus	*Ps. pyocyanea*	*Bact. coli*	*Staph. aureus*	Skin coccus	*Ps. pyocyanea*	*Bact. coli*	*Staph. aureus*	Skin coccus
0·5	0	0	+	+	0	0	+	0*	+	+	+	+
1·0	0	0	0	0	0	0	+	0*	0	0	+	+
2·0	0	0	0	0	0	0	+	0*	0	0	+	+
4·0	0	0	0	0	0	0	0	0*	0	0	+	+

* Results open to doubt (see text).
\+ = Growth—i.e., not sterilised.
0 = No growth—i.e., sterilised.

CHLOROS

'Chloros' in 70% Ethyl Alcohol.—Chloros is said to represent approximately a 10% solution of chlorine in water, so that a mixture of 3 parts of chloros and 7 parts of ethyl alcohol would give about 3% of chlorine. It should be noted that a heavy deposit was formed on making the mixture, which was filtered before use. Skin areas treated with a suspension of *Ps. pyocyanea* were exposed to the filtered mixture for 30 sec. Of 10 areas so treated none was virtually disinfected, though the viable bacteria were very greatly reduced. A somewhat longer exposure would doubtless be successful, but it is clear that chlorine in this form is less effective than iodine.

Chloros in Aqueous Solution.—In our previous paper (Gardner and Seddon 1946) full-strength chloros was shown to be incompletely effective in 1½ min. Further experiments, with exposures of 4–5 min. gave the following figures:

Chloros 100%: 20 tests with skin-coccus; 18 virtually disinfected.

Chloros 50%: 20 tests (10 coccus, 10 *Ps. pyocyanea*); all 20 virtually disinfected.

Chloros 25%: 10 tests with the coccus; only 3 virtually disinfected.

Prolongation of the time of treatment with the 25% solution to 9 min. only slightly improved the results to 5 virtual disinfections out of 10 tests. Thus chloros at 50% is effective in 5 min. Possibly the 2 failures out of 20 with 100% chloros were experimental errors.

DETTOL IN 70% ALCOHOL

Undiluted aqueous 'Dettol' was shown (Gardner and Seddon 1946) to be unsuccessful in killing epidermal cocci on the skin in the 5 min. which it takes to dry.

Further tests showed that even 15 min. exposure was not enough. Dilution with water 1 in 2, 1 in 4, and 1 in 8 did not improve the results. But a great reduction in the viable bacteria took place in 5 min. with 100% and 50% dettol; hence it seemed possible that alcoholic solutions might show a rapid action.

Tests were therefore made with a mixture of 30 parts of dettol and 70 of ethyl alcohol, using both *Ps. pyocyanea* and a skin coccus as test organisms. In neither case was virtual disinfection of all areas attained in 30 sec., though a high proportion were disinfected; and one area out of 9 (*Ps. pyocyanea*) showed growth even after a minute's application. Thus a rapidity of action equal to that of alcoholic iodine was not observed.

MISCELLANEOUS EXPERIMENTS

Petrol, as sold in garages in England in May, 1947, showed no obvious disinfecting power on *Ps. pyocyanea* in either 30 sec. or 2 min. (10 areas tested in each case).

Acetone, similarly tested for the same time, was ineffective, though it caused a moderate reduction in the number of living microbes on the skin.

Propyl alcohol.—A 50% solution, as used for disinfecting the shaved skin of animals in some laboratories, was compared with 70% ethyl alcohol in parallel tests when acting for ¾ min. or 2 min., an epidermal coccus being the test organism. In all experiments the propyl alcohol proved the less efficient in a given time. But it has quite a strong action, and if applied for 3–5 min. it would probably disinfect well. It is alleged to be less irritating than ethyl alcohol when repeatedly applied to an animal's skin.

Brilliant Green and Crystal Violet, 1% of each in 75% Methylated Spirit.—This mixture is used at the Wingfield-Morris Orthopædic Hospital, Oxford, for maintaining the sterility of skin areas. It is not used for rapid disinfection.

Experiments showed that, as expected, it failed in 30 sec. to disinfect 10 out of 10 skin areas experimentally infected with *Ps. pyocyanea*; and when applied for 30 sec. and left for 5 min. in the dry state it was not completely successful, only 3 of 5 areas so treated being virtually disinfected. But when, after application wet for 30 sec., it was left dry on the skin for 30 min., all 5 areas so treated were virtually disinfected (though one area, which yielded 5 colonies, was only just up to the standard).

It may be judged from these experiments that this dye mixture, if applied from time to time to skin which is then kept covered with sterile dressings, can produce and maintain a state of virtual disinfection.

DISCUSSION

Though great rapidity of skin disinfection is indispensable only in certain circumstances, such as emergency incisions and the inoculation of many persons in a short time, there is little object in using slow methods for any surgical operation when quick ones are as good or better. The washing or scrubbing of the skin, and various other methods of preparation, sometimes extending to the day before the operation, seem to make altogether unnecessary demands on the time and energy of nurses, for there is no evidence that they achieve any greater sterility of the skin than does the single ½ min. application of an effective disinfectant immediately before the operation (Price 1938).

Prof. H. J. Seddon (private communication), acting on the evidence of our first publication, has used 2% iodine in 70% alcohol for some two years in orthopædic operations, applying it only once just before the operation, without washing the skin except when it seemed unhealthy. No infections attributable to infected skin have occurred at operations during that time, and only an occasional mild dermatitis has been caused by the iodine.

There seems little justification for using slow disinfectants, such as merthiolate or the flavines (Gardner and Seddon 1946). These are usually applied in alcoholic solution, and it has been shown that ethyl alcohol alone will virtually disinfect skin in about 2 min. (table I). There is no evidence that slow disinfectants dissolved in it have any useful effect at all.

SUMMARY

The power of 2% iodine in 70% ethyl alcohol to achieve virtual disinfection of flat areas of unwashed clean skin in ½ min. or less is confirmed, and it is shown that, if a full 30 sec. is allowed, the iodine may be reduced even to 0·5%.

The detergents, zephiran 30%, and cetrimide 10%, both in 70% ethyl alcohol, give satisfactory disinfection in 30–45 sec.

Ethyl ether, chloros, various mercury preparations, and some other substances have either a slower or an otherwise imperfect disinfecting power.

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"... A rough estimate of problem families for England and Wales gives 80,000 containing approximately 300,000 children. This is arrived at using the average incidence of Rotherham (3 per 1000), Luton (2 per 1000), and Herefordshire (1 per 1000). Thus it seems likely that at least 60,000 children now being cared for by local authorities and voluntary bodies away from their parents come from problem homes, being about one-fifth of the total children living in comparable circumstances."—Dr. C. FRASER BROCKINGTON, addressing the Royal Institute of Public Health and Hygiene on Oct. 27.

POTENCY AND "TOXICITY" OF SOME SYNTHETIC ŒSTROGENS

CLINICAL ASSESSMENT

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STILBŒSTROL, dienœstrol, and hexœstrol were synthesised in 1938 by Dodds and his associates (1938a and b, Campbell et al. 1938). These compounds are now extensively used clinically, and it has become customary to assume that stilbœstrol, though a highly effective œstrogen, readily produces "toxic" symptoms, whereas dienœstrol and hexœstrol, though possibly equally potent, are less "toxic." There have, however, been few serious attempts to determine or compare the potency of these substances in man.

Of forty papers reporting the use of stilbœstrol at the menopause, in menstrual disorders, or to inhibit lactation, only seven refer to its strength in relation to that of the natural œstrogens, though in none of these did the methods of assessment seem to justify definite conclusions.

We have found only nine records of the clinical use of hexœstrol, and five of dienœstrol. In these it is generally agreed that both show a low incidence of "toxicity," and that hexœstrol is less potent than stilbœstrol (values range from a tenth to a third), when given by mouth. In only two of the reports on dienœstrol is it compared with stilbœstrol. Barnes (1942) states that it is ten times more effective than stilbœstrol in suppressing lactation, and Rakoff et al. (1947) suggest that the action of dienœstrol in inhibiting pituitary activity is greater than that of stilbœstrol, whereas stilbœstrol is more effective in its action on the endometrium and vaginal epithelium.

Other œstrogens, apart from the naturally occurring substances œstradiol, œstrone, and œstriol, have been used clinically. One of these, bis-dehydro-doisynolic acid (Meystre and Miescher 1944) has been considered in this investigation.

METHOD

The œstrogen was given by mouth in daily doses for a fortnight to induce "withdrawal bleeding" within fourteen days of the last dose, the usual interval being from two to four days. The first course consisted of a "sighting" dose (usually 2 mg. daily in the case of stilbœstrol). Depending on whether the response was positive or negative, the daily dose of the second course (the "first bracketing" dose) was either lowered or raised—usually halved or doubled. The daily dose of the third course (the "second bracketing" dose) was similarly adjusted according to the response of the first bracketing dose. In this way a "therapeutic unit" was obtained, being the mean of the daily doses of two courses, one of which consisted of the highest, and the other of the lowest, daily dose to fail or succeed, respectively, to produce a withdrawal bleeding.

The patients selected had primary amenorrhœa, or secondary amenorrhœa of at least some months' standing.

In general an attempt was made first to determine the therapeutic unit of stilbœstrol, and subsequently the therapeutic unit of one or more of the other œstrogens, on the same patient.

The œstrogens used in the investigation were stilbœstrol, dienœstrol, hexœstrol, and bis-dehydro-doisynolic acid.

RESULTS

Of the 168 patients studied 146 had secondary amenorrhœa and 22 primary amenorrhœa; 997 courses of œstrogen were given; 79 therapeutic units of stilbœstrol, 48 of dienœstrol, 30 of hexœstrol, and 19 of doisynolic acid were obtained.

A wide range of therapeutic units was encountered for each œstrogen in different patients. The series of cases was consequently too small to permit the mean therapeutic unit to be used as a basis for statistical comparison of the various œstrogens. Thus it was impossible to take the average of all the 79 therapeutic units of stilbœstrol, for instance, and compare it with the average of all the 48 therapeutic units obtained for dienœstrol.

The ratio between the effective doses of any pair of œstrogens determined on individual patients was, however, found to be much more uniform. The statistical analysis of the results is therefore based on the logarithms of these individual ratios, the comparisons being made with the therapeutic unit of stilbœstrol expressed as unity. In other words, the effect of each of the other œstrogens was compared with that of stilbœstrol on the same patient. This was possible in 75 cases. The results were as follows:

Substance	*No. of comparisons*	*Mean ratio*	*Fiducial limits of error (P = 0·05)*
Dienœstrol	36	0·261	0·205–0·334
Hexœstrol	23	0·056	0·042–0·074
Doisynolic acid	16	0·214	0·147–0·311

From this it will be seen that dienœstrol is about a quarter, doisynolic acid about a fifth, and hexœstrol about an eighteenth, as potent as stilbœstrol.

Though the mean therapeutic unit is of little significance, some interest attaches to the approximate median therapeutic unit (the daily dose on which half the patients bled), for it may give some indication for the choice of the sighting dose in subsequent investigations. For stilbœstrol it was 1·5 mg., dienœstrol 2·5 mg., hexœstrol 10 mg., and doisynolic acid 2·5 mg.

"*Toxicity.*"—It was hoped to collect sufficient data to calculate regression lines of "toxicity" on dosage for each substance, so as to compare accurately the "toxicity" of each œstrogen at various dose levels. (By this means the percentage incidence of "toxicity" at various dose levels is plotted as a curve with percentage "toxicity" as ordinates and dose, or log: dose, as abscissæ.) Unfortunately this has been possible only in the case of stilbœstrol. Here the probit-of-percentage-"toxicity"/log dosage relationship was found to be linear, with a very good fit, giving a regression line

$$y = 1{\cdot}388366\,x + 2{\cdot}196176.$$

The departure from linearity gave a χ^2 value of 4·0317, on ten degrees of freedom, giving a probability of 0·90–0·95 of linearity. This type of relationship is a common biological one and in this case indicates that "toxicity" depends virtually on dosage. No similar relation could be shown for the other substances, because of the smaller incidence of nausea in relation to the size of the series, but probably a larger series would reveal a relation of the same type.

Because of this failure to express "toxicity" weight for weight in the case of the other œstrogens, a simpler method has been used comparing the "toxicity" of effective doses. This comparison has been restricted to patients in whom uterine bleeding has been produced. Since care has been taken throughout the investigation to exceed the minimal effective dose as little as possible, the comparison is as near as one can get to a statement of the "toxicity" of doses of equivalent therapeutic effect.

The numbers of patients responding to treatment with each substance, together with the numbers complaining

of nausea at any time during the treatment, were as follows:

Substance	No. of patients responding	No. of patients nauseated
Stilbœstrol	92 ..	36
Dienœstrol	63 ..	4
Hexœstrol	40 ..	2
Doisynolic acid	26 ..	3

The results of a series of χ^2 tests on these data were as follows:

Substance	χ^2	df	P
Stilbœstrol v. dienœstrol ..	19·310 ..	1 ..	0·001
Stilbœstrol v. hexœstrol ..	14·220 ..	1 ..	0·001
Stilbœstrol v. doisynolic acid	5·783 ..	1 ..	0·01–0·02
Stilbœstrol v. all others ..	32·284 ..	1 ..	0·001

These results indicate a highly significant difference between the "toxicity" of stilbœstrol and those of dienœstrol and hexœstrol. The lower degree of statistical significance attaching to the difference between stilbœstrol and doisynolic acid is almost certainly due to the smallness of the series. It therefore seems clear that, to produce equivalent clinical effects with stilbœstrol, one must run the risk of encountering a much greater incidence of nausea than with any of the substances considered.

DISCUSSION

Choice of End-point

Œstrogen withdrawal bleeding in amenorrhœa has been chosen as the end-point for this investigation. The mechanism involved—i.e., the effect of œstrogen on the endometrial vessels—represents only one level of œstrogenic response. There are, however, others, such as the replacement of the waning activity of the ovary in the treatment of the menopausal syndrome; conversion of an atrophic to an œstrous type of vaginal smear; suppression of lactation; and arrest of the symptomatic progress of carcinoma of the prostate. It would therefore be desirable to compare the œstrogens used in the present investigation using end-points devised to demonstrate these other levels of œstrogenic response, for it is not improbable that the ratio of doses of the various œstrogens would differ for the relief of menopausal symptoms or the suppression of lactation from that which we have recorded for the production of withdrawal bleeding.

We have, however, failed to devise satisfactory end-points for these other conditions, for the following reasons:

(1) The manifestations of the menopausal syndrome are entirely subjective and therefore difficult to assess quantitatively. It might, however, be possible to persuade the patient to keep a record of her daily hot-flush count, and to use this as the end-point. To do so it would be necessary to establish a base-line by giving the patient inert control tablets for a fortnight. This would be followed by various therapeutic courses to determine the minimal effective dose of at least two of the œstrogens to be tested. Alternating with each therapeutic course control tablets would have to be given to allow the hot-flush count to return to the base-line. The many incalculable factors which might modify the hot-flush count; the length of time necessary to establish a therapeutic unit of two or more œstrogens in a condition in which the level of response might alter as time goes on; and the disinclination of the patient to submit to periodic exacerbation of her symptoms due to the alternating courses of control tablets, render this method, in our opinion, impracticable.

(2) The end-point in the vaginal smear would be the conversion of an anœstrous into an œstrous smear. Many menopausal women show an anœstrous smear. In few, however, is the smear sufficiently labile to undergo the necessary change, and then to revert to the anœstrous condition on control tablets, to enable one in practice to establish therapeutic units of at least two œstrogens in a reasonable period of time.

(3) Suppression of lactation seems to us an unsuitable method for the clinical assessment of œstrogens, for the administration of only one course of œstrogen is possible, and that either does or does not suppress lactation. To establish the minimal effective dose of one œstrogen, therefore, would require a large series of cases, and to compare the effect of another œstrogen would necessitate the use of another equally large group of patients. The same is true of carcinoma of the prostate.

For these reasons, therefore, we have found it possible to use only one end-point, the induction of bleeding in amenorrhœa, and it should be emphasised that our results refer only to this one level of œstrogenic response.

Suitability of Œstrogen Withdrawal Bleeding in Amenorrhœa as an End-point.—Not only did we conclude that we could devise no other suitable end-point than the production of bleeding in amenorrhœa, but also we were at one time doubtful whether even this would give significant results. First, there was the probability of spontaneous periods occurring as a coincidence after a therapeutic course and consequently being recorded as withdrawal bleedings. Secondly, it seemed likely that the level of response in any one patient might alter during the investigation, which lasted sometimes for more than a year. To test this possibility the same dose of stilbœstrol was readministered to individual patients on 74 occasions, on 59 of which the response was unchanged, though several courses of œstrogen, and sometimes many months, intervened between the original course and readministration. On the 15 occasions where the response was altered, 14 were in cases in which the dose concerned probably represented the bleeding threshold of the patient. In these cases larger doses consistently produced bleeding, and smaller ones consistently failed to do so. In one case only was the response so uncertain as to make it impossible to determine a bleeding threshold. Finally, we were doubtful about the justification for including cases of primary and secondary amenorrhœa in the same series, for it was felt that the cause of the condition might be fundamentally different in these two groups. Actually there was no significant difference between the mean therapeutic unit for primary and secondary amenorrhœa (2·1 and 2·2 mg. of stilbœstrol respectively). When the results of the investigation were analysed, Dr. Emmens made the following statement: "The degree of precision of the comparisons, as revealed by the fiducial limits of error shown, is of the order usually attained in biological assays in which moderately large groups of animals are used." This seems to justify our choice of this particular end-point for comparing the potency of œstrogens in man.

SUMMARY

A method is described for comparing the potency of œstrogens in man. It consists in giving the œstrogen daily by mouth in fourteen-day courses to amenorrhœic women and recording whether œstrogen withdrawal bleeding takes place.

The results obtained indicate that dienœstrol is about a quarter, doisynolic acid about a fifth, and hexœstrol about an eighteenth, as potent as stilbœstrol.

Investigation of the incidence of "toxicity" indicates that stilbœstrol is more likely to produce nausea in therapeutic doses than are dienœstrol, doisynolic acid, and hexœstrol.

Reasons are given for choosing this end-point, and for the failure to devise any other suitable method of assessment at different levels of œstrogenic response, such as the relief of menopausal symptoms, the production of an œstrous vaginal smear, and the suppression of lactation.

We wish to thank Sir Jack Drummond, F.R.S., for the facilities he has put at our disposal to enable us to carry out

this work; and Dr. W. L. M. Perry for help on the statistical aspects of the investigation after the departure of Dr. Emmens for Australia.

The œstrogenic preparations used in these experiments were supplied by British Drug Houses Ltd., Messrs. Ciba Ltd., and Boots Pure Drugs Co. Ltd.

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ACTIVITY OF SOME SYNTHETIC ŒSTROGENS DETERMINED BY EXPERIMENTS ON RATS

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WORKERS on the relative activity of three synthetic œstrogens—stilbœstrol, dienœstrol, and hexœstrol—using ovariectomised rats or mice, have published widely different results. For example, Emmens (1938) reported that dienœstrol given by mouth to mice was four times as active as stilbœstrol, whereas Kemp and Pedersen-Bjergaard (1943) found it to have half its activity. Campbell et al. (1939) found the activity of hexœstrol given by mouth to be 80% that of stilbœstrol, whereas Kemp and Pedersen-Bjergaard (1943) found it only 10%.

Bishop et al. (1948) have established the relative clinical efficiencies of these three œstrogens, and it seemed desirable to try and correlate the clinical and biological results. Because of the conflicting results previously reported, we have repeated the assays, using a sufficiently large number of animals to permit a reliable estimate to be made of the error of the observations. We have also included in some of our assays a new water-soluble synthetic œstrogen, potassium hexœstrol sulphate, and record our results here.

Inbred ovariectomised rats of the Wistar strain 7–8 weeks' old and weighing about 100 g. at ovariectomy were used. After ovariectomy the rats were rested for about ten days, and thereafter vaginal smears were examined daily for the next ten days. A sample of the vaginal cells was removed with a round-ended metal spatula moistened with a drop of water before insertion. A thin smear was made on a glass slide, fixed in methyl alcohol, and stained with a 1% aqueous solution of methylene-blue. A smear was scored as positive if it consisted exclusively of cornified cells, or of cornified cells with sporadic nucleated epithelial cells. Animals which had been shown to be in anœstrous throughout the whole period of smearing were used for assay once every two weeks.

TABLE I—RELATIVE ACTIVITIES OF ŒSTROGENS GIVEN BY MOUTH

Œstrogen	Present investigation		Kemp and Pedersen-Bjergaard (1943)	Campbell et al. (1939)
	Activity	P = 0·95 limits of error	Activity	Activity
Stilbœstrol	100	(assumed)	100 (assumed)	100 (assumed)
Hexœstrol	10	8·5–11·7	10	80
Dienœstrol	68	63–73	100	100
Potassium hexœstrol sulphate	7·3	6·7–8·0	—	—

ORAL ASSAYS

Stilbœstrol, hexœstrol, and dienœstrol were given in arachis oil, and potassium hexœstrol sulphate in aqueous solution.

The arachis-oil solutions were prepared by dissolving a weighed quantity of the œstrogen in acetone and adding the acetone solution to a known volume of arachis oil. The vessel containing the mixture was surrounded with a jacket of warm water, and a rapid stream of nitrogen was passed through to mix the solution and drive off the acetone. Further dilutions were prepared from this stock solution, mixing being in all cases effected with a stream of nitrogen. Oil solutions were prepared freshly for each assay and were stored during the test period in a refrigerator; aqueous solutions of potassium hexœstrol sulphate were prepared freshly each day.

The required dose for each animal was divided into three equal parts, and each part was given in a volume of 0·5 ml. once daily by stomach-tube; dosing was therefore spread over three days. Several doses of each sample were given, the doses being so adjusted that their logarithms were in arithmetical progression. This simplified subsequent arithmetic for the calculation of potencies. In the earlier assays smears were made on the fourth, fifth, and sixth days of the assay; but, since no additional information was obtained from the sixth-day smears, these were discontinued. A positive smear obtained on either day or on both days was recorded as a positive response.

TABLE II—RELATIVE ACTIVITIES OF ŒSTROGENS GIVEN BY SUBCUTANEOUS INJECTION

Œstrogen	Series I		Series II		Series III	
	Activity	P = 0·95 limits of error	Activity	P = 0·95 limits of error	Activity	P = 0·95 limits of error
Stilbœstrol	100	(assumed)	100	(assumed)	100	(assumed)
Hexœstrol	64	61–68	64	60–68	70	66–74
Dienœstrol	26	24–27·4	27	25–29	33	31–35
Potassium hexœstrol sulphate	0·98	0·91–1·05	—	—	—	—
Œstrone	—	—	30	28–32	28	26–29

The total number of positive responses in each dosage group was summed and expressed as a proportion of the total number of rats receiving that dose. From these results potencies and limits of error were calculated by the method for quantal responses described by Gaddum (1933).

A few preliminary tests were made with each œstrogen to determine the optimal dose range. The animals were then divided into sufficient groups to allow each œstrogen to be given at three dosage levels. In general the doses used were greater than those used by Campbell et al. (1939).

Results.—The mean potencies calculated from these assays, and their fiducial limits, are shown in table I together with the potencies found by other workers. The potencies of hexœstrol, dienœstrol, and potassium hexœstrol sulphate were all expressed relative to stilbœstrol, which was assigned the value 100. The total number of observations contributing to the mean potencies was for stilbœstrol 256, hexœstrol 86, dienœstrol 341, and potassium hexœstrol sulphate 313.

TABLE III—RELATIVE SUBCUTANEOUS POTENCIES OBTAINED BY VARIOUS WORKERS

Œstrogen	Present investigation			Kemp and Pedersen-Bjergaard (1943)	Campbell et al. (1939)
	I	II	III		
Stilbœstrol ..	100	100	100	100	100
Hexœstrol ..	64	64	70	80	122
Dienœstrol ..	26	27	33	30	87
Œstrone ..	—	30	28	36	43

SUBCUTANEOUS ASSAYS

Three series of assays were made with aqueous solutions. In the first series stilbœstrol, hexœstrol, dienœstrol, and potassium hexœstrol sulphate were compared; in the second and third series œstrone, hexœstrol, and dienœstrol were compared with stilbœstrol.

The preparation of the animals and the preparation and scoring of the smears were the same as described above.

The aqueous solutions of stilbœstrol, hexœstrol, dienœstrol, and œstrone were prepared by diluting with distilled water stock solutions in absolute alcohol; aqueous dilutions were prepared every day, and stock solutions freshly made for each test. The stock solutions were stored in a refrigerator during the period of the test, and the aqueous dilutions were similarly stored between the times of dosing. Aqueous solutions of potassium hexœstrol sulphate were prepared freshly each day.

The total dose for each animal was divided into six equal parts, and each part was given in a volume of 0·5 ml. on the morning and afternoon of three successive days. Smears were made on the fourth and fifth days. The results were treated as described above.

Results.—Three series of assays were made, each series consisting of a large number of observations. In the first series hexœstrol, dienœstrol, and potassium hexœstrol sulphate were compared with stilbœstrol, the potency of which was assigned the value 100. In the second and third series œstrone was substituted for potassium hexœstrol sulphate.

The results obtained in the three series of assays are given separately in table II to show the order of the agreement which may be expected in separate assays of this type. The mean potencies compared with the values obtained by Kemp and Pedersen-Bjergaard (1943) and by Campbell et al. (1939) are given in table III. In all cases the results are shown relative to stilbœstrol, which has been assigned the value 100.

DISCUSSION

Our findings that the relative potencies of stilbœstrol, dienœstrol, and hexœstrol given by mouth are 100, 68, and 10 do not agree with those of Campbell et al. (1939), who found hexœstrol almost as active as stilbœstrol. They do, however, agree with those of Kemp and Pedersen-Bjergaard (1943).

This is the more interesting since the mode of administration used by us duplicated that used by Campbell et al., but differed from that used by Kemp and Pedersen-Bjergaard. It seems from this that the mode of administration—i.e., solvent, arrangement of doses, &c.—may have less influence on relative potency than has been assumed. It is also interesting to note that our results are in close agreement with the clinical results reported by Bishop et al. (1948).

Similarly, our results for the relative subcutaneous potencies show close agreement with those obtained by Kemp and Pedersen-Bjergaard, though they differ from those reported by Campbell et al.

SUMMARY

Large-scale experiments designed to assess the œstrogenic activity of some synthetic œstrogens have been made with ovariectomised adult female rats.

Hexœstrol given by mouth has only a tenth of the activity of stilbœstrol, dienœstrol two-thirds, and potassium hexœstrol sulphate a fourteenth. Potassium hexœstrol sulphate was given in aqueous solution; the others were dissolved in arachis oil.

Injected subcutaneously in aqueous solution hexœstrol has about two-thirds, dienœstrol less than a third, and potassium hexœstrol sulphate a hundredth of the activity of stilbœstrol. Œstrone has about the same activity as dienœstrol.

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RATE OF FLOW OF VENOUS BLOOD IN THE LEGS

MEASURED WITH RADIOACTIVE SODIUM

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VENOUS thrombosis has long been known to be influenced by three main factors, commonly known as Virchow's triad—changes in the constitution of the blood, damage to the blood-vessels, and disturbances of the circulation. The conception of phlebitis as a factor in thrombosis was introduced by John Hunter (1793), and Hayem (1889) first recognised the rôle played by the platelets. Baillie (1793), Laennec (1819), and others emphasised stasis of the blood as a factor in thrombosis, and Lancereaux (1875) postulated this law: "Thromboses are always found at the level of the points where the blood has the greatest tendency to stasis, that is, at the limit of the action of the forces of cardiac propulsion and thoracic aspiration." Though the first two of Virchow's three factors are now well established experimentally and recognised in clinical practice, the participation of the third has hitherto remained largely inferential.

The introduction of radioactive tracers, however, has made possible the direct measurement of the rate of blood-flow in a limb by introducing such a tracer at one point and determining its arrival at some other point with a suitably placed Geiger-Müller (G-M) counter sensitive to the type of radiation emitted. In the present study radioactive sodium, Na^{24}, was used to determine the rate of flow of venous blood up the leg in normal people. The findings are interesting and furnish valuable controls for comparative studies in various pathological states later.

Tracer.—A radioactive isotope of sodium, Na^{24}, was prepared by the neutron irradiation of 'Analar' NaCl, which becomes, after neutron capture, partially converted into $Na^{24}Cl$. The dry crystals were first assayed to determine their activity; usually, on arrival, 1 g. contained 1–2 millicuries of Na^{24}, corresponding to about 5 atoms of radioactive isotope per 10^{10} atoms of stable Na. The crystals were made into sterile solution so that 1 ml. contained 10–20 microcuries. Immediately after delivery this concentration corresponded to about 1% NaCl; but, since the half-life of Na^{24} is only 14·8 hours, it was necessary, on successive days, to use higher concentrations of saline solution to achieve the same specific activity of Na^{24}. This solution, which

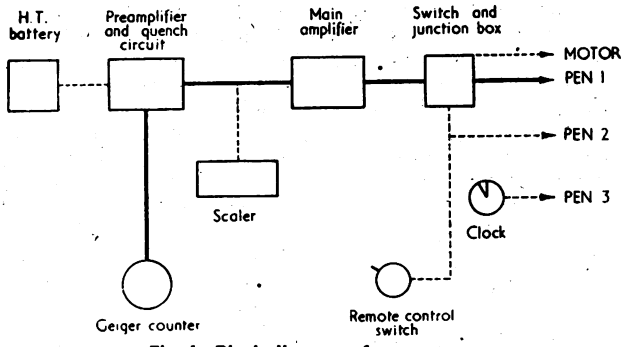

Fig. 1—Block diagram of apparatus.

never exceeded a concentration of 5%, was used for intravenous injection.

Apparatus.—The apparatus * consists essentially of a gamma-ray G-M counter, carried on an adjustable gantry. The counter is inserted into a tubular cylindrical lead block with a slot in the lower surface. All rays except those from vertically below are therefore subject to absorption by 4 cm. of lead, the thickness of the cylindrical wall. The counter is arranged so that the slot in the screen lies transversely over the femoral vein in the groin, and is pressed down as close to the body as possible without impeding the venous flow. Each pulse from the G-M counter is recorded on a motor-driven kymograph drum in such a way that any significant change in counting-rate becomes immediately evident. Fig. 1 is a block diagram of the apparatus, and fig. 2 shows a typical tracing obtained in a normal person and the method by which it has been interpreted.

INVESTIGATION

In the present study we examined 121 normal people aged 17–48 years, most of them falling within the 20–30 years age-group. The majority were students and probationer nurses leading active lives. No person with clinically observable varicose veins was included. The flow time was measured with the subject in the supine position, care being taken to ensure that the foot was at the same level as the heart, and that the head was not raised. The subjects were rested for at least 20 min. under a warm electric blanket so that their foot temperature approximated as nearly as possible to that of patients in bed—i.e., 33°C. To see whether skin temperature had any pronounced effect on the foot-groin time, 10 people were examined on two occasions, first in the way just described and again with the foot and leg immersed to the knee for 20 min. in a water-bath at 45–48°C.

A prominent vein on the dorsum of the foot was selected for injection, and a cuff, raised to 40 mm. Hg, was placed on the ankle above. A fine-gauge needle (no. 20) was inserted into the vein, without an injection being made. At this moment the drum was started and, after the " background " had been recorded for 15–20 sec., 1 ml. of $Na^{24}Cl$ solution was injected into the vein as rapidly as possible. The duration of the injection, about 3 sec., was recorded on the tracing. Flow times have been measured from the start of the injection period, since it is obvious that the solution first entering the vein will normally be the first to pass under the G-M counter. At the moment the radioactive material reached the groin the counter indicated an increase in counting-rate, and this was recorded immediately as a change of slope in the tracing. The moment of change was usually clear-cut, and, from a knowledge of the time of injection, the time of arrival at the groin, and the length of the leg (measured from the internal malleolus to the inguinal ligament over the femoral triangle), the average rate of flow could be calculated. It was found most convenient to express the result as foot-groin time in seconds, after correction for length of leg to a standard of 80 cm.

* For a detailed account of the circuit and of the recording device used in this study, together with a discussion of the accuracy of recording and analysing the data obtained, see Osborn and Wright 1948.

RESULTS

The foot-groin times for the 121 normal people are shown in fig. 3. The average flow time for the group was 18 ± 0·9 sec. The mode of the group was at 13 sec. It can be seen that the observations form a skew curve with a range of 4–50 sec. When abscissæ are logarithms of the flow times, however, the data fit a normal distribution curve ($\chi^2 = 11{\cdot}65$; $P = 0{\cdot}074$). This type of log-normal curve is often found in biological data (Gaddum 1945).

The data obtained have been further analysed for statistical differences between (1) males and females and (2) right and left legs, as follows:

	No. of cases	*Average flow time (sec.)*	*Range of observations (sec.)*
Males	50	18·5	4–47
Females	71	17·6	6–50
Right leg	54	18·4	4–50
Left leg	67	17·4	6–47

There is thus no significant difference between these groups, nor does any group differ significantly from the series as a whole.

Finally it was shown that the results obtained in the 10 people examined in the standard manner and again after vasodilatation had been induced by immersion in hot water showed no significant change when analysed by Fisher's (1944) method. The times observed were as follows:

Subject	A	B	C	D	E	F	G	H	I	K
Flow time (sec.):										
At standard temp. ..	11	13	13	8	8	11	13	15	11	15
After immersion ..	10	11	10	4	10	13	11	14	15	20

DISCUSSION

The present study offers a direct and objective method of measuring the rate of blood-flow in a particular section of the vascular system. The method avoids subjective errors by either the patient or the observer; but there remain certain other possible errors which need consideration. Since these are discussed more fully elsewhere (Osborn and Wright 1948), it need only be stated here that the combination of the errors introduced both by the random fluctuations of the " background " and by the fitting of a line to the slope of the kymograph tracing may be about 1 sec. in flow

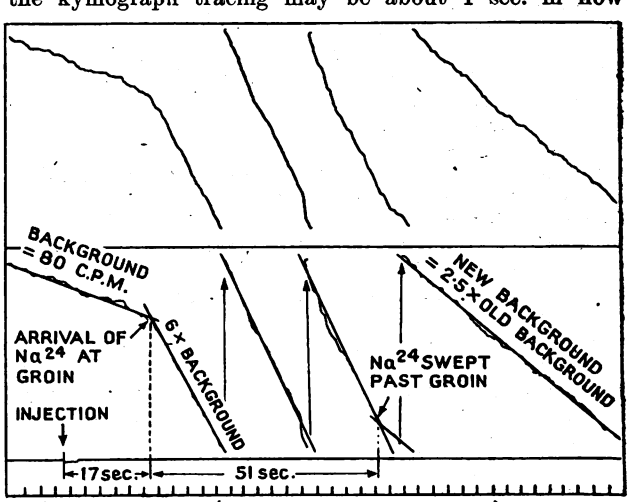

Fig. 2—Typical tracing obtained in a normal person, and method of interpreting it.

times of 10 sec. or less and may increase up to 3 or 4 sec. in cases with long flow times of about 50 sec.

The end-point, when the slope of the tracing changes from that of the "background" to the new rate produced by the $Na^{24}Cl$ arriving under the G-M counter, is very clear when 10 microcuries or more is used, but with less amounts the concentration may be insufficient to produce so pronounced an alteration of slope. The injected solution is considerably diluted as it passes up the vein, especially in cases with a slow flow. This is shown by the fact that with a slow flow the change of slope is similar to that obtained when a more dilute solution of $Na^{24}Cl$ is injected in a person with a rapid flow, since the angle of the slope depends solely on the quantity of $Na^{24}Cl$ under the counter window. The time at which the slope changes, however, is independent of the concentration of $Na^{24}Cl$ used, provided it raises the count above the "background" sufficiently to be detected; the magnitude of the change of slope is the only variable depending on the concentration of the radioactive material at the counter.

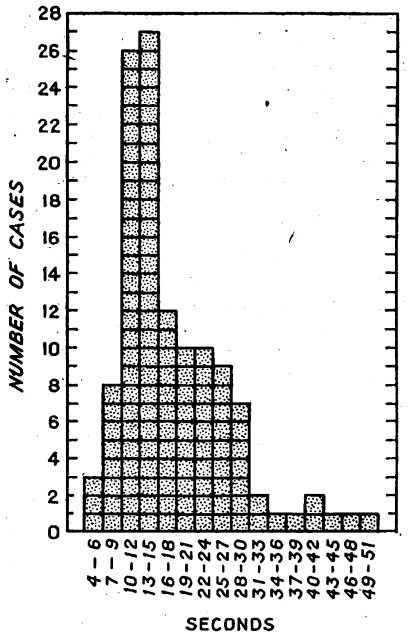

Fig. 3—Foot-groin times of blood-flow in 121 normal people.

A further feature of interest is the persistence of the raised counting-rate at the groin after the arrival of the $Na^{24}Cl$. Fig. 2 illustrates this clearly. It can be seen that, compared with the duration of the injection (about 3 sec.), a long time is required for the blood containing $Na^{24}Cl$ to pass the counter. We believe that the reasons for this are (1) that the radioactive material is diluted by blood flowing into it from tributary veins as it passes up the leg; and (2) that the viscous flow causes the blood in the centre of the vein to travel along much more rapidly than that at the periphery. By the time all the $Na^{24}Cl$ has passed through the vein under the G-M counter the first part of the injected $Na^{24}Cl$ may well have become mixed with the circulation and be returning under the counter in the femoral artery. In this way the slope often trails off only slowly towards that of a new "background" level.

The observed range of flow times in the present series of normal people under standard conditions of rest and temperature has shown a wider variation than was expected by comparison with the recorded figures of other workers. Blumgart and Weiss (1927) used a radioactive substance (radon) in their observation of arm-arm times in normal and in diseased persons. They did not record any foot-arm measurements. Thompson et al. (1928), using vital brilliant red, found a range of foot-arm times from 30 to >75 sec., whereas Smith et al. (1940), using sodium cyanide, reported a range of 20 to >70 sec. in normal people for foot-carotid time. It is difficult to compare our average time of 18 sec. with those reported by these workers, since our measurement is of a direct foot-groin time, whereas other methods give foot-heart or lung-heart-artery times, and the time proportions of such a circuit can at present be estimated only approximately. Nevertheless it seems clear from the figures obtained by subtracting the arm-carotid from the foot-carotid times in the same person that our figure of 18 sec. is of the same order as those found by the indirect methods.

The much larger range of observed times in our series may be due to the sensitivity of the method. In such tests as that with sodium cyanide, where the end-point is determined by the observer noting a dilatation of the alæ nasi followed by a deep inspiration, it is likely that a proportion of cases will be noted as "no end-point," owing to a poor reaction to the drug; such cases would therefore be recorded as having exceeded the upper limit. In our entirely mechanical method of recording, however, even end-points with a minimal change of slope can be detected, and consequently a case showing no end-point is rare.

An increase of circulation-rate when the temperature of a limb had been raised was recorded by Kvale and Allen (1939) and by Smith et al. (1940). Significant changes were noted by these workers when the skin temperature rose from 20 to 33°C. We obtained no significant alteration of flow time, however, in the group examined at 33°C and again immediately after immersion in water at 45°C. The range of temperature change was about 10°C in both cases, but it is possible that our lower temperature, which was definitely "warm," had already evoked considerable vasodilatation and little further change took place when the temperature was raised to 45°C. Smith's lower figure of 20°C, however, might be considered as "cold," and a much greater vasodilatation would follow a rise over their temperature range. This suggestion is borne out by the observations of Roth et al. (1940) on the degree of vasodilatation produced in the extremities of limbs at different temperatures. We chose 33°C as a standard temperature because it approximates closely to the skin temperature of persons comfortably warm in bed, and our observations on normal people have been collected and analysed primarily to be a basis for the assessment of possible changes observed in pathological conditions in patients confined to bed. The extension of this work is in progress.

SUMMARY

A direct method of measuring the rate of venous blood-flow in the leg with the radioactive isotope Na^{24} is described.

In 121 normal people the mean foot-groin flow time under standard conditions was $18 \pm 0{\cdot}9$ sec. The extreme range of the observations was 4–50 sec.

The accuracy of the method is discussed and a comparison made with the findings by other methods of measuring rates of blood-flow.

We wish to thank Prof. W. C. W. Nixon, director of the Obstetric Unit, University College Hospital Medical School, for his interest and support; Mrs. M. Merrington, of the Galton research department, University College, London, for advice and help in the statistical analysis; and the students, nurses, and colleagues who volunteered as subjects for this investigation.

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FURTHER OBSERVATIONS ON THE RESULTS OF SYMPATHECTOMY OF THE UPPER LIMB

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PREGANGLIONIC section of the sympathetic nerve-supply to the arm (Smithwick 1940) is designed to leave a wide gap between the cut fibres. That sympathetic function can be regained, even to a small extent, seems at first sight difficult to believe; yet there is good evidence that this is so (Simmons and Sheehan 1939, Haxton 1947, Barcroft and Hamilton 1948). The question is of such fundamental importance to the surgery of the sympathetic nervous system that we describe below some further evidence in favour of it.

In our previous work (Barcroft and Hamilton 1948) vasomotor and sudomotor reflexes were completely absent in seventeen limbs tested 1–6 months after operation. Sixteen of these limbs have now been re-examined 1–1$^1/_2$ years later, and the results compared with those obtained earlier.

Vasomotor Test.—Warming the feet elicits a reflex increase in blood-flow in the hands, the efferent limb of the reflex arc being from the vasomotor centre through sympathetic fibres. In the absence of sympathetic connexions to the limb heating of the feet does not alter the blood-flow. The details of the test were described in our previous paper. The results are expressed as the ratio $\frac{\text{Blood-flow during heating.}}{\text{Blood-flow before heating.}}$ This heating ratio is 3 or more in normal hands; in completely sympathectomised hands it is 1.

Sudomotor Test.—The resistance to the passage of an electric current through the body is located almost entirely in the skin and is determined chiefly by the activity of the sweat glands. This activity depends on nervous excitation mediated through sympathetic fibres. In practice the test we used previously (Barcroft and Hamilton 1948) was simplified and was as follows. The feet were heated to encourage free sweating. The currents which flowed through the pads of the thumb and middle and little fingers were measured in μA, and the average of them was called the current difference. Normal hands have current differences of 20 μA or more, since the skin is moist. In fully sympathectomised hands current differences are negligible, since the brain cannot elicit sweating. (The absence of any humoral mechanism for excitation of sweating is proved by the fact that ulnar-nerve block reduces the current through the little finger to less than 1 μA.)

RESULTS

Vasospastic Attacks.—All the sixteen limbs had been operated on for frequent severe vasospastic attacks. The clinical condition at the time of the first and second tests was:

Time after operation	*No recurrence of attacks*	*Attacks less disabling*	*Attacks as bad as before*
1–6 months	14	2	0
1–2 years	12	4	0

Vasomotor Test

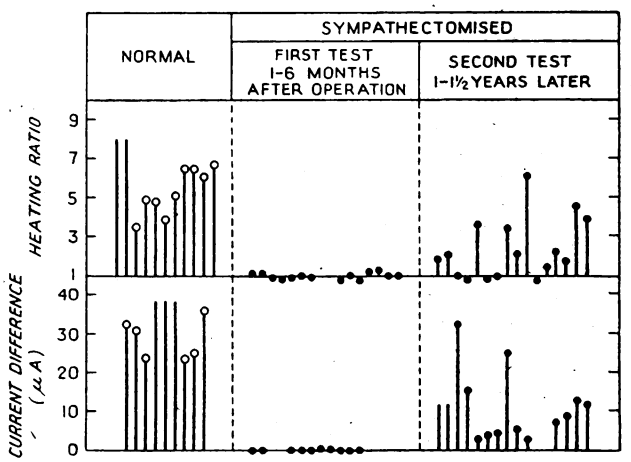
The heating ratios of some normal hands and those of the sympathectomised ones are shown in the upper half of the accompanying figure. Heating produced vasodilatation in all normal hands, the blood-flows being increased at least threefold.

The ratios of the sympathectomised limbs are arranged in two groups, 1–6 months after operation (the first test), and 1–1$^1/_2$ years later, when the tests were repeated. In each group the ratios are arranged in order of the length of time between the operation and the performance of the first test, those tested soonest after sympathectomy being on the left. As noted in the previous paper, all hands tested within six months of operation had heating ratios of about 1—i.e., indirect heating had no effect on the vessels of the hands. In contrast to this, many of the same hands, when tested a year or more later, had heating ratios considerably greater than 1—i.e., in these vasodilatation could once more be produced in the hands.

Sudomotor Test

The current differences of the same normal and sympathectomised hands are given vertically below their heating ratios in the lower half of the figure. All the normal hands showed large current differences due to the low resistance of the moist test skin and the relatively larger resistance of the dry control skin. The results from the sympathectomised limbs are arranged in the same groups, 1–6 months after operation and 1–1$^1/_2$ years later. All the hands tested within 6 months of operation had very small current differences. When retested many of these same hands showed quite large current differences.

The figure shows conclusively that there was no evidence of any sympathetic nervous connexion between the brain and the hand for several months after sympathectomy. A year or more later, vasomotor and sudomotor reflexes were obtainable in many hands. This confirms the findings of Simmons and Sheehan (1939), Haxton (1947), and Barcroft and Hamilton (1948).



Results of vasomotor and sudomotor tests obtained in sympathectomised hands.

It will be seen that clinical improvement persisted in all hands, though reflexes had reappeared in most. Therefore the new nerve path formed is probably functionally poorer than that present before sympathectomy.

SUMMARY

Sixteen limbs, sympathectomised for frequent vasospastic attacks, were each examined twice after operation.

At the first examination, 1–6 months after operation, attacks had not recurred in 14; they had recurred but were less severe in 2; and vasomotor and sudomotor reflexes were absent in all the hands.

At the second examination, 1–1$^1/_2$ years later, attacks had not recurred in 12; they had recurred but were less severe in 4. Vasomotor and sudomotor reflexes, though absent in some limbs, had returned in many.

The persistence of the excellent clinical results in these limbs, in spite of the reappearance of the reflexes in most, signifies that the new nerve path is functionally less efficient than that present before operation.

Once more, we acknowledge our gratitude to Prof. J. R. Learmonth, Mr. P. Fitzgerald, and Mr. J. S. Loughridge for putting us in touch with their patients; Mr. D. B. Smith for technical assistance; and the Medical Research Council for defraying expenses.

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A METHOD OF TESTING ANALGESICS

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EARLY in 1947 Messrs. Roche asked the Central Middlesex County Hospital to perform a clinical trial of their analgesic preparation 'Saridone.'* This paper describes an attempt to judge the effectiveness of these tablets by as impartial and accurate a method as possible. It is notoriously difficult to assess the power of different analgesics. There are three main methods—animal experiments, experiments on human volunteers with artificially produced pain, and clinical trial on patients with naturally occurring pain.

Animal experiments are useful in initial tests to select a substance for further trial, but they assess properties only remotely connected with the purpose of an analgesic. A patient wants a tablet that makes his pain better and not only one that stops a rat from twitching its tail away from a painfully hot lamp (a common laboratory test for analgesic properties is to measure the time taken before a rat moves its tail from an increasingly hot beam of light).

Experiments on artificially produced pain have disadvantages too. First, the subjects have not the same mental attitude to the pain as ordinary patients have. It is a pain of their own choosing, and so they suffer none of the anxiety, resentment, and irritability that usually attend naturally occurring pain. Their discomfort is somewhat modified too by the pleasure of feeling slightly heroic and by the curiosity of being experimented on.

Clinical Trials

The danger of clinical trials is that a perfectly controlled test is so hard to arrange. Also, the more elaborate the arrangements, the less closely do the conditions of taking the tablet resemble normal bedside administration. For any fair trial a control inert tablet should be given, but if the identity of the tablet is known to the doctor supervising the tests or to the nurses giving the tablets, their own attitude may much influence the attitude of the patients and so corrupt the results. Consciously or unconsciously a nurse giving a substance she knows to be inert may convey her distrust of the tablet to the patient by manner, gesture, or word. The way people can be unconsciously influenced by a word is well shown by the results of an American bureau of salesmanship who found that when a salesman said "Ice-cream, sir? Large?" he sold over 50% more large ice-creams than when he said "Ice-cream, sir? Large or small?" It is therefore essential that the identity of substances under trial be not known by anybody until all the tests are completed. As well as a control tablet and the substance being investigated, it is useful to include a substance of established reputation so that we can answer two questions: (1) does the substance work? and (2) does it work any better than what we are using at present?

In the present trial three kinds of tablets were used: saridone, an inert tablet, and tab. codeine co. (N.W.F.), which is perhaps better known as 'Veganin.' Messrs. Roche kindly made up these three substances in tablets of identical appearance, except that they were coloured red, white, and blue (not necessarily respectively). For the second half of the experiment they supplied another set of tablets in which these colours were changed round. There was no possible way of knowing which colour corresponded to which tablets. The key to the identity of the tablets was provided in a sealed envelope which was kept locked in a drawer until after the whole trial was completed, when it was publicly opened by the chairman (Dr. Avery Jones) at a meeting of the clinical society of the Central Middlesex County Hospital. Messrs. Roche also printed for me a corresponding number of cards bearing on one side instructions to the nurse and on the other side instructions to the patient. The instructions to the nurse were as follows:

These tablets are to be given for the relief of pain, not for sleeplessness without pain. Two tablets of the same colour are to be given. Only one pair of tablets may be tried by each patient. Please hand this form to any patient who is given these tablets.
Please complete this side of the form first and see that the patient fills in the other side properly.

Name of Patient .....
Ward .....
Description of Pain and/or Diagnosis .....
Colour of Tablets Supplied .....
(Different coloured tablets may not be given together.)

The instructions to the patient were as follows:

You are asked to try these tablets which are for easing pain. Please help us to judge them by filling in this form. Do not fill it up for at least two hours after taking the tablets.

1. Was the pain (*a*) Slightly eased? .....
(*b*) Completely relieved? .....
(*c*) Not changed at all? .....
Put a cross against one of these answers.
2. How soon after taking the tablets did you get any benefit? .....
3. Did you notice any other effects from the tablet? If so write them here. .....

EXPERIMENT I

Two hundred pairs of tablets from the first set were distributed to the wards with the same number of cards, and an explanation of the experiment was given to the nurses. They were asked to give the tablets to patients to whom they would normally have given aspirin or codeine tablets, but not to patients with severe pain needing morphine. They were not told that any of the tablets were inert, but most of them guessed that at least one colour of the three kinds would be inactive. They were only told one deliberate lie—that different wards were being given different sets of tablets. I did not want rumours, such as "blue are the duds," to spread from ward to ward; so I left them believing that what was blue in one ward might be white in another. Further I feared that tablets might be lent by one ward to another, which would muddle results if different sets were used (and this actually happened). It was interesting to hear the different reputations of the various colours. In one ward the sister told me "I am sure the white have nothing in them; so I only give them to patients I don't think have really got a pain." In an adjacent ward the sister swore by the blue and restricted their use to the

* Saridone, according to the makers, is an effective and balanced combination of analgesics, rapid in action and free from disagreeable effects. It is recommended for headache, toothache, rheumatism, &c. The formula is:

Isopropyl antipyrine ..	150 mg.
Phenacetin	250 mg.
'Persedon'	50 mg.
Caffeine	50 mg.
Weight of tablet	600 mg.

patients with the worst pain. It became more and more obvious what a good thing it was that nobody really knew which tablet was which, and that the different wards thought they had different tablets. Until both lots of tablets were all used I did not add up the results from the cards, and so I had no idea which were the inactive tablets.

Of the 200 cards issued 141 were suitable for analysis. The others had been lost or were inadequately or ambiguously complete. The results of these tablets are shown in table I. The column marked "strict" gives a strict criterion of relief, and the column marked "wide" gives a wide one—i.e., in the "strict" column relief means that "completely relieved" was recorded, and no relief that "not changed at all" or "slightly eased" were recorded; in the "wide" column relief includes both "completely relieved" and "slightly eased," and no relief means "not changed at all."

From the total results at the bottom of the table it is easy to see, without statistics, that the pink tablets are far less effective than the other two—i.e., over half the patients got no relief from them, whereas from the other tablets more than nine-tenths got relief (in its widest sense). Taking relief in the strict sense the conclusion is the same though not quite so obvious (the pink tablets gave 31% complete relief compared with 55% and 65% for the other two). I was thus almost certain, after adding up these results, that the pink were the neutral tablets. The other deduction is that the blue and the white tablets do not significantly differ in power, for they give 92% and 94% relief (wide criterion) and 55% and 65% relief (strict criterion) respectively. Statistical analysis of the figures confirms these self-evident results.

TABLE I—RESULTS OF TRIALS OF ANALGESIC TABLETS (EXPERIMENT I)

Ward	Effect	White tablet		Pink tablet		Blue tablet	
		Criterion of relief		Criterion of relief		Criterion of relief	
		Strict	Wide	Strict	Wide	Strict	Wide
Annexe	Relief ..	..	..	1	1	1	2
	No relief..	..	..	0	0	1	0
C3	Relief ..	5	6	0	3	4	4
	No relief..	1	0	5	2	1	1
D2	Relief ..	1	2	0	1	1	2
	No relief..	1	0	1	0	1	0
C4	Relief ..	3	5	2	2	4	5
	No relief..	2	0	0	0	1	0
D3	Relief ..	3	3	0	0	1	3
	No relief..	0	0	5	5	4	2
B4	Relief ..	4	5	2	2	0	4
	No relief..	2	1	2	2	4	0
A2	Relief ..	2	2	0	0	1	3
	No relief..	1	1	3	3	2	0
A1	Relief ..	4	5	3	3	3	4
	No relief..	1	0	1	1	2	1
O2	Relief ..	2	5	0	1	3	5
	No relief..	3	0	4	3	2	0
O1	Relief ..	2	4	4	4	3	5
	No relief..	2	0	1	1	2	0
D1	Relief ..	1	4	0	1	2	4
	No relief..	4	1	4	3	2	0
C1	Relief ..	5	5	1	3	4	4
	No relief..	0	0	4	2	0	0
Total	Relief ..	32 (65%)	46 (94%)	13 (31%)	21 (49%)	27 (55%)	45 (91·8%)
	No relief..	17 (35%)	3 (6%)	30 (69%)	22 (51%)	22 (45%)	4 (8·2%)
	Total ..	49		43		49	

TABLE II—RESULTS OF TRIALS OF ANALGESIC TABLETS (EXPERIMENT II)

Effect	Pink tablet		White tablet		Blue tablet	
	Criterion of relief		Criterion of relief		Criterion of relief	
	Strict	Wide	Strict	Wide	Strict	Wide
Relief	22 (42%)	43 (83%)	11 (28%)	28 (70%)	20 (40%)	40 (80%)
No relief ..	30 (58%)	9 (17%)	29 (72%)	12 (30%)	30 (60%)	10 (20%)
Total ..	52		40		50	

When the key to the identity of the tablets was opened it revealed that the pink tablets were inert, the white tablets were codeine co., and the blue tablets saridone. This experiment therefore suggests the following:

(1) Tab. codeine co. and saridone are very effective in relieving various kinds of moderate pain.

(2) There is no significant difference in their effectiveness, but tab. codeine co. was slightly more successful in this experiment (and it is also about a quarter the price of saridone).

(3) An inert tablet can give some relief in 50% of cases.

(4) Small experiments are useless in judging analgesic effects—note the widely differing results in different wards.

It cannot be assumed that the 50% effectiveness of a dummy tablet is due to suggestion; a proportion is doubtless due to spontaneous remissions of pain. It would be impossible to measure this proportion without a further series of patients who were given nothing for their pain—not even a dummy—and such people might be too disgruntled to complete their cards properly.

EXPERIMENT II

When the first experiment had been completed (but not computed), the second lot of tablets were used to confirm the previous findings. In this second experiment, because it was troublesome dealing with many different wards, only the two maternity wards were used. Consequently this series contained a high proportion of "after pains" and "headaches" and is not strictly comparable with the assortment of pains tested in the first experiment. Nevertheless the conclusions were much the same—see table II, which records another 142 trials.

The white tablets were obviously less effective than the pink and blue tablets, giving only 28% complete relief compared with 42% and 40% with the others. White was correctly deduced as being the dummy. The pink tablets were saridone, and the blue tablets codeine co. Therefore, as before, saridone and veganin were about equal in effect, giving complete relief in 42% and 40%, and some relief (wide criterion) in 82·8% and 80% of cases, respectively. All these figures are lower than those of the first experiment and suggest that after pains do not respond so well to analgesics as do other varieties of pain. Nevertheless, these women got much more relief from inert tablets than did the patients in the other series—70% compared with 49%. This may mean that women are gullible and more easily duped, but I think more probably it shows that after pains and headaches very often clear spontaneously.

OTHER FINDINGS

No significant effect from colour was noted—i.e., the relative efficacy of the tablets was the same in both experiments—but there is possible evidence that a dud white tablet is better than a dud pink one (some patent-medicine merchants may be interested to know this).

No significant side-effects were noted with any of the tablets, and no information was obtained about the speed of action of the different tablets, partly because so few patients filled in the sections asking about these matters.

COMMENT

This investigation was fairly easy to carry out, and I suggest that the tricolour method or a modification of it should be used as a standard method of testing various drugs. Uncontrolled tests give results so variable as to be valueless. Such controversies as that about the effect of vitamin E in angina or in the myopathies might well be settled in this way. Any substance deserving to be used by clinicians ought to be discernible from a dummy without its identity being known, and to show some advantage over other active substances serving the same purpose.

My thanks are due to Messrs. Roche, who supplied the tablets and cards; the medical staff who allowed me to try these tablets on their patients; and Dr. George Discombe and Dr. Richard Doll for help in the presentation of the results.

Medical Societies

NORTH OF ENGLAND OBSTETRICAL AND GYNÆCOLOGICAL SOCIETY

Early Stages of Cervical Cancer

AT a meeting of this society in Manchester on Oct. 8, with Mr. J. E. STACEY, the president, in the chair, an address on Early and Precursory Stages of Cervical Cancer was given by Prof. EMIL NOVAK (U.S.A.).

Last year, said Professor Novak, 18,000 women in the U.S.A. died from cancer of the uterus. It would appear that as regards the development of malignant disease there are three classes of people: (1) those whose inherent predisposition is so strong that they are predestined to suffer cancer irrespective of any other circumstances; (2) those in whom the predisposition is less prominent and in whom an exciting factor is required for development of the growth (the factors possibly exciting the uterus being injury, infection, and œstrogenic hormones); and (3) those who have no predisposition and who will never develop cancer even when exposed to those activating factors which determine the onset of the disease in class 2.

The relationship of œstrogens and carcinoma is difficult to define. Judging by the well-known effects of these hormones, they might reasonably be supposed to cause cancer in susceptible women; but this action could operate only in respect of the breast, uterus, vagina, and vulva. Experimentally cancer of the breast has been produced with œstrogens only in mice. Cervical changes in animals after the administration of œstrogens can be prevented by giving progesterone, which seems to have some protective effect against the carcinogenic action of œstrogen. Though agreeing that there might be hesitation in employing œstrogen therapy in the presence of a precancerous lesion, or in a woman with a strong family taint of malignant disease, Professor Novak said that he did not know of a single case in which œstrogens had been shown to have caused cancer in women.

Turning to pathological features, he observed that leucoplakia of the cervix is now generally held not to predispose to malignant change. The most important lesion is intra-epidermal carcinoma, alternatively known as Bowen's disease or carcinoma in situ. In this the cells of the epidermis take on malignant features, but the disorder may remain localised for many years, ultimately breaking through the basement membrane to assume typical malignant characters. When this condition is found in one part of the cervix, fully established carcinoma is commonly found in another part when a thorough search is made. Nevertheless, with routine and careful examination of cervices it should be possible to find and treat this lesion while it is localised. Amputation of the cervix is probably sufficient, though in Professor Novak's clinic total hysterectomy is usually carried out—partly for the purpose of having all the material for study and research. Another change in the cervix which may be significant is unusual activity of the basal cells of the epidermis. This may be a reaction to a hormonal stimulus. Such a change, and even pseudomalignant features, are to be seen in the cervix sometimes during pregnancy; they are reversible and may well be associated with the profound hormonal changes of pregnancy.

In the early diagnosis of malignant and premalignant states the Schiller test with iodine has little application, since it indicates merely the site of pathological change and not its nature. Vaginal-smear studies are in vogue but are extremely difficult to interpret; even the few experts with adequate experience admit a comparatively high percentage of errors in diagnosis. Cervical biopsy still remains one of the most reliable methods, particularly when the modification known as "surface biopsy" is adopted. By this method large areas of the superficial layers of the epithelium are removed by scraping with a curette or sharp spoon. This is a most satisfactory way of revealing intra-epidermal carcinoma.

New Inventions

A MONOCHROMATIC HALOMETER

THE halometric determination of red-cell diameters is capable of considerable precision provided the diffraction halo is reduced to its simplest form and a sound method of measurement is adopted. The halo appears as a central bright disc surrounded by a bright ring—the fainter outlying rings can be ignored. The problem is to measure the angular diameter of the bright ring. The ring fades off indefinitely inwards and outwards, and when, as is usual, an ordinary lamp is used, it ranges through the spectrum from blue on its inner side to red on its outer side. It is impossible to define at all simply what one means by the diameter of such a ring. If, however, a monochromatic light is used the ring will appear of a uniform colour fading off inwards and outwards from a brightest central zone. One is thereby provided with a perfectly definite diameter —that of the brightest zone.

The most popular method of measurement is to use two lights and thus produce two halos. By adjusting the distance between the lights one attempts to bring the two rings into contact, when the angular distance between the lights will equal the angular diameter of either ring. If the rings were thin circles of light this method would be ideal, but that is not so with diffuse rings. Even with monochromatic halos it is extremely difficult to estimate when the brightest zones coincide, owing to overlapping of the edges; but with coloured halos the overlapping colours reduce the procedure to mere guesswork.

Early last century Thomas Young measured halos by a most effective method which seems to have been forgotten. He introduced between the blood film and the light a screen containing a central aperture surrounded by a ring of pinholes, so that the pinholes appeared superimposed upon the halo. By adjusting the distance of the screen, he placed the pinholes on the brightest part of the coloured ring. The distance between the eye and the screen was then proportional to the diameter of the red cells. If a monochromatic light is substituted for the white light, one can place the pinholes on the brightest zone of the monochromatic ring with much greater precision.

An instrument incorporating a monochromatic light and Young's perforated screen has been in use in my laboratory for twelve years, and its theoretical advantages have been fully borne out in practice. The design has recently been modified and the completed instrument has been built for me by Kaylene Ltd., of Cricklewood. A mercury lamp with choke is enclosed in the apparatus and can be plugged direct into the alternating-current mains. Part of the beam passes through a filter to produce a green or yellow monochromatic halo; another part remains unfiltered and illuminates the pinholes which thus appear as whitish points standing out sharply against the green or yellow halo. To obtain the highest accuracy the brightness of the halo is con-

trolled by an iris diaphragm and that of the pinholes by a movable "occulting disc." An aluminised mirror turns the rays through 90° so that the film to be measured is in a *horizontal* position. In this way one can also measure cells in the wet state. The cells suspended in a salt solution or in their own serum are run into a chamber provided for the purpose and allowed to settle down on its floor. Both cm. and μ scales are provided, the latter ranging from 5·0 to 10·0 μ.

When anisocytosis is slight the halometric diameter corresponds to that given by the peak of the Price-Jones curve. With increasing anisocytosis the halometric diameters tend to be somewhat larger, but the halometric diameter is always a perfectly definite quantity which the measures of different observers can very closely reproduce.

It is found that cell suspensions give even more consistent results than dried films, in which unequal shrinking is so liable to occur. Already interesting results are being obtained on the manner in which cell diameters vary with changes in their suspending media.

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Reviews of Books

Dupuytren's Contraction

With special reference to ætiology and improved surgical treatment. TORD SKOOG. *Acta chir. scand.* 1948. **96.** Suppl. 139.

SOME 355 authors have contributed to this subject, the first as early as 1614. None, however, has dealt with it as thoroughly as the writer of this monograph. He gives a minute description of the anatomy and embryology of the palmar aponeurosis, a detailed survey of the incidence and symptoms of the disease, and an original discourse on its pathology and pathogenesis, supporting his arguments with some convincing photomicrographs and electron-microscope observations. He relates the condition to some similar changes in connective tissue, and to epilepsy, and finally surveys the history of treatment and gives a complete description of treatment by modern surgery. His monograph will be valuable to surgeons and teachers.

Proteins and Amino Acids in Nutrition

MELVILLE SAHYUN, M.A., PH.D., biochemist consultant, Charles Godwin Jennings Hospital, Detroit, Michigan. New York: Reinhold Publishing Co. London: Chapman & Hall. 1948. Pp. 566. 45*s*.

EACH of the fifteen chapters in this book is by a separate author or authors, and each deals with some aspect of protein metabolism. The last two are on the protein nature of toxins, antitoxins, and related substances, and the protein nature of filtrable viruses. The last-named, by Max Lauffer, is one of the best in the book.

The opening article, on the historical aspects of proteins in nutrition, shows how the work of the pioneers such as Magendie, Mulder, Boussingault, Claude Bernard, Voit, and Rubner led up to the contributions of the great men of more modern times like Atwater, Kossel, Hopkins, Osborne, and Mendel. H. H. Mitchell has contributed a sound chapter on the biological utilisation of proteins and protein requirements, and Deuel one on caloric, vitamin, and mineral requirements, with particular reference to protein nutrition. A study of the economic aspects of food proteins by Lela Booher is thoughtful and clearly presented. The chapter on the amino-acid requirements of birds, by Almquist, will interest those whose interests have been confined to mammals. Abraham White deals with the relation of hormones to protein metabolism, and the remaining chapters are on plasma proteins, protein deficiency, and protein and amino-acid requirements —in children, in surgical patients, in cases of burns, and in relation to fluid balances and mineral salts. The best chapters are written by those who have themselves made outstanding contributions to their subjects.

The book is an all-American production and suffers in places from isolationism. It is misleading, for instance, in a review of nutritional œdema, to neglect entirely the fundamental work done in Germany between 1915 and 1925. It never has been, and never can be, superseded. A little repetition here and there might have been avoided by stricter editing. It is questionable if the inclusion of the Chatfield and Adams tables of food composition or those of the Bureau of Human Nutrition, occupying 90 pages of text, was justified. The book has a distinctly clinical flavour, and in no way competes with the recent series of volumes on "Advances in Protein Chemistry." A second edition in a few years' time would be welcome.

Nouvelle pratique chirurgicale illustrée

(Fascicule 1.) JEAN QUÉNU. Paris: Doin. 1948. Pp. 274. Fr. 550.

THIS atlas of surgical operations, accompanied by a few notes on methods and indications, is really a continuation of those excellent books originally written by Pauchet. The illustrations, by the same artist, are clear and explanatory. This first volume ranges over a number of departments of surgery. Dr. Quénu, the chief editor, presents abdominoperineal excision of the rectum and hysteropexy, giving indications for the latter. He considers fixation of the isthmus of the uterus to be preferable to round-ligament fixation or suture of the fundus; but of course, in order to do this operation, the surgeon must be able to bring the isthmus up to the abdominal wall above the pubes. The other operations selected, described by his associates, are radiotherapy of the uterus, the cure of vesicovaginal fistula, the treatment of non-union of a fracture of humerus and of the neck of femur, and arthroplasty for osteo-arthritis of the hip—the method of dealing with the hip being original. All these operations are of interest to English readers.

Occupational Marks and other Physical Signs

FRANCESCO RONCHESE, M.D., instructor in dermatology, Boston University. New York: Grune & Stratton. 1948. Pp. 181. $5.50.

Dr. Ronchese has brought together, by means of some 250 photographs and diagrams, examples of characteristic body marks, common and uncommon. Here are the callosities of barbers, tailors, carpenters, jewellers, plasterers, cooks, and surgeons, the boxer's cauliflower ear, the golfer's finger-joint, and the violinist's neck-mark. The book's subtitle is "A Guide to Personal Identification." The author warns us that his pages will not turn every practitioner into a Sherlock Holmes, but he offers us these records of diversified medical practice, having found them useful as an aid to the scientific identification of unknown bodies and hoping that they may stimulate others to make further contributions.

Modern methods such as the use of protective gloves may nullify the value of some of these occupational stigmata; some marks are becoming obsolete. The ischial bursitis known as "weaver's bottom," now rare, may have been common in the days of hand-weaving. (Dr. Ronchese remarks, by the way, that Shakespeare's choice of the name Bottom for his rustic weaver may have had this association.) There is a short chapter on deceptive markings and legal problems; the question whether a callus entitles the patient to compensation is touched upon. A brief foreword by Prof. John G. Downing emphasises the value of developing the faculty of correct observation and correct interpretation. The law reports, he remarks, contain cases of mistaken identity resulting in injustice. "It is possible to change the colour of the hair, remove teeth and alter the appearance in other ways, but the stigmata of occupation last for a long time." Such physical marks are useful evidence for identification. "Good physicians must be good detectives also to solve the riddle of disease."

A Synopsis of Regional Anatomy (6th ed. London: J. & A. Churchill. 1948. Pp. 436. 18*s*.).—Prof. T. B. Johnston's synopsis has reached its venerable position because it is useful and accurate. The new edition finds space for a summary of the extrapyramidal system, and other new matter has been added. The student can perhaps be trusted to find out the pleasures of the book. Professor Johnston, following the principle laid down in the old advertisement for 'Monkey Brand,' contents himself with a warning: "the book should not be consulted at all," he says, "until the actual work of dissection is completed and revision is being undertaken." That is indeed a moment when most students are glad of a little topographical guidance.

THE LANCET

LONDON: SATURDAY, NOV. 13, 1948

A World Influenza Centre

Two related happenings have emphasised the need for better international collaboration in the field of influenza. First, promising reports of successful vaccination against this disease in 1943 and 1946 have been followed by the disappointing news of almost total failure in 1947. Eight unfavourable reports have lately been published in America [1] and one in Britain.[2] All observers agree that this sad result is probably due to the emergence of an antigenic type of influenza virus A not closely related to those used for making the vaccine. Apparently, serological races of A can differ from each other widely enough to vitiate attempts at vaccine prophylaxis. Second is the evidence suggesting that influenza viruses may be capable of spreading rather quickly across the world. Influenza B apparently did so in 1945–46 and a type of virus A which caused trouble in America in 1947 is apparently identical with strains recovered in Britain, Holland, and Sweden at the same time and possibly with one isolated in Australia in 1946. There is thus an obvious need for study of the "global epidemiology" of influenza.

As an outcome of informal discussions on this matter held at the International Microbiological Conference in Copenhagen in 1947, the World Health Organisation is supporting a World Influenza Centre. The Medical Research Council has agreed that this shall be set up at the National Institute of Medical Research at Hampstead under Dr. C. H. ANDREWES, F.R.S. As a beginning, the centre hopes to obtain prompt news of the prevalence of influenza anywhere in the world and to collect strains for study. Such strains will be examined and compared at Hampstead or sent to interested laboratories elsewhere. The success of the scheme depends on establishing contact with workers in other countries. The hope is that a number of countries will designate laboratories as regional centres, which will be able to decide by serological tests whether local outbreaks are due to viruses A or B, and to isolate and dry new strains and send them to the centre. Countries not equipped to establish regional centres will be asked to appoint observers who will keep the centre informed of the local activity of influenza and if possible send specimens by air to the nearest regional laboratory. In the United States an organisation along similar lines has been begun. About 35 laboratories have been invited to act as "watch stations" or "listening posts," and these will send new strains to a national influenza strain study centre in New York. Close coöperation will be maintained between this centre and the one in London.

The present set-up is designed primarily to acquire information; as yet it has neither the knowledge nor the authority to try to stop the spread of epidemics. It will try to find whether we are right in guessing that these strange serological races of flu are globe-trotters. It aims to learn whether there are limited numbers of serological types of influenza or whether the virus has limitless powers of variation. Maybe the information gained will be such that we can later hope to foresee the advent of a new strain from abroad and have time to prepare a homologous vaccine to greet it; such hopes are decidedly premature at present. Let us hope that the centre will justify itself and prove how great are the possibilities of fruitful international collaboration under W.H.O.

1. cf. Loosli, C. G., Schoenberger, J., Barnett, G. *J. Lab. clin. med.* 1948, 33, 789.
2. Mellanby, H., Dudgeon, J. A., Andrewes, C. H., Mackay, D. G. *Lancet*, 1948, 1, 789.

Hospital Manners

SOME hospitals have a name for making patients welcome, and take a pride in keeping it. What starts such a tradition? Doctors with a friendly manner? An enlightened matron? Well-chosen sisters? Contented nurses? Whichever it is—and all must play a part—such a tradition is of great moment to the sick. Moreover, it is not easily broken, for every newcomer to the staff breathes it in and learns to pass it on. But unfortunately bad traditions are as easily inherited and as hard to break as good ones. Our correspondent on p. 782, who has tried both, gives an instructive account of life in a hospital where the tradition was a poor one. There is nothing unfamiliar about the picture she draws: she got the sort of treatment we are all apt to get nowadays in shops, restaurants, and hotels—grudging unwilling service. The cause of this attitude can hardly be debated here; some blame CROMWELL, others wars, fatigue, national poverty, or even the licensing laws; but it marks a decline from our status as Merry England and from former standards of kindness. This decline has to be checked. Happily there are a few hotels left where the staff seem actively pleased to see the traveller; there are still some hospitals where the patient's comfort does not take second place to administrative convenience—or at any rate not all the time; and from these islets of good practice regeneration might begin. The danger is that a spread of bad practice will outstrip the healing process.

One strikingly bad practice noted by our correspondent is that of leaving the patient in the dark about his condition. "They don't tell you anything" is a serious allegation against any hospital, and especially against the doctors, since it ascribes to them an almost 19th-century concern with the purely physical facts of the case, coupled with a 20th-century disregard of the rights of the individual. Consultants who cannot, or will not, spare time to explain the patient's illness to him in a few private words, or who do not insist that their housemen explain it, are out of date in their medicine. Even the family doctor too often protects himself by oracular silence, leaving the patient to make his own painful or alarming guesses. It is increasingly clear that recovery

is often bound up with the mental attitude of the patient towards his disease; but modern studies in psychosomatic medicine must appear strangely unreal to the student who sees his teachers ignoring the elements. The embarrassment some patients feel at exposure of their abdomens to a class of students is nothing compared with the anxiety that can be created by an exchange of obscure and alarming terms over their heads. While some teachers never lose sight of the patient's feelings, others are courteous but aloof, others again friendly but careless, and some, in the give and take of bedside teaching, forget the patient entirely, exposing him physically to draughts and mentally to fear while they compare his condition with other grave disorders, and make technical jokes when a student blunders. To teach and treat simultaneously is a most difficult art; but those who undertake it must remember that their technique will be learned by students no less conscientiously, though much less consciously, than their opinions.

Meanwhile a patient is far from being a passive observer of human nature in action. Accustomed to think of himself as an adult citizen of a free country, he holds that he should be told not only what his symptoms mean, but what the doctor hopes the treatment will achieve, and why. He dislikes being launched on some new course of treatment without any understanding of its form and purpose. The example given by our correspondent of two women who worried for twenty-four hours about a new kind of treatment, only to find it was merely a different sort of medicine, is a case in point. Fearing to give trouble, they mentioned their anxiety only to other patients. It never entered the heads of the houseman and sisters that they might be afraid. The houseman, presumably, had never been taught to think like that; yet the ability to ask the right question at the right moment can be taught as directly as percussion and auscultation. These two patients had a clear-cut fear which would have been readily disclosed in friendly conversation; others may have more obscure fears at which the doctor can only guess. But sometimes even gross signs of fear are ignored as long as possible: "the patient's physical reactions were studied," our correspondent remarks; "his mental reactions received no attention till they caused trouble." Trouble, that is, to other people. But fear is apt to give itself away, especially in the pulse-rate; any houseman can learn to spot the initial signs of fear, and he should act on them at once; indeed, he should act first, whenever possible, by explaining the patient's illness and treatment to him, for this can almost always be done in a manner to allay rather than increase alarm. Patients may be childish at times, but they are not imbeciles.

What happened to the nursing staff in the first hospital our correspondent describes? What petty frustrations or prolonged fatigue had reduced them to a mood of antagonism towards their patients? It is noteworthy that the mood had spread to the patients themselves. Hens have been shown to have a peck order, the strongest pecking the next strongest, and so on, until one wretched hen, at the lowest ebb of strength, gets pecked by all. It is a fair surmise that a nurse who is sharp with her patients is hen-pecked. Unfortunately even the most junior student nurse is not the most feeble chicken in the roost: there is still the patient. But apparently the mood was different in our correspondent's second hospital, where the nursing was good. This is a small hospital with a reputation for friendliness. Relations between members of the medical staff have always been cordial, and the matron and sisters take a personal interest in the patients. Since the hospital is not a complete nurse-training school, the matron has some difficulty in getting nurses: but none, it appears, in keeping them. The nurses' home, an ordinary house not far from the hospital, is not outstanding; but it is under the charge of a married warden who is not a nurse and has a family of her own. The moral seems evident enough: contented nurses make contented patients. Moreover, they tend to stay in their profession.

Apart from doctors and nurses, the patient has to adjust himself to many other people in the hospital—to the porter who receives him, the clerk who takes his particulars, the almoner, the chaplain, the radiographer, the students, the pathology technician, the ward-maids—all of whom, except perhaps the last, may ask him questions and none of whom expects to be asked any back. This anonymous approach can be exasperating to anyone accustomed to ordinary standards of good manners; it dates back to the time when the patient was a derelict. So too do the lack of rest, of quiet, and of good food, which have still to be endured so commonly: though these are perhaps less important than failures in human behaviour. What is wrong with our spirit that we accept these failures? In other walks of life it may be that a man sells his time but not his good humour—his ability to work but not his ability to make friends and crack jokes while he is about it. But what has this to do with medicine and nursing, professions in which good humour is an essential qualification? If the rest of our countrymen want to water down their offering to the common good that is their affair; but surely doctors and nurses should say, with Noah, "I don't care where the water goes if it doesn't get into the wine."

Insult to Injury

IN childhood most of us have borne, stoically or otherwise, the application of iodine to abrasions of knee or elbow. Our parents had no doubt that they were saving us from sepsis or worse. Iodine (as the linimentum iodi) first appeared in the *British Pharmacopœia* in 1885, but there is a record of its use in the treatment of wounds as early as 1839. That it should have been used in the pre-Pasteur age is empirical evidence of its utility. The later argument is clear: the unpleasant sequelæ of wounds are mostly due to bacterial infection; iodine kills bacteria; therefore iodine (or whatever local antiseptics were favoured by authority and fashion from time to time) must encourage natural healing. The experiences of 1914–18 raised some doubts. ALMROTH WRIGHT showed that the bactericidal antiseptic was also leucocidal. The Commission on the Health of Munition Workers reminded the profession that infection may enter a wound at any time after its infliction, and that there-

fore the logical treatment of a "clean" wound is to cover it quickly. Nevertheless, since most wounds are probably infected from the start—and because we must do something!—local antisepsis has remained with us and countless gallons of tincture of iodine, "blue paint," picric acid, and the flavine and phenol compounds have been applied to mankind for prevention or cure.

From time to time attempts have been made to devise techniques, in vitro and in vivo, to assess the usefulness of this procedure and to compare the value of the various antiseptics. The late war gave renewed stimulus to this work, and a mass of information has been published. But the subject is far harder to study than superficial consideration would suggest, and it cannot be said that observations on natural wounds carry much conviction. The term "wound" covers a wide range of injuries; and efforts to define the extent, severity, and even site of a wound must depend on personal judgments. While staphylococci, streptococci, and the coliform organisms make up the major invading force, other organisms are almost constantly present, of whose importance, if any, we are less well informed. Moreover, the antiseptic may be applied in so many forms and concentrations that comparisons are hazardous. To the surgeon it is axiomatic that no two wounds are alike, and human capacity makes it certain that no one observer will see more than a small sample of wounds of all sorts. Thus investigations are usually restricted to the cruder statistical processes. Tests on the intact skin are of course, less subject to these errors and limitations, as is shown by the satisfactory examples which Professor GARDNER reports in this issue.

Experimentally, however, wound, infection, and treatment can all be standardised; and, by using mice, tests can be repeated often enough to give full scope to the statistician. In an investigation at Leeds [1] large numbers of mice were subjected to a uniform wound, which was infected with pure cultures of organisms whose virulence for the animals was constantly reviewed by control experiments. The effects of several local antiseptics in varying concentrations were observed. As far as possible all the pitfalls were avoided, and though the unambiguous answer on the value of local antiseptics still escapes us, it seems clear that the early use of certain antiseptics on wounds infected with streptococci is justified. Sulphanilamide, "blue paint," and some flavine compounds gave the best results, while iodine and the phenol compounds were apparently less useful; but performances were often inconsistent. A promising newcomer was 'Quininal'—a new form of dye derived by sulphonation from 2 (*p*-dimethylaminoanil) 6 methylquinolinemethochloride. This was particularly effective in vitro against *Bacterium coli* but was toxic in vivo in the form used. Once more the wisdom of the surgeons was confirmed by the poor results obtained from injection of the antiseptic into deep and closed wounds. After all, debridement and full exposure mean no more than the conversion of a deep to a superficial wound.

If we are to translate this valuable investigation into everyday practice there is still some guessing to be done. No local treatment saved all experimental animals from death; no local antiseptic was far better than the others. There is also much work to be done on the pharmaceutical side, and the technique used at Leeds might be profitably employed in seeking the most generally useful method of compounding flavine and the sulphanilamide compounds. Moreover, the work lately recorded in our columns [2] shows once more that diamidine derivatives should have a full trial. Since human wounds are not standard, and the infecting organisms are a fairly inclusive selection from the catalogue of schizomycetes, we must not hope that experiments such as these will immediately bring to light the ideal local antiseptic. However, there is little doubt that small boys show sound judgment in preferring proflavine to tincture of iodine on their bare and bloody knees.

1. Gordon, J., McLeod, J. W., Mayr-Harting, A., Orr, J. W., Zinnemann, K. *J. Hyg., Camb.* 1947, **45**, 297.

Annotations

A FAMILY MATTER

PROBLEM families, unlike problem plays, seldom confine themselves to one problem at a time. They bristle with problems, and hook them like burs into any passing coat. A few years ago Dr. C. P. Blacker made a list [3] of the problems they present, and the people who may be called upon to solve them. Thus the children of a problem family may be delinquent, or may have been removed from their unsatisfactory parents; or they may be lousy, scabietic, dirty, neglected, or ill treated; or the family may have high miscarriage, stillbirth, and infant-mortality rates; or it may be chronically dependent on public funds; or some of the members may show the features mentioned in the Wood report—mental defect, backwardness, mental disorder, epilepsy, drunkenness, prostitution, unemployability, and crime or recidivism. Those who encounter problem families in one or other of these manifestations are medical officers of health, school teachers and medical officers, school nurses and attendance officers, N.S.P.C.C. inspectors and heads of other voluntary bodies including the Family Welfare Association, health visitors, sanitary inspectors, district nurses and midwives, public-assistance officers, probation and relieving officers, chief constables, borough treasurers, directors and social workers of child-guidance clinics and of psychiatric clinics for adults, superintendents and social workers of mental hospitals, and officials of labour exchanges. What is needed is some means of pooling their information and dealing with the family as a unit; and Dr. Blacker suggested that the proper thing to do was to make some one person in each area responsible for receiving reports on problem families, ministering to their needs, and endeavouring to reclaim them.

As a step towards this end the Problem Families Committee, of which he is chairman, has lately undertaken six pilot inquiries,[4] with the primary intention of establishing a serviceable method of investigation. First, people, bodies, and departments likely to come into touch with problem families are to be invited to submit names and brief particulars of any such families known to them. The number of times a single family is mentioned by different bodies will give some indication of the size of the problem it presents. A consolidated list of families will be prepared under the direction of the M.O.H., in which the families will be set out in terms of the number

2. Wien, R., Harrison, J., Freeman, W. A. *Lancet*, 1948, i, 711. Kohn, F., Cross, C. D. *Ibid*, Oct. 23, p. 647.
3. *Eugen. Rev.* 1946, **38**, 117. Reprinted, June, 1948.
4. Problem Families: Six Pilot Inquiries. Issued by the Problem Families Committee, 69, Eccleston Square, London, S.W.1. Pp. 16.

of their "mentions"; and a conference will then be arranged of the people and bodies who contributed the names. It may turn out that many "mentions" do not necessarily mean a problem family, and this is one of the things the survey sets out to test. Some of the families on the consolidated list will probably be excluded as outside the range of the inquiry, and a shorter list of possible problem families will be compiled and assessed at first hand by a health worker. As a result of her visits to the home the list will doubtless be still further reduced. For each of the remaining, authentic, problem families a card will be filled in and sent to the committee's headquarters where the results will be examined and analysed. The six areas to be surveyed are Bristol, Warwickshire, Luton, Rotherham, West Riding, and Kensington—a reasonable cross-section of England, since they include a port, a metropolitan borough, two administrative counties in the Midlands, a county borough, and an actively growing industrial town. (Two of the areas include rural districts.) These surveys should widen our knowledge considerably and clear the way for the next step—treatment.

SCHOOL FEEDING

Mr. F. Le Gros Clark sees school meals as more than a useful safeguard of the nutrition of children. In a new booklet [1] on the history of their development he comments on two important educational aspects of the service: it must establish, over the course of a generation, a flexible and wholesome set of food habits, and it must initiate the child into good social habits at the same time. "We cannot," he says, "make the child tolerant, self-reliant and easy-mannered in the abstract; we have to choose some medium through which these qualities can be imparted to him. For such a purpose the meal table is ideal."

School feeding, like so many other social services, was begun by voluntary bodies. In the late '80s of the last century schemes for providing free school meals were numerous and increasing; and in 1889, on the initiative of the London School Board, a School Dinners Association was formed. By 1906—when the first Act permitting the provision of these meals by local authorities was passed by Parliament—Manchester, Birmingham, Bradford, Glasgow, and several other boroughs were already supporting private funds of some size. The first Provision of Meals Act, which gave local authorities the power to supply meals to necessitous children from the proceeds of a ½d. rate, had plenty of opposition. Taxpayers, it was said, were already overburdened, and the families of children who were freely fed would be pauperised. The Board of Education, however, was quietly determined that the provision of meals should be a medical and educational measure; and this was achieved, though, as result of opposition from the Lords, Scotland was excluded from the Act. Nevertheless, the business of deciding which children were necessitous enough to be fed was still claiming more attention than was the type of food to be provided or the manner in which it was to be served. When the School Medical Service was founded, a year or two later, the task of selecting children was placed in the hands of the school doctor; but there were administrative difficulties about this. Moreover, the necessitous child was fed only on school days and went hungry during holidays. Nevertheless the numbers of children being fed rose gradually if not spectacularly—in London from 29,000 weekly in 1906 to 41,000 weekly in 1911; but as might be expected charitable donations towards school meals declined, falling from £17,000 in 1908 to £950 in 1914 when the next Act was passed. Under this Act, the powers of the local authorities to provide meals were still permissive, but they were no longer expected to do it on the yield of a ½d. rate. A bad time followed: the Act was passed on the day war broke out, and Government policy at that time was the reverse of that in the recent war. During the first year of war 420,000 children received meals, but by the last year only 43,000 were getting them, and this decline was encouraged by the Minister of Food. In the postwar depression the Geddes axe aimed another dangerous blow at the scheme: in 1922 the board's grant was restricted, and authorities were instructed to show economies. During the whole period of the peace the proportion of children receiving meals rarely rose above 3·5%, and sometimes fell to 2%. Towards the close of the '20s the custom of providing milk in schools became more general, and a growing number of authorities accepted this partial measure as a solution of their difficulties.

In the '30s a change came; the boroughs were beginning to concentrate on the provision of free meals for poorly nourished children, while the counties, though providing meals on payment in a few rural schools, were making little attempt to provide free meals. The parents, too, still hung back, seeing free school meals as a form of charity. The 1939–45 war had the effect of reversing this prejudice, we may hope for good. The Government's policy of feeding the children led to a wide development of the school meals service, at first in the reception areas and later throughout the country. It was an extraordinary achievement, raising the percentage of elementary-school children receiving meals from 11·4 in 1942 to 33·8 in 1945. Even so, the parents had to be persuaded to accept the scheme by a completely fresh approach. The figure is still far below the 75% proposed as a target by the Government, but it represents an advance in our sense of social responsibility which it would have been hard to imagine a hundred, or even fifty, years ago.

1. Social History of the School Meals Service. Published for the London Council of Social Service by the National Council of Social Service, 26, Bedford Square, London, W.C.1. Pp. 28. 2s.

TREATMENT OF THYROTOXICOSIS

WHEN the Medical Society of London discussed thyrotoxicosis eighteen months ago,[1] most speakers preferred surgical methods to treatment by thiouracil. Dealing with the same topic last month, members of the Liverpool Medical Institution took a rather more kindly view of this drug. Neither method, as Mr. Philip Hawe pointed out, is ideal; and each is used best only by careful selection of cases. He suggested that all well-defined nodular goitres and most goitres in elderly patients, especially when associated with cardiac complications, should be considered for operation, while the young patient with a diffuse goitre should have a trial of thiouracil; for the many intermediate cases there can be no hard-and-fast rule. He has had gratifying results in preoperative treatment with thiouracil followed by a course of iodine. Since the war, he observed, post-operative crises seem almost to have disappeared, possibly because of improved preoperative care. Mr. A. M. Abrahams mentioned his impression that the disease itself has become less severe.

Some of the essential factors in causation are still unknown; and Prof. Henry Cohen remarked that the clinical picture of thyroid affections shows that thyrotoxicosis and hyperthyroidism are not synonymous, though the former includes the latter. Moreover, the diverse patterns of thyrotoxicosis suggest that it may be the expression of more than one ætiological factor, and that the susceptibility of different tissues to thyroxine, and their capacity to use it, may modify the clinical picture. Thiouracil and radioactive iodine do not attack extrathyroid causative factors; but despite toxic hazards, the risk of mechanical difficulties from swelling of the goitre, and the possibility of overlooking malignant

1. See *Lancet*, 1947, i, 376.

disease, thiouracil, in Professor Cohen's view, has a place in treatment. It will be remembered that in our issue of Oct. 30 Sir Carrick Robertson, comparing surgical and medical results in a series of 350 cases, recommended thiouracil for young people with Graves's disease, for elderly people who are serious surgical risks, for cases with predominance of nervous symptoms other than depression, for cases of thyrotoxicosis recurring after operation, and as a means of preoperative preparation.

STANDARDISATION OF TRANSFUSION EQUIPMENT

AT a meeting in Oslo last month representatives of Norway, Sweden, and Denmark decided to adopt a common standard for equipment used in blood-transfusion. The equipment chosen is similar to the British, and any part can be used with a British set. The benefit of this arrangement is that standard bottles filled in any one of these countries can be readily used for transfusion in either of the others. In the Inter-Nordic Standards Association the Scandinavian countries have an effective body for the arrangement of agreed standards. The obvious advantages of standard equipment may persuade the countries of the Western Union to follow Scandinavia's example.

THE HYPERTENSIVE'S LIFE-SPAN

DESPITE the prevalence of essential hypertension, doctors are still unable to estimate with any confidence its effect on the expectation of life. A report published lately in the United States suggests that this effect is far less than is usually supposed. From his private case-records, dating back to 1914, Burgess [1] chose the first hundred patients with essential hypertension who were found to have a blood-pressure of 180/100 mm. Hg or more and who were alive eight or more years afterwards (aiming in this way to exclude any cases of malignant hypertension). Of these hundred patients ninety were found to have had hypertension before 1932, while the remainder were first observed between 1934 and 1936. In 1947 forty-seven were still alive, while fifty-three had died. Of those alive, the average duration of life since the hypertension was discovered was 16·9 years, compared with an average expectation of life of 21·6 years. The comparable figures for those who had died was 14·2 and 17·8 years. Taking all patients together, the figures were 15·7 years for the actual duration and 19·8 years for the expectation. Every patient who was 65 years or older when the hypertension was first noted attained the life expectation.

Of greater interest is the analysis of the thirty-two patients in whom the hypertension was discovered at or before the age of 50. Of these, twelve had died, having lived an average of 15 years, compared with an expectation of 26 years. The twenty survivors had lived an average of 18 years since the hypertension was first noted, compared with an average expectation of 29·4 years; all but three of these patients are leading normal lives without symptoms. Of the twenty-seven patients with a systolic pressure of 250 mm. Hg or more at some time or other while under observation, the duration of life for the nine still alive had been 19·1 years (compared with an average expectation of 22·9 years), while the eighteen who had died had an average duration of 16 years (compared with an expectation of 18·5 years). The significance of these observations is enhanced by the fact that the five patients in whom a reading of 300 mm. Hg or more was recorded on one or more occasions, had an average duration of life slightly in excess of the normal. In striking contrast is the position of those with severe diastolic hypertension. Of fifty patients with a diastolic pressure of 120 mm. Hg or over, twenty were still alive, with an average duration of life of 17·8 years (compared with an expectation of 24 years). For the thirty who had died the comparable figures were 14·6 and 21·7 years. Of those with diastolic pressures under 120 mm. Hg, twenty-seven were alive with an average duration of life of 16·2 years (compared with an average expectation of 20 years), and twenty-three had died having lived an average of 14·7 years since the hypertension was first noted (compared with an average expectation of 16·6 years). Taking the group as a whole, the shortest duration of life after the discovery of hypertension was 9 years and the longest was 25 years. In other words, the patient with the type of hypertension dealt with in this report usually lives to within 3–4 years of his normal expectation of life. The younger the age at which hypertension develops, the less likely is the individual to live out his full life-span; yet the average expectation of life for those developing hypertension under the age of 50 is over 15 years.

This study suggests that, irrespective of age, sex, or whether or not the diastolic pressure is below 120 mm. Hg, these patients will probably live for 14–19 years. Though based on a small series the analysis raises the question, which Burgess himself asks, whether any patient with non-progressive benign hypertension should be subjected to such a serious operation as sympathectomy. As Dr. Horace Evans remarked last month to the Devon and Exeter Medico-Chirurgical Society, surgical treatment for the relief of high blood-pressure is nowadays too lightly undertaken.

SICKNESS IN THE POST OFFICE

Too often the reporting of morbidity statistics becomes first a formal routine and then a meaningless ritual; but there is nothing mechanical about the report on the health of Post Office workers by their chief medical officer, Dr. Cecil Roberts.[1]

As Roberts says, sickness-rates cannot be intelligently interpreted except against a background of the policies of personnel management and the selection and invaliding standards of the medical advisers. Thus, in the long history of sickness recording in the Post Office since 1891, the annual sickness-rate is clearly associated with the invaliding policy effective at the time; an invaliding-rate raised by the discharge on medical grounds of the chronic-sick absentee was associated with a low sick-absence rate, and vice versa. Purely statistical factors also enter the picture. Studies by the Government Actuary's department have reaffirmed the prime importance of age and sex composition in determining a population's sickness experience. As in the country as a whole, the Post Office has been facing the problems of an ageing working population. Some, if not all, of the increase in sickness absence in recent years derives from the increase in the average age of Post Office workers, and the rise in sick-absence rates between the wars need not have been attributed to failure in morale. Had age-sex standardisation of the rates been carried out, much of the apparent increase would no doubt have been eliminated.

Unfortunately the lack of the basic data for such a correction also impedes the comparisons made between the sickness experience of different occupational groups within the Post Office, but some interesting distinctions have nevertheless been drawn. "The hard core of male sick-absence problems is to be found among the big battalions of the postmen"—and the reason is not far to seek. During the war postmen were not on the reserved schedule; young fit men were called up and replaced by women and elderly men who were unequal to the consistent monotonous grind of the postman's day. Sickness among engineering workmen, on the other

1. Burgess, A. M. *New Engl. J. Med.* 1948, **239**, 75.

1. *Mon. Bull. Min. Hlth P.H.L.S.* September, 1948, p. 184.

hand, was remarkably low. This was not entirely the result of a lower average age but was more the expression of the satisfaction which those men (by nature, training, and occupation all skilled craftsmen) derived from the completion of their duty and the camaraderie of the groups in which they worked. Whether that work was a light intricate indoor task or arduous labour in rough weather seemed irrelevant, and morale was the decisive factor. Sorting clerks and telegraphists also had a favourable sickness experience—the result, Roberts thinks, of the smoothly efficient unharassed routine of skilled work in a comfortable environment.

Regional differences appear to exist. Scots will be gratified, if not surprised, by the statistical demonstration of their race's hardihood in the relatively low sick-absence rates obtaining there in all grades of the service. In England, the Home Counties have the best record, but London itself, although better than the North-West region is worse than the remainder of the country. Indeed, sick-absence rates seem to be almost proportional to the size of the town where offices are sited.

Environmental manipulation, however, is not the only concern of the industrial physician. More and more, men and machines must be fitted together by the precise assessment of each man's capabilities and limitations, whether physical or psychological, and by the design of machines which make the least demands on human skill and endurance. In this and other human problems of the manifold occupations of the Civil Service, Roberts believes, there is a limitless opportunity for extension in the field of medical care, where the Post Office has been so notable a pioneer.

RATE OF BLOOD-FLOW

To ascertain the rate at which blood flows through the vessels, various injectable substances have been used. As early as 1927 Blumgart and Weiss [1] were employing a radioactive substance, thorium X, and in our present issue Dr. Payling Wright and her colleagues describe their findings with the radioactive isotope Na^{24}. Their object was to discover how quickly this substance passed from a vein in the foot to the femoral vein, temperature being roughly controlled by warming the subject under an electric blanket until the foot temperature was approximately 33°C. The results show a wide scatter, and there was no change in the time values when the leg was further heated at 45–48°C. This rise in temperature would be expected to increase skin and muscle blood-flow; but if the capacity of the particular venous pathway under investigation increased in parallel with the blood-flow, then the rate of movement might well show little change. The capacity of the veins is known to depend on temperature, pressure, and nervous influences; and the factors influencing the circulation-rate are no doubt complex. In the heart interpretation may prove to be even more difficult. Prinzmetal and his associates [2] found that, with a Geiger-Müller counter over the precordium, intravenous injection of Na^{24} was followed in normal subjects by two main waves, due to the presence of tracer element in the right side and then in the left side of the heart; while in heart-failure a prolonged monophasic curve was observed. With this condition and with considerable cardiac enlargement, mixing difficulties probably play a part.[3] Smith and Quimby [4] found that the arm-to-sole-of-foot Na^{24} time was actually below normal in some cases of Buerger's disease, and for assessing arterial disease of the legs they appear more recently [5] to have discarded the measurement of circulation-time in favour of the uptake-rate in the sole of the foot. The information obtainable by measurement with radioactive agents could of course be supplemented by concurrent use of established techniques for measuring blood flow and pressure.

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2. Prinzmetal, M., Corday, E., Bergman, H. C., Schwartz, L., Spritzler, R. J. *Science*, 1948, **108**, 340.
3. Nylin, G., Malm, M. *Amer. J. med. Sci.* 1944, **207**, 743.
4. Smith, B. C., Quimby, E. H. *Surg. Gynec. Obst.* 1944, **79**, 142.
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VISCEROPTOSIS AND PAIN IN THE LEGS

NEURITIS affecting the lateral femoral cutaneous nerve as an isolated syndrome was first described by Bernhardt [1] in 1895, and soon afterwards it was named meralgia paræsthetica by Roth.[2] Its causes have always been a bit of a puzzle. A suggestion from the Argentine is that some cases are due to pressure of the viscera on nerves during their intra-abdominal course. Guilhe, of Buenos Aires, found that in one patient with meralgia paræsthetica the pain disappeared if he stood behind the erect patient and embraced the lower part of his abdomen, and that it reappeared when the viscera were allowed to drop again. The meralgia also disappeared when the patient lay on his back. Obarrio and Guilhe [3] have seen 6 further cases, all in middle-aged people with a lax pot belly, and all have been immediately relieved by an abdominal belt. Subsequently Obarrio [4] saw 3 cases in which sciatica associated with pain suggestive of intermittent claudication was relieved by an abdominal belt. Two of these patients also had meralgia paræsthetica, which was similarly affected. Lately he and his colleagues [5] have described 2 cases of "intermittent claudication" and "abdominogenital neuritis," one of which was complicated by meralgia paræsthetica on the same side and sciatica on both sides. These patients were women, and in both the pain disappeared on lying down and was permanently relieved by an abdominal belt.

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2. Roth, V. K. *Medits. Obozr. Sprimona*, 1895, **43**, 678; Meralgia Paræsthetica. Berlin, 1895.
3. Obarrio, J. M., Guilhe, B. J. *Bol. Acad. nac. Med. B. Aires*, 1946, p. 605.
4. Obarrio, J. M. *Prensa méd. argent.* 1948, **35**, 387.
5. Obarrio, J. M., Schärer, A. J., Obarrio, J. M. jun. *Ibid*, p. 1849.

EMPIRE RHEUMATISM COUNCIL

IN industry alone rheumatic disease accounts each year for the loss of 3 million weeks of work, and the annual cost to industry is about £20 million. This estimate was given last week by H.R.H. the Duke of Gloucester, presiding at the Empire Rheumatism Council's annual meeting at St. James's Palace. The rheumatic diseases, he said, had in the past been "the most neglected of all human afflictions in the field of research." As chairman, Lord Horder reported the continuance of the council's full-scale investigation into the causation of rheumatoid arthritis, and of its research into the allergic aspects of rheumatism. The council has lately issued a standard case-sheet which, Lord Horder suggested, may soon become the accepted case-sheet for world rheumatic practice. The council has also extended its educational responsibilities by increasing the lecture courses given at the Apothecaries' Hall; these have been well attended. Integration with medical bodies in other countries is constantly improving. For example, the Canadian Rheumatism and Arthritis Society and the Royal Australian College of Physicians are considering affiliation as autonomous branches; and a New Zealand branch is to be inaugurated with a two-day meeting at Rotorua on Nov. 18 and 19. During the past year the council's income has fallen considerably—owing, the finance committee suggests, to a popular misbelief that voluntary contributions are no longer needed.

Dr. E. D. PRIDIE has been appointed Chief Medical Officer, Colonial Office.

THE next session of the General Medical Council will open on Tuesday, Nov. 23, at 2 P.M., when Sir Herbert Eason, the president, will deliver an address.

Special Articles

SIMPLE STATISTICS OF CANCER *

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I BEGIN with the story of a failure which points a moral. It is told at length in two volumes published by the League of Nations Health Organisation (1925).

It had been noted that, at that time, the rates of mortality from cancer of the breast in age-groups were much lower in the Netherlands than in England and Wales; indeed in some age-groups the rates in England and Wales were more than 50% greater than in the Netherlands. It was tempting to suppose that this contrast might be due to causes—such as earlier resort to hospitals in the Netherlands—which could be brought to light by statistical investigation.

An international committee of experts, statistical, pathological, clinical, and administrative, was appointed and worked in complete harmony for many months. Many interesting statistical tables were compiled, but in the end no conclusion was reached. The Dutch experts were "inclined to admit that in England cancer of the breast is a more malignant process than in the Netherlands," but they recognised that this conclusion was vague, and it certainly recalls the candidate's answer to the question: "*Quare opium facit dormire?*"—"*Quia est in eo virtus dormitiva.*". Perhaps the failure of the inquiry was due to the difficulty, amounting to impossibility, of making a point-to-point comparison of *all* the circumstances in the ordinary lives of women of two countries which might be relevant. What seemed a simple problem was too difficult.

Between 1920 and 1930 the Ministry of Health issued reports dealing with cancer of the breast, uterus, and rectum and the "natural" duration of cancer. The general plan was to assess, by comparing survivorships, the benefits of treatments of different kinds and instituted at different stages of the disease.

The logician will ask for a control—i.e., an adequate number of patients, observed from the onset of the disease until death, who had received no treatment which could reasonably be supposed to influence the course of the illness. As all medical men know, data satisfactory to the logician cannot be had. Greenwood (1926) published the best available; they recorded the lengths of life of a large number of patients who had not been radically treated from the date of reputed onset of the disease. The numbers were respectable—651 with cancer of the breast, 1749 with cancer of the uterus, and 887 with cancer of the rectum.

The returns from different institutions were remarkably consistent. Thus five different recorders contributed data of cancer of the breast; the mean duration in the total was 38·3 months, and the range from 30·2 (a very short series) to 39·8. But this control is vulnerable to both medical and statistical criticism. Medically speaking, all we know is the date when a patient said he or she had first noticed something wrong. Not only might his memory be at fault, but also the power of recognising signs and symptoms must be a function of the patient's psychological make-up; a more observant or more sensitive person will give an earlier date of onset than will one of more stoical or stolid mould, though in both the pathological evolution may be at the same point. Statistically speaking, one must object that most of the data relate to patients in institutions; they are a selection, not a random sample of patients with cancer, and the average durations may be too long if cases of rapid evolution are under-represented.

These data were published in 1926. May we not expect better data soon? Methods of recording and mechanically tabulating have greatly improved, and it is hoped that pooling of information will become general. It will never, I think, be possible to avoid indetermination of the exact onset, but it will certainly be possible to remove the suspicion of bias in the sample, if the data assembled are numerous enough.

Apart from "natural" duration as a control of the results of operations, a thorough statistical-medical study of the course of inoperable cancer is of value. There have been in the past, and will be in the future, beliefs that some substance, natural or artificial, will reduce the pain of operable cancer, lead to arrest of the growth, or produce some other beneficial result. Often clinical records of such benefits have been cited, but our profession was never impressed. All medical practitioners of wide experience knew that the vicissitudes of mortal sickness, whether of cancer or cardiac disease, were almost infinite. They did not think it necessary to collect statistical evidence and the public did not expect them to do so.

STATISTICS

In the last forty years the public has become statistically minded—perhaps at a faster rate than our profession. If the inventor of a cure or a palliative is able to produce statistical data consistent with his claim that in a sensible proportion of his patients the swelling has diminished, that there has been less pain, or some other improvement has followed the exhibition of his remedy, then a public accustomed to statistical arguments is not satisfied by a general rejoinder that all these things may and do happen without the use of any remedy. The retort is—Where are your statistics?

Where are they? The answer is that the raw material of such statistics is to be found in the case-books of some practitioners and the notes—perhaps the ward sister's reports—of hospitals and institutions harbouring patients incurably sick. No statistics exist, because from the medical point of view it has not been worth while to collate the information. It would be a laborious task and give no help at all in treatment. But it might have great value in another field; it might convince an unprejudiced layman that changes attributed to a new treatment *did* often occur without it; it might save bitter disappointment.

We live in an age of mechanism and technicians; coding of clinical notes and mechanical tabulation can now save human labour to such an extent that what, in my submission, is required can be had without any waste of time which could be better employed.

ASSESSMENT OF SURGICAL RESULTS

The reports already mentioned contain impressive evidence, presented in the statistical form which is now acceptable to many more readers than a generation ago, of the value of early treatment. Reporting on the late results of operation for cancer of the breast, Dr. Janet Lane-Claypon (1928) gives a table showing the proportions surviving from operation per 1000, and the survivorship of the general population of women aged 50 (about the average age at operation). Of the general population, 936 out of 1000 will survive at least five years, and 852 out of 1000 will survive ten years. Of women operated on without infection of the axillary glands (pathologically verified) 730 survived at least five, and 603 at least ten, years. Of 1000 operated on when the disease was no longer local, 266 survived at least five, and 142 at least ten, years. I cite no more figures, because the results of twenty years ago may be obsolete,

* Abstract of a lecture delivered at the Royal College of Surgeon of England on March 4, 1948.

and I need not discuss the importance of following-up in detail.

It is obvious that if, a year after operation, of 1000 patients 800 are still alive, 100 are dead, and nothing is known of the fates of the remaining 100, the true proportion of survivors cannot be more than 900 or less than 800, and is probably a little nearer 900 than 800. In actual work the number lost sight of is not usually of the order of magnitude suggested in the example, at least in the first few years after operation. But it is important to remind statisticians without medical experience who handle surgical data that in the past a primary factor of successful following up has been the interest of the surgeon. There is still gratitude in the world, and patients are sometimes grateful to their surgeon, willing, even anxious, to answer a letter from *him*. They will neither owe nor feel any gratitude to a statistical officer or even a research committee. This is well brought out by Fulton (1946) in his biography of Harvey Cushing. After quoting some letters, Fulton writes :

> "This exchange is mentioned to illustrate H.C.'s unusual faculty for remembering his patients and keeping in touch with them. During 1905 he began to request all his neurosurgical patients to write to him on the anniversary of their operations. This practice enabled him over the years to collect data concerning the end-results of his operations, and ultimately to learn of the probable life expectancy of patients having any particular type of tumour. At the time of his death in 1939 he was following nearly 1000 of his living cases of verified brain tumour. If by any chance a patient did not write on the anniversary of the operation, a reminder was promptly sent."

Provided there is a cordial partnership between surgeon and statistician, I suggest that within another decade we might have surgical statistics which would solve many practical problems and also save many lives by educating the general public. But there are difficulties to be overcome ; we must recognise the limitations of the statistical method and the anfractuosities of human temperament.

A statistical analysis can answer the question whether, on the average, method A gives better results than method B, and no other question. To answer that question we must pool the results of many surgeons using method A and pool the results of many surgeons using method B—enough to weaken if not obliterate the influence of personal equation. Suppose we have done this and obtained a difference in favour of method A which is highly significant in both the statistical and colloquial sense of that over-worked adjective, it does not follow that even an authoritarian government should forbid the use of method B. Surgery is an art as well as a science ; and, even when the material, the patient, does not change—as it always does—a preference for a particular technique which, on the average, gives worse results, may be justified by the special skill of the surgeon or particular features of the case. The Evans gambit is seldom played in the chess tournaments of modern masters, but were Tchigorine still alive he would probably often play it and win ; even in his time statistics were against him, but he could take risks and win. He was an artist. Averages are for the instruction of ordinary people. Not to recognise that is as unwise as to fly to the opposite extreme and to credit the great artist with infallible judgment. The latter mistake was made often enough forty years ago, when clinicians and pathologists despised mere statisticians ; but now statisticians, if still regarded as nuisances, are accepted as inevitable nuisances, and there is even a danger that the clinician may expect too much from the mere statistician.

In my view useful clinical statistics can only be produced by the coöperation of surgeon (or physician) and statistician. It is not asking too much of the statistician who has had no medical training to expect him to have read carefully an account of the general principles of surgical treatment in malignant disease and so far to have mastered it that he can listen intelligently to a surgeon's criticism of the planning or interpretation of a statistical analysis. Even a very busy surgeon allergic to algebra would not find the principles of random sampling too difficult to master ; the collaborators can surely be in charity one with the other.

The statistical investigations described here are simple, but they will not be carried out quickly or easily and they will not lead to dramatic epoch-making discoveries. Yet they will, I think, save human lives. Perhaps in these times of excitement we are apt to despise simple things.

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TWO HOSPITALS

BY A PATIENT

A FEW months ago I spent some weeks as a patient in two London voluntary hospitals. I have been wondering ever since how much doctors know about the effect of hospitals on patients. I am not a doctor and I would not presume to judge the medical care I received. Standards were probably high, as I was in teaching hospitals of great reputation. When I saw the whole machinery of medicine in action, I was impressed. No effort and no expense seemed to be too great. But there seemed to be an almost unbridgeable gulf between those who occupied the beds and those who did the work, and I could not help comparing the efficiency of a great hospital at work with its comparative neglect of human needs.

I do not know how far my own experiences are typical. I can only say that they were confirmed by many of my friends. I was unhappy and annoyed about the same things as other people, but I could not share the view of so many resigned ex-patients that nothing at all could be done about it. Why should hospitals have different standards and a different scale of values from those accepted outside ?

It is natural that people should fear operations or painful forms of treatment, but why should they fear being in hospital ? I had never shared this general fear and had always prided myself on being reasonable. When I fell ill I was eager to be admitted and cared for by trained people. Today I am less reasonable. If I had to go again, I would be afraid.

THE OUTPATIENT

When my doctor provided me with a hospital letter, he said "This is a hospital with an appointments scheme, and waiting has been practically abolished." He did not know that some words have different meanings in hospital and elsewhere. The appointments list was overcrowded and my first visit was delayed for three weeks. When I entered the large, light waiting-room with its coloured chairs and its tea-counter in the corner, I was pleasantly reassured. There was no sign of the

narrow forms and draughty corridors of which I had heard. But the appointments system proved a disappointment. Its primary purpose seemed to be to prevent an accumulation of too many people on any one day; there was apparently no intention that patients should see their doctors at the appointed time. Many people were given appointments for the same doctor at the same hour, and only a few lucky ones early in the day were promptly attended.

One day, after waiting for two hours, I had to leave without seeing the doctor, because I had another engagement. When I complained to the receptionist, she replied: "I am always telling patients that they must expect to spend the whole morning in hospital; if they finish earlier, they are lucky." I realise, of course, that this is an ideal state of affairs compared with conditions in some hospitals where people may have to wait the whole day. One large teaching hospital, I am told, still applies the principle of men first in its outpatient clinics. Women are supposed to have nothing important to do, and they have to wait indefinitely, often with their small children. It is almost unbelievable that an institution which employs the latest devices of medicine should ignore the obligations of women.

My own hospital was not as bad as that, but it bore many traces of the past, when the sick poor formed its clientèle. What private doctor would ask his receptionist to call three patients into his consulting-room at the same time? Some of these patients sought advice on gynæcological complaints. Their conversations with the doctor were in whispers, and they were embarrassed by the presence of other people at the back of the room. Those who wait for medical care are the last to underestimate the value of a doctor's time, but there are limits which neither hospital nor doctor should exceed. The appointments system appeared to be based on the principle that a minute of the doctor's time was more valuable than an hour of the patient's.

THE INPATIENT

My first two impressions on entering hospital were loss of personality and noise. They remained with me all the time I was there. Nothing softened the first shock—for it is a shock to enter a 20-bed ward, however much one may have known before about large public wards. The nurses were too busy to bother much about the new arrival. A friendly word just then would have been welcome. It would have been a relief to know that the doctor would be round later in the day—as he was—or that tea would soon be forthcoming. Nobody seemed to know that a patient, on arrival, needs more than a bed to lie in and a case for her clothes. It took time to establish contact with the adjoining beds. People kept themselves to themselves, at least as far as newcomers were concerned.

In hospital many of the rules and politenesses of ordinary human relationships are suspended. You are asked questions by all kinds of people whom you have never seen before and who do not tell you who they are. You have to distinguish between a variety of uniforms and white coats: sisters and nurses, house-physicians, medical students, physiotherapists. When matron makes her daily round, there is a hush in the ward; you are expected to know her and to give an optimistic answer to her question about your health. Gradually you learn all these things from whispered conversations with other patients. It would be so much simpler if these people, when they address you with your name, would also mention who they are, just as they would in ordinary social or business life. I fear it is no accident that this is not done. As a hospital patient, you have a different human status from the one you had outside.

TEACHING MATERIAL

The bedside lecture, although I had expected it, was an ordeal, and I wonder whether the same educational purpose could not be served at smaller human cost. I remember lying in bed motionless, waiting for the event. Its significance had been impressed on me by a change of the top sheet and a last-minute tidying. When doctors and students had gathered around, I was politely asked how I was and where the pain was. Then I was disregarded. For ten minutes or more they talked about me and similar cases as if I were not there. At the end of their incomprehensible conversation, when all my fears and suspicions had been aroused, they left me suddenly, without an explanation or so much as a nod of their heads.

I did not see the teaching specialist alone. I did not have a single private word with the doctor in charge of my case. I never saw him, except in the presence of at least three students, two other doctors, and the ward sister. He is, no doubt, a busy man, but should it not be part of his job to answer his patients' questions? I recognise the demands of medical education. Whenever students asked me questions and examined me, I felt an obligation to be as helpful as possible, even when I was tired. I even accept the bedside lecture as an unavoidable necessity. But I do object to being turned from a human being into medical teaching material. This is a question of manners and approach. Today there is no special group of patients compelled to pay for their medical care by accepting inconvenience and perhaps even indignity. Medical education depends more and more on the voluntary and ready coöperation of sick people of all classes, and later, when I was transferred to another hospital, I saw that a different approach is possible. There a patient told me how she had been asked, as a favour, to attend in the lecture hall. It had been made clear to her that she could refuse if she wished. "They had been so kind to me; I felt I wanted to help them." Her case was discussed in the presence of many students for half an hour, and before she was wheeled back to the ward the professor expressed his appreciation of her helpfulness. He saw her alone in the ward on his usual round later on.

THEY DON'T TELL YOU ANYTHING

Why should an adult cease to be regarded as a normal and reasonable human being merely because he is in hospital? I am not talking about patients who are desperately ill or in great pain, but of people in full command of their senses, some of them out of bed for part of the day. They were all treated more or less like children, with firm friendliness and occasional severity. They were ordered about, humoured, talked down to, but they were rarely taken seriously. I sometimes felt like a prisoner, surrounded by an impenetrable wall of enforced, artificial cheeriness.

In and out of hospital, doctors tend to appeal too little to the patient's reason. Sometimes a pat on the back and a bottle of medicine may be the best treatment; it is certainly the most time-saving and the easiest in the short run. It is much more difficult to adapt explanations and answers to the psychological and intellectual capacities of the patient. In hospitals, where doctors and nurses know practically nothing about the individual patient, there is even more temptation to choose the simplest way. "They don't tell you anything," was the complaint of practically every patient to whom I talked. It came spontaneously, as the first reaction to every doctor's round.

Do doctors realise how much unnecessary worry and fear can be caused by the failure to say the right thing at the right time? I shall not easily forget the two elderly women who had been told that a new method of

treatment would be started with them the next day. They were worried the whole evening, and they slept little at night. In the morning, after nurse had given them each a glass of watery tasteless liquid to drink, they asked anxiously when the course of treatment would begin and whether it would be very painful. They would not have asked if I had not encouraged them to do so. "But you have just taken the first dose," the nurse answered. Nobody had thought of telling them what to expect.

This failure to inform the patient seemed to be part of the hospital's failure in human relationships. The patient's physical reactions were studied; his mental reactions received no attention until they caused trouble. Even then, a few meaningless soothing words or a sleeping tablet were usually preferred to a sensible explanation. If only doctors and nurses would understand what a humiliating and sometimes frightening experience it can be to be treated like a semi-imbecile at a time when one is physically helpless. I do not believe a doctor loses authority if he says: "I do not know, but I am doing my best to find out." A day or two before my discharge from the second hospital, I tried to get a general explanation of my case from the house-physician, as the specialist had been more or less unapproachable in the presence of students. He answered my questions readily. It may not have been the full truth, but it satisfied me at the time. When he came again the next day, he asked me smilingly: "Any more questions?" The patient who asks questions in hospital is an unusual phenomenon.

NOISE

When a person is ill at home, people walk on tiptoe and talk with subdued voices. Everybody takes for granted that the rest of a sick person is sacred. In hospital it is different. When I entered I longed for peace and complete rest. Immediately on arrival I received a shock. The noise in the ward almost reduced me to tears.

I soon noticed that its main cause was the stone floor. The nurses told me later how hard it was on their feet. It was also hard on patients' nerves. Things were often dragged over it with a thundering, screeching, and rattling which would have drowned the noise of half-a-dozen typewriters and telephones. I do not know how often I was jerked out of a dose by volumes of sound and hid myself under my blankets to escape. Gradually I learned to distinguish between the rattling of the screens being dragged from one bed to another—their metal wheels were not covered with rubber—the screeching of beds pulled from one end of the ward to the other, and the terrific thunder of a heavy trolley, covered with clattering glass and metal containers. The nurses were so used to the noise that they did not even notice its painful effect upon the patients. In this type of ward even the wish to create a quiet atmosphere disappears, and the patients' need for rest is forgotten. Hospital routine is more important, and patients who fall asleep during the day may be wakened without compunction for unimportant purposes. What was needed was a smaller ward, a different kind of floor, differently fitted trolleys and screens, and greater respect for the patients' comfort.

The hospital day began at an unearthly hour. I know that there are too few nurses to change this now, but the custom existed long before the nursing problem reached its present crisis. It should be abolished as soon as possible. Townspeople do not usually rise shortly after 5 A.M. and fall asleep at 9 P.M.; and they cannot easily adapt themselves to this new daily rhythm. Sleeping tablets were often used—I found them generally far too plentiful. More than once I was aroused from my early sleep to take them.

FOOD AND TOBACCO

To see good food turned into badly planned, carelessly served, uninspiring meals is always a pity. In hospital, where meals are important events and should form part of the patients' treatment, it is felt even more painfully. Everything connected with the meals showed lack of interest, and there was a vague atmosphere of the poor-law about it. Even the crockery and cutlery were so cheap and bad that the patient was not left in doubt about his social status. The food itself was either lukewarm or cold; it was served hurriedly by probationers with the help of ambulant patients.

The classical hospital dish, I am told, used to be rice pudding. Since the war its place has been taken by semolina. I had it for dinner as milk pudding on five consecutive days; on one of them it was preceded by semolina-cheese which formed the main dish. In retrospect, this sounds laughable; at the time it seemed like an insult. There were no tomatoes, no fresh fruit, and only one or two lettuce leaves a week, when all these things were abundant on the market. The diet was clearly built up on the principle that visitors would provide what was missing.

Most hospitals allow smoking between certain hours, but in my hospital the matron "did not like it." Doctors seemed to have no influence in the matter. Even on the large balcony adjoining our ward, where many patients spent part of their day, smoking was prohibited. One day, a lonely private patient, sitting in the sun among the others, blew rings into the air, unknowingly arousing widespread class antagonism. I still regret that I did not take up the cudgels there and then and light a cigarette. But hospital discipline is strong, and the smokers among the patients chose an easier way out. The lavatories, however, had no locks, and the danger of discovery was great, though on the whole the crime seemed to be quietly tolerated because little else could be done.

A DIFFERENT KIND OF HOSPITAL

When I was discharged, I felt as a prisoner must feel on the day of his release. But my spell of freedom was short. After a few blissful days at home, I had to go to another voluntary teaching hospital for observation. When I received their printed notification that a bed was available, I expected the worst. The form had to be signed in different places. It was addressed to me, the patient, and it provided for every contingency, including burial costs.

Fortunately, this first impression proved to be entirely wrong. The form had survived, but the spirit that produced it had disappeared. A wave of warmth and friendliness surrounded me the moment I entered the ward. There were nine beds, and the patients welcomed me as a new member of their community. I was offered the most comfortable chair by those who were out of bed, and in the presence of a smiling nurse everybody started to tell me straight away what a pleasant hospital it was.

When lunch arrived a table was laid with mats, glasses, and cutlery for those who were not in bed; it could have been a table in a good hotel. A large heated trolley was pushed into the ward and the food was not only well cooked—"We have a chef here, you know"—but also piping hot. Sister herself shared out, with the help of two nurses, and individual wishes were taken into account. The meal was a happy social occasion.

There was a spirit of comradeship among the patients, and if one of them seemed worried or depressed, tactful attempts would be made to help. Visitors' gifts were often shared, and cakes from friendly relatives turned our afternoon teas into a succession of parties. We were convinced that our ward was the happiest in the hospital, but the neighbouring ward made a similar claim. Our

sister did many things which, in current opinion, might have undermined her authority; in fact they only strengthened it and made us like her more. One of the cleaners told me what a kind, understanding person matron was, and the cleaner herself was introduced to me by one of the patients as "our ray of sunshine." The house doctors seemed to be on excellent terms with the nurses and ready to lend a hand at difficult moments. These happy relationships between the different members of the staff were, I felt, reflected among ourselves.

This hospital, like the other, suffered from severe staff shortages. Yet there was time for sister to supervise patients' meals and for a friendly word where it was needed to make the patient feel at home. It is true that here, too, questions were not encouraged and the background of the patients remained unknown, the specialist was difficult to approach, and the day started at dawn. But these things were easier to bear because the patient was treated as a person and felt like an individual.

In the first hospital an elderly nurse once said to me: "The trouble with you is that you should have gone into a private ward." This remark showed more effectively than any description the kind of approach which made that hospital so unattractive. The other can, perhaps, be best described by quoting the private patient who said to me on her discharge: "I wish I had gone into the public ward."

ACCIDENTAL INJURIES

Treatment and Prevention

SPEAKING before the section of epidemiology and State medicine of the Royal Society of Medicine on Nov. 1, Mr. W. GISSANE suggested that accident cases were too often treated too late or by medical personnel inadequately trained for the task. In hospitals suitable structural arrangements and modern equipment were required for this purpose, and team-work was necessary for even reasonably good results. Adequate after-treatment and follow-up were desirable, preferably by the same team. He felt that while prevention of the actual accidents might be a very stubborn problem, the prevention of crippling results was something which could be tackled immediately.

Dr. LEONARD COLEBROOK, F.R.S., analysed a Birmingham series of 736 accident cases, of which 504 occured in the home and 232 in industry. The fatality-rate of the home accidents was six times that of the industrial accidents, and the average stay in hospital approximately 25% longer, owing largely to the more serious nature of accidents in the home, and especially to burns and scalds in children and old people. Epilepsy accounted for a third of the home burns, which were due mainly to tea and other hot liquids, coal fires, electric and gas fires, baths left unattended, and inflammable liquids; electrical faults and conflagrations were very infrequent causes. Dr. Colebrook emphasised the need for prompt admission to hospital without prior treatment apart from protection of the damaged part.

Dr. C. A. BOUCHER said that more than 8000 people were killed every year in England and Wales as a result of accidents at home and in everyday pursuits. Of these fatal accidents 6000 took place in the home—which represented about 40% of all fatal accidents, including road accidents, transport accidents, and mine accidents. There had been no fall in the figure since 1938; and in the age-groups under 5 and over 65 there had been an increase. In 1945 some 20% of fatalities were in children under 5, and about 50% in people over 65, falls being the main cause in the latter group. Overcrowding in the home was an important causative factor, especially in accidents affecting children. Dr. Boucher drew attention to the perils of neglect of the dangers in the home and of using cheap and faulty appliances which looked tempting in the shops. The Royal Society for the Prevention of Accidents had shown great energy and imagination in drawing attention to the dangers. Furthermore, in 1947, an Interdepartmental Committee on Accidents in the Home had been set up, and a domestic accidents panel of the building requirements subcommittee of the Ministry of Works was already at work. Many local authorities held exhibitions to promote home safety, while local education authorities encouraged teachers to inform the children; films on this subject were circulated by the Central Office of Information. Education and propaganda offered a better hope than legislation. One example of the ineffectiveness of legislation was the provision in the Children and Young Persons Act, 1933, by which anyone over the age of 16 having charge of a child under the age of 7 who was seriously injured or killed because of an insufficiently guarded open firegrate is liable to a fine of up to £10. Nobody could penalise a woman, particularly a mother, for so tragic an accident. He thought that education should be personal rather than impersonal, and felt that the aim should be to make the public critical of goods which they buy, in the hope that in time public opinion would demand safe articles.

Dr. PERCY STOCKS believed that general appeals were unlikely to succeed and that each cause would have to be attacked in detail. It was first necessary to obtain good statistics, and the General Register Office was working to that end. Coroners' certificates were providing more detail than hitherto of the circumstances of fatal accidents; a classification both by nature of injury and cause of accident had been grafted on to the International List, which was not designed for morbidity statistics; and the teaching hospitals were being asked to pay more attention to the causes of accidents.

TRANSVAAL HOSPITALS DISPUTE

FROM A SOUTH AFRICAN CORRESPONDENT

THE dispute which has been going on for three months between the South African Medical Association and the Administration of the Transvaal[1] has at length been settled with the help of Mr. Justice De Villiers, appointed by the minister of health to act as mediator.

Since Aug. 1 the Provincial Administration had been adamant in its intention to implement the Hospital Ordinance, allowing free hospital care to all, and the doctors had been just as adamant in their intention not to operate the scheme unless a "means test" was imposed. Towards the end of October it became obvious that the continual statements from each party, having front-page publicity in the press, were disturbing public confidence. When therefore the parties agreed between themselves to have mediation, and approached the minister of health in the matter, they found that the minister, while making immediate arrangements for a judge to act as mediator, also made an earnest appeal that no more press statements should be issued. The sudden cessation of angry statement and counter-statement in the daily press was very noticeable. Discussions behind closed doors continued for several days before a press statement was issued that "with pleasure and relief we announce the settlement of the dispute between us."

Agreement has been reached that patients unable to pay shall be given free hospital treatment, while "those well able to afford to pay" will be required to do so. This is a statement on very general lines, and further meetings will have to be held to hammer out the details of the scheme. But agreement and cordiality have been reached, and an indication of this

1. See *Lancet*, Oct. 23, p. 661.

is the South African Medical Association's intention to operate the ordinance at once while waiting for the administration to amend it. This means that full hospital services are now in operation again, although it will take some time for the Transvaal Administration to ratify their agreement and alter the legislation. It is proposed that those parts of the ordinance offering free hospital treatment to all should be suspended for three years.

The opinion of the average patient would probably be that "the doctors have won." The S.A.M.A. states, however, that it "was full of admiration for the ordinance; our only submission was that it was premature to try to introduce it in full at present." And looking to the future Dr. J. H. Harvey Pirie, chairman of the augmented executive of the S.A.M.A., has said: "Both the Province and the Medical Association regard this as being in all probability a temporary step towards the establishment of a national health scheme."

Medicine and the Law

Swab Left at Operation

ON Nov. 3 the Manchester City coroner inquired into the death of a woman of 27 who died at the Manchester Royal Infirmary. Her gall-bladder and appendix having previously been removed elsewhere, she last year underwent an operation at the Royal Infirmary; after which, the surgeon said, her condition improved steadily for a time. But pain and jaundice later returned, with frequent attacks of fever, and when she re-entered hospital last month she was deeply jaundiced and anæmic. The second operation, to join together two ends of the bile-duct, was performed on Oct. 20: it was very difficult and lasted five hours. After it the patient seemed to be settling down nicely, but complications developed. Post mortem a swab was found, but in the surgeon's opinion its presence had no connexion with the woman's death, which, he would say without hesitation, was due to necrosis following leakage from the pancreas and acute liver failure. A pathologist testified that he found the swab when he was removing the liver: it was like a ball $1^1/_2$ in. in diameter. The clot of blood and gauze was not infected, and in his view had nothing to do with the death. The patient had died from hæmorrhagic necrosis of the duodenum, following leakage of pancreatic fluid, and acute liver, failure.

The theatre nurse said that she began with 24 swabs and later added another 24. Still they had not enough; so she had to cut rolls of gauze to provide 84, making 132 in all. She checked the instruments and swabs after the operation and counted 132 swabs. She had not the slightest doubt they were all there. She could only account for the swab being found by the fact that it might have been a loose strip of gauze, which was sometimes found in a roll. Another nurse suggested that the piece of gauze might have been a piece tucked underneath a roll, to make up the weight, or a piece of the gauze might have been torn from another piece as it was being used.

The coroner said that the final operation was clearly a difficult and hazardous one, but it was a last effort to save the woman's life. It was the duty of the theatre staff to check instruments and swabs correctly, and it was unfortunate that a piece of gauze had been overlooked because it made it necessary for an inquest to be held. According to the medical evidence the presence of the swab had not accelerated death in any way, and he must accept that evidence. He recorded a verdict of death from natural causes.

Conviction for Neglect Quashed

In the Court of Criminal Appeal on Nov. 8 the Lord Chief Justice, Mr. Justice Humphreys, and Mr. Justice Lewis allowed the appeal and quashed the conviction of Miss G. E. Sherwood who was sentenced to one day's imprisonment at Hertfordshire quarter sessions last July for neglecting one of the children in her home at Potters Bar (*Lancet*, July 31, pp. 190 and 200).

In England Now

A Running Commentary by Peripatetic Correspondents

It is written: "At the end of an infinite search the philosopher finds himself clinging to laughter as the best of human fruit." Meredith is something to cling to when running an African hospital in the bush.

A common Sunday afternoon patient is the piccin with scalds of head and neck. As a gesture of selfless generosity (or maybe just atavism) they fall into pots of boiling soup. The law heartlessly disallows any more piccin soup, so the chop-mammies pull them out and bring them here. We used sulphonamide ointment until a nurse was found smearing on sulphur ointment; since then we have preferred penicillin cream as less liable to confusion.

The counter-irritant cuts made by the witch doctors are sometimes remarkably effective. It would delight the professors to see a patient complaining of pain in the loin, vomiting, fever, and headaches displayed before students with the precise surface markings of L.2 mapped out in neat juju scars.

Umbilical hernias are looked on as adornments and rarely cause trouble. Indeed they are a valuable alternative to the rectum for palpating deep in the pelvis through the thin burnished skin. On arrival my cook was promptly christened Umbo and my steward boy Abdo for conspicuous anatomical reasons. They could not understand what I was laughing at when they told me that "quickly" was *tum-tum*.

* * *

The October meeting was over and the doctors, having dined convivially in the verandah restaurant overlooking the Avon, now sat in ordered composure to watch the final rendering of the Tragedy of Hamlet. White heads, grey heads, and bald heads contemplated with mute admiration the excellent and realistic production; nor did Victorian whiskers and frock coats seem out of place in the court of the ignoble Claudius; indeed, we had come prepared for the New Look and an automatic telephone on the royal desk, but these we were spared. It was only right that we, as doctors, should pass judgment on this appalling tragedy, for was not a doctor originally to blame for it? Was it not the Pathologist-Royal at the court of Elsinore who tripped up on that all-important autopsy? Had he searched the King's body meticulously for evidence of the presumed serpent bite? Had he examined the external auditory meatus with a hand lens?

We tolerated the tiresome Polonius, the fickle Gertrude, and the platitudinous Horatio, in order to enjoy the philosophical gravedigger who so honourably upheld Adam's profession. Each particular hair stood on end as the darkling officers of the guard watched the pallid and aphonic ghost fade in the cheerless air of early dawn: like them we were "distilled almost to jelly with the act of fear" as this emphysematous spectre poured out a whole packet of trouble for young Hamlet. As the tragedy unfolded and the news of Ophelia's death was told, our sympathies were with the miserable Prince of Denmark. Two hours later, the compulsion neurosis spent and the greed of Claudius rewarded, our sympathies were entirely with the coroner for Elsinore, for now, our pulses quickened by Robert Helpmann's final display of athletic histrionism, we viewed a stage littered with corpses and sullen survivors.

On the homeward journey through the Warwickshire countryside we prepared depositions and pink certificates for our friend the coroner. The old King's amended certificate now reads: 1. (*a*) Intravascular clotting, due to (*b*) Instillation of cursed hebona into portals of ear; verdict of Wilful murder ("most foul") against Claudius. Polonius died of: 1. (*a*) Hæmopericardium, due to (*b*) Cardiac tamponade (sword-wound), due to (*c*) Eavesdropping, with 2. Cerebral arteriosclerosis (he was a stupid old man) as a contributory cause; verdict of Misadventure, "and in bringing in this verdict I should like to say that no blame whatever attaches to His Royal Highness, who was clearly under the impression that *no-one* was hiding behind the curtain. (Decent chap, this coroner.) At the same time I should like to

express on behalf of this court our sympathy with the family of Polonius, and in particular his daughter, who, I am sorry to hear, is indisposed as a result of her sad bereavement."

Ophelia, poor child, seems to have died of: 1. (*a*) Asphyxia, due to (*b*) Drowning, due to (*c*) Acute schizophrenia, with 2. Infatuation for Hamlet as runner-up; verdict Accidental death. (The coroner for Elsinore is, of course, aware of the evidence suggesting that the deceased met her death at her own hands; he knows, too, of the parallel case of Catherine Hamlett of Stratford-on-Avon, who, when William Shakespeare was yet a boy, fell out of a willow tree while attempting to water flowers, circumstances which could only be interpreted as felo-de-se but which, out of respect for her family, were recorded as death by accident.) Gertrude ("What a falling off was there") died of: 1. (*a*) Aspirin, or perhaps barbiturate, poisoning due to (*b*) Anxiety neurosis; verdict Accidental death.

The next three verdicts are all variants on the same theme. Laertes's certificate reads: 1. (*a*) Multiple abdominal injuries (rapier-wounds); 2. Intravascular hæmolysis due to snake venom; verdict of Misadventure. Contrast this with that of Claudius which reads: 1. (*a*) Syncope from fear, as a result of (*b*) being called an "incestuous, murderous, damned Dane" and being made to drink aspirin (or perhaps barbiturates); 2. Abdominal wounds and intravascular hæmolysis; verdict of Justifiable homicide against Hamlet. Finally there is the complex case of Hamlet himself, whose ticket should read: 1. (*a*) Intravascular hæmolysis, due to (*b*) Abrasion on back, and 2. Aspirin (or barbiturate) poisoning as a contributory cause; almost certainly this would be returned from Southport with the question "how was the abrasion caused?" The verdict in this case (it's very difficult) would be Wilful murder against Laertes, later softened down by a lenient jury to Culpable homicide against Hamlet, and also Suicide while of unsound mind (this is stretching a point in a compulsion neurosis, but it saves our friend the gravedigger from working overtime at the crossroads). Those unfortunates, Rosencrantz and Guildenstern, become the concern of a "crowner's quest" in England, but our impulsive Prince Hamlet can hardly escape a charge of being an accessory before the fact.

As this dreadful series of inquests concluded we could not help feeling sorry for that principal witness, Horatio, who, during the play, himself so nearly took a swig at the aspirin. But all these lamentable deaths would have been prevented had the first autopsy been more thoroughly carried out. Will pathologists who read these words please remember in future to examine the portals of the ears?

* * *

The dining club described by your correspondent of Oct. 16 has certain resemblances to mine, which is now approaching the age of 25. We started with six students—four of them medical—sharing "digs" in a Bloomsbury Square whose name the club bears; but later we added six so-called honorary members, friends and relations of the founders. At first four annual meetings were attempted, including a summer meeting at Bisley where the secretary annually tries to win the King's Prize—and once nearly succeeded—and a "pyrotechnic" provincial meeting in November. (Some 17 years ago a club yacht was purchased, but only the more leisured members patronise this sport.) Now that we are all getting older and busier we have settled into a routine consisting of the annual general meeting in Town in January and the more hilarious pyrotechnic meeting at some small town in the southern half of the country. At the latter, the procedure is as follows: (1) 6.30 P.M. arrival of members from divers directions (with fines for lateness); (2) dinner; (3) the company proceeds to some local eminence or place of historic interest, where pyrotechnics are exploded; and (4) return to the hotel, where the secretary reads the minutes and we reminisce over the minute-books. Should any reader have heard the sound of pyrotechnics being exploded on a hill above a well-known Thames-side town last Saturday about 9 P.M. there was no cause for alarm. It was only us.

Letters to the Editor

MEDICAL GROUP PRACTICE

SIR,—The report in your last issue of the activities of a partnership of five who are described as "general-practitioner specialists" raises questions of consequence to the public and the profession.

The group is stated to work in a country town of 10,000 inhabitants with a population of 15,000 in the surrounding country district. Fifteen miles away is a city with a large non-teaching hospital. The partners pool income from all sources. "The division is assessed mainly on two factors: (1) age and seniority in the group; and (2) the recognised higher earning capacity of surgeon-specialists." The partners are "a surgeon-obstetrician (F.R.C.S.E.), a physician (M.D., M.R.C.P.), an anæsthetist (M.B., D.A.), an assistant anæsthetist (M.B.), and a second surgeon (F.R.C.S.E.). The five members of the group all have specialist experience, four out of five having served in the war as specialists in the Services; four out of the five are members of the B.M.A. part-time consultants roll. All members of the group undertake general practice; all, except the senior partner, undertook N.H.I. work." They form five of the seven members of the staff of the local hospital of 50 beds.

The first object of the group is stated as "to provide a comprehensive medical service for the patient in his own locality." The group "heartily endorse" an American opinion in favour of group practice because "consultant's opinion and treatment can be made available without delay and with the minimum of expense." Again, it is stated: "When a consultant is required for an opinion or an operation, the patient is free to choose any specialist inside or outside the group." It is therefore clear that the partners regard themselves as "consultants" or "specialists." Exactly what they tackle is not so clear. It is said: "All routine general surgical and gynæcological operations and abnormal obstetric cases are undertaken, except the more uncommon and the most extensive, which are passed on to specialists with greater experience of these departments. Thoracic and cerebral operations and the more specialised orthopædic procedures are not undertaken." Only two specific cases are mentioned: details are given of how the group's surgeon operated upon a diagnosed carcinoma of the cæcum. Elsewhere there is reference to "a difficult diabetic."

Surely, Sir, such a partnership of "general-practitioner specialists," feeding patients to one another and yet financially linked, is bad both professionally and morally.

In modern medical organisation a man should not be both general practitioner and specialist. The attempt leads to his being an inferior and lopsided G.P. and a pseudo-specialist.

One realises that financial gain is not the main initial motive of such a group. The impulse comes more from professional keenness and a mistaken impression that the pure G.P. is in some way inferior to the specialist, which he certainly is not; he is or should be the equal. The true G.P. is the salt of the profession. The hybrid tends to deem himself too good for the doctoring side of his work, which he is always hoping to shed; his pre-occupation with his specialty prevents balanced development of his general medical knowledge.

A consultant or specialist is not just a man with a higher qualification acquired in his younger days. He is a man who genuinely specialises for the bulk of his professional life and who is on the staff of a large hospital. Incidentally, it would be a valuable advance if every intending consultant was compelled to do six months of general practice (not as a "general-practitioner specialist") as part of his training.

The genuine consultant draws his patients at least from scores, usually from hundreds, of doctors, and he spends his whole time within his specialty in which his range of experience and standard of work is inevitably much higher than is attainable by the "general-practitioner specialist."

One of the most important functions of the family doctor is to send his patients needing specialist advice to the specialists likely best to help them. In this he should be completely unfettered in his choice. How

can partners in such a group really do this? If they do not send patients to each other, especially to senior and surgical partners, they risk mutual acrimony and incur financial loss since all earnings are pooled.

A significant paragraph reads: "The success of this group has been built on complete freedom of action as a group, and on the much-discussed personal-profit motive. How greatly it will be affected by restrictions imposed on part-time consultants practising in groups where some members have G.P. contracts with local executive councils, remains to be seen. Any official attitude which prejudices the free action of the general-practitioner consultant is likely to be fatal to medical group practice." In this particular matter the duty of those responsible for the administration of the National Health Service would seem clear.

The criticisms above are not directed against general-practitioner partnerships, which are obviously desirable because of the advantages of covering duties during periods of leisure and holidays and the sharing of running expenses and practice facilities. Nor is it unreasonable for members of a G.P. partnership to develop, within limits, special bents and to seek higher qualifications. Like most worth-while things in life it is a matter of balance and where the line is drawn.

CONSULTANT.

TUDOR EDWARDS MEMORIAL

SIR,—In June, 1947, you were good enough to publish a letter inviting contributions to a fund for the establishment of a memorial to the late Mr. Arthur Tudor Edwards. The fund was closed on March 31 last and reached £4000, with which the Royal College of Surgeons of England and the Royal College of Physicians have consented to form and administer a trust to found a Tudor Edwards lectureship to be given alternately at the two colleges. It is hoped that the lectures will reflect Tudor Edwards's wide interests, and that they will embrace not only the surgery and medicine of diseases of the chest, but also the allied studies of anatomy, physiology, pathology, and anæsthetics applicable to thoracic surgery.

HORDER
Chairman.
COURTAULD-THOMSON
Treasurer.

London, W.1.

SICKLING RAPIDLY DETECTED

SIR,—I have just noticed the statement in an annotation [1] that Singer and Robin [2] have introduced a new test for the presence of the sickle-cell trait.

I should like to point out that this test was introduced by me in 1945.[3]

G. ROBINSON
Senior Pathologist.

Medical Research Institute, Accra.

LIFE AND DEATH IN A CONCENTRATION CAMP

SIR,—As my late husband's assistant and companion in Theresienstadt concentration camp may I be allowed to reply to Dr. Juraj Oravec's letter in your issue of Sept. 18?

At Theresienstadt the unboiled potatoes often eaten by the internees were usually already putrified for the most part, and were thus a probable cause of many cases of diarrhœa.

From my own experiences, I disagree with Dr. Oravec's opinion that "nocturia" and "polyuria" are not deficiency diseases, but the consequence of the consumption of considerable quantities of watery soups distributed to the internees as food. During the $2^1/_4$ years of my internment I ate no soup and only consumed a moderate amount of liquids. Yet, like many of our comrades, I suffered from this very awkward inconvenience after a certain time during which other symptoms of deficiency had already appeared. Improvement only came after liberation. The same symptom was observed in Germany, especially in 1946–47. It was indeed alarming to see the water balance of many patients so seriously disturbed, some indeed being beyond medical help.

ELSE WOLFF-EISNER.

Munich.

1. *Lancet*, 1948, 1, 874.
2. Singer, K., Robin, S. *J. Amer. med. Ass.* 1948, **136**, 1021.
3. Robinson, G. *Trans. R. Soc. trop. Med. Hyg.* 1945, **39**, 264.

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SIR,—The theme of Dr. Wyburn-Mason's letter of Oct. 2 is that in my article (Sept. 4 and 11) I have "confounded the effects of intraneural and intra-arterial injection"; that in fact such drug injection was into either the major nerves or the perivascular nerve network, and that the arterial thrombosis and other circulatory effects could be adequately explained by such neurological damage. But his reasoning flaunts some important physiological facts, and it is my duty to confute him with some vigour.

1. Blood is not aspirated from major nerve or perivascular tissues. Yet blood was aspirated, according to the anæsthetists' reports, in most of the cases.

2. Patients do not fall asleep after injections into the perivascular tissues or major nerves, as followed in these cases. Thiopentone may be a general anæsthetic, but locally it is a profound irritant; much local pain, sloughing, or abscess formation are the well-known effects of such spillage. Distal circulatory pathology does not follow such an accident.

3. Massive limb œdema, blisters, punched sloughing ulcers, as in some of the cases, Dr. Wyburn-Mason would have us believe are "familiar to neurologists" as "identical with . . . e.g., in brachial neuritis and causalgia" and the "initial effects of 'Proctocaine' injection." Such bizarre "neuritic" behaviour effects have not, however, been observed by my neurological friends or myself.

4. It is difficult to account for the complete limb palsy after such injection by any mechanism other than ischæmia. Otherwise, it does mean the separate blocking of the radial, ulnar, and median nerves; even the stiletto skill of a Borgia could not achieve that with 4 ml. Anæsthetists have a reputation for kindly disposition to surgical retort and insult, but it is presuming too much to suggest that in their search for the median cubital vein they injected the ulnar nerve.

I fail to understand why Dr. Wyburn-Mason is so reluctant to accept the effects of ischæmia on nerve conduction; the uncurtained iron facts are on view in any *Index Medicus*. Nerve conduction is an active metabolic process requiring oxygen, and if blood-flow be interrupted nerve conduction cannot continue.

5. Dr. Wyburn-Mason's concept of such extensive gangrene as being of the class of "trophic lesions," comparable to the tabetic ulcer and bedsore, would require the imagination of a Salvador Dali. The fact, of course, is that in 1936 the requiem for trophic nerves was sung in the experimental laboratory by Grant [1] and in the human by Lewis and Pickering.[2] They showed that changes ascribed in the past to the interruption of "trophic" nerve-fibres are in reality secondary effects to the loss of movement or sensation.

6. The pale hand, the cyanosed fingers, the flushed skin, the gangrene Dr. Wyburn-Mason explains with ease as simply the effects of irritation of the vaso-constrictor and vasodilator fibres; but we are not told how such stimulation paralyses the sensory and motor fibres at the same time.

To suggest peripheral vasodilatation as primarily responsible for the limb death, implies a strange and disordered behaviour of a multitude of physicians and surgeons in their management of the ischæmic limb, for such is their aim and endeavour.

7. According to Dr. Wyburn-Mason the intraneural injection of thiopentone "stimulates the vasodilator fibres, liberates acetylcholine in the blood-vessels," and as "acetylcholine accelerates blood-clotting" this "initially precipitates thrombosis." This is of course pure hypothesis unbrushed by the lightest touch of the wings of fact.

Firstly, peripheral vasodilatation is believed to be due to the inhibition of vasoconstrictor impulses; active vasodilator fibres (if they exist in human skin), have a very limited functional significance.[3]

Secondly, there is no evidence that acetylcholine, even if thus liberated, could find its way into the arterial stream

1. Grant, R. T. *Clin. Sci.* 1936, **2**, 1.
2. Lewis, T., Pickering, G. W. *Ibid.* p. 149.
3. Sarnoff, S. J., Simeone, F. A. *J. clin. Invest.* 1947, **26**, 453.

in any quantity; indeed, its rapid hydrolysis renders this virtually impossible.

Thirdly, injection in the human of up to 80 mg. acetylcholine intra-arterially has not been followed by thrombosis.[4] Dr. Wyburn-Mason does not give the authorities for his statement that acetylcholine "accelerates" blood-clotting; Zunz and Vesselowsky [5] have shown that with high concentrations such as 1/1000 to 1/50, clotting was actually slightly retarded.

Wilson and Stoner [4] found that the intra-arterial injection of 40–80 mg. of acetylcholine in 2 ml. was followed in the majority of cases by "burning," "crushing pain," muscle spasm, and a skin flush—very similar to that of other accidental drug injections—and, be it noted, despite 2% procaine peri-arterial infiltration. These effects were attributed to the "muscarine" responses of the acetylcholine, but I am given to understand that the above solution has a pH of about 3·5 and this may be the explanation. Pain and other effects were not a constant feature; as in other accidental drug injections, this probably depended, as Wilson and Stoner observed, on whether the solution was distributed to skin or muscle. Quite obviously thrombosis has nothing to do with the pain.

8. Finally, Dr. Wyburn-Mason presents a case which developed the "signs of brachial neuritis" after thiopentone injection, and comments: "it is difficult to explain as due to arterial damage." I quite agree, but find it even more difficult to interpret as due to local injection around the brachial artery or major nerves. I have never known the brachial plexus to palsy itself as a sympathetic gesture to one of its irritated branches. Similar "shoulder-girdle syndrome" cases have been described following T.A.B. and other inoculations, and oddly enough, after operations. Dr. Wyburn-Mason has himself contributed to the subject; the condition has been called "neuralgic amyotrophy" by Parsonage and Turner.[6] They attribute the effects to brachial-plexus perineural œdema, and the complications of intravenous injections may be one of many mechanisms responsible for this.

It has been well said that an hypothesis, even if wrong, dies an honourable death if it has provoked thought and discussion.

London, W.1. SOL. M. COHEN.

ABORTION, STERILISATION, AND THE LAW

SIR,—The letter from Dr. Haire in your issue of Oct. 23 provides an opportunity for reference to the clarification of abortion law during the trial of Dr. Eleanor Bergmann and Dr. Mary Bell Ferguson, who last May were acquitted of criminal abortion after a four days' hearing at the Old Bailey.

In his summing-up the judge quoted the following words from the Bourne case (1938):

> "If the doctor is of opinion, on reasonable grounds and with adequate knowledge, that the probable consequence of the continuance of the pregnancy will be to make the woman a physical or mental wreck, the jury are quite entitled to take the view that the doctor who, under those circumstances and in that honest belief, operates, is operating for the purpose of preserving the life of the mother." And he added: "I fully adopt those words and invite you to bear them very much in mind."

Later on he told the jury:

> "You are not concerned with the question as to whether Dr. Ferguson arrived at the right conclusion; you have not to decide whether Dr. Ferguson did or did not make a mistake. Between medical people there may often be differences of opinion; sometimes it is difficult to assert which of two opinions is to be preferred, but you are not here to weigh up whether Dr. Ferguson was correct or incorrect in the view that she had formed. You have to be satisfied by the prosecution that she expressed a dishonest opinion, and that when she advised, if you think she did advise, the termination of pregnancy by her letters in these two cases, you will have to consider whether you are persuaded by the evidence called by the prosecution that that lady gave a dishonest opinion, did not act in good faith, and was therefore advising something that was unlawful."

After this remarkable legal pronouncement, does it not seem unlikely that, on the grounds described by Dr. Haire, a jury would convict a medical practitioner who had "in good faith" performed or advised the operation? And therefore the risk of imprisonment and loss of livelihood by doctors who show courage in relation to the practice of therapeutic abortion, would seem to be now considerably less than formerly.

ALICE JENKINS
Hon. Secretary,
Abortion Law Reform Association.

53, Gloucester Terrace,
London, W.2.

DENTURES AND ANÆSTHESIA

SIR,—Some of your correspondents seem to have difficulty in getting an airtight fit for the edentulous.

A thick piece of 'Gamgee' will mould to fill all except the most hollow cheeks. Clamping a face-piece on without any padding has been condemned in the past for producing nerve palsies; but rubber face-pieces can be moulded slightly in the hands to give a better fit. I have found stuffing the sides of a face-piece less effective and more easily dislodged than the more usual and simpler gamgee with a hole in it for the nose and mouth. As for packing round an air-way or tube, why increase the number of items which can be "left behind," except of course when a pack is essential as for a dental operation? The large masks suggested last week by Dr. Barnard increase the "dead space" in which carbon dioxide and other gases can collect in too large proportions.

Lastly, many of the old and toothless have small and shrunken faces.

Manchester. S. SHUBSACHS.

PROPRIETARY MEDICINES UNDER THE NATIONAL HEALTH SERVICE ACT

SIR,—It was, of course, to deal with such difficulties as borderline cases (which Dr. Forster says I omitted to consider) that I suggested an expert advisory committee to the Minister. I cannot quite see how Dr. Forster can state, as he did in his letter on Oct. 30, that "proprietary articles ordered on N.H.I. and private prescription were all of the truly ethical type," and yet fail to find anything significant in the fact that practitioners were effectively discouraged from prescribing such "truly ethical" preparations. (Average of proprietary medicines prescribed in the three areas quoted by me: private 31·5%, N.H.I. 6·2%.)

Dr. Forster's criticisms of the Chemists Federation would not, I think, have been made had he been better acquainted with its work over the past few years. (The federation, for example, has concerned itself little with price protection.) Following the adoption of a selective policy the standards committee have applied the federation's rules in respect of formulæ, conditions of manufacture and presentation, and claims made on labels and packings and in literature and advertisements. Preparations on the list before the adoption of standards have also been reviewed with the result that much unsound literature has been revised and certain products removed altogether from the list. This work has required the sacrifice of a great deal of time by the members of the standards committee, whose qualifications are pharmaceutical, scientific, and legal. Medical advice, including that of a permanent medical adviser, is readily taken. In addition, specialist medical opinion is sought wh never necessary.

I think it is important to remember that there are two related but distinct problems: (1) to establish the safety of "domestic" proprietaries for use by the public, and (2) to ensure that "ethical" proprietaries have sufficient merit to justify the State paying for them under the National Health Service. An almost complete solution to the first problem may be found in the further development of the work of the Chemists Federation, advertising associations, and other interested bodies, always provided that the services of the pharmacist are fully utilised.

The high standard of the information services provided by the great majority of the manufacturers of "ethical"

4. Wilson, A., Stoner, H. B. *Quart. J. Med.* 1947, **16**, 237. Harvey, A. M., Lilienthal, J. L. *Bull. Johns Hopk. Hosp.* 1941, **69**, 566. Ellis, L. B., Weiss, S. *J. Pharmacol.* 1932, **4**, 235.
5. Zunz, E., Vesselowsky, O. *Arch. int. Pharmacodyn.* 1938, **60**, 146.
6. Parsonage, M. J., Turner, J. W. A. *Lancet*, 1948, i, 973.

proprietaries and the specialised knowledge of the doctor reduce the second problem to small dimensions, and there is certainly less reason in this country than in America for the setting up of such a body as the Council on Pharmacy and Chemistry. An advisory committee to the Minister, together with the existing machinery for dealing with excessive prescribing under the Act, would provide, in my view, all the means of control which are required.

Finally, may I suggest that those concerned with the solution of these problems should bear in mind that the vitality of the industry, the professional freedom of the doctor, and the public welfare are all involved, and that the use of "ethical" proprietaries under the National Health Service concerns the lifeblood of the *Pharmacopœia* itself.

London, N.W.10. E. W. GODDING.

TESTING ANALGESICS

SIR,—It is interesting to note from their article on Oct. 30 that Dr. Hewer and Dr. Keele in testing analgesics have chosen the method of pain-induction by means of contraction of ischæmic muscles rather than cutaneous pain elicited by heat radiation as described by Hardy and others.

Workers who have used both methods have expressed decided preference for the latter. Thus Jones and Chapman [1] regard the "muscle ischæmia pain" method as less accurate and highly subjective. Similarly, Chapman, Arrowood, and Beecher,[2] in assessing on 15 subjects, the analgesic effect of 20% nitrous oxide as equivalent to that of gr. 1/4 of morphine sulphate, say:

"Two types of pain production have been studied: (*a*) pain arising from heat radiation on the skin of the forehead. Our principal conclusions are based upon those observations. (*b*) Pain arising from muscle ischæmia as a result of exercise of the hand under conditions of vascular occlusion by a cuff tourniquet on the arm. Here, the observations are highly subjective and have been used only as supplementary support for our conclusions."

It seems that the problem of testing analgesics is a thorny one in view of their side-effects—notably that of euphoria. After administration of some drugs (particularly of the opiate group, pethidine, and 'Physeptone') the pain is still discernible but the attitude towards it is changed, inasmuch as the "alarm reaction" is reduced. Thus a question suggests itself: Are the analgesics as such really tested, and can the analgesic and euphoric effects be separated? This vexed question was the subject of a symposium in the U.S.A. in 1943.[3]

London Hospital, E.1. BERNARD KENTON.

OVULATION AND THE MENSTRUAL CYCLE

SIR,—In his critical survey last week of the evidence concerning the time of ovulation within the menstrual cycle, based on the study of tubal ova, early embryos, and endometrial histology, Professor Davies describes a case in which ovulation appears to have occurred on the 9th or 10th day of a cycle in a woman whose history indicated regular cycles of normal length (28 days).

It is commonly assumed that if ovulation occurs unusually early in a cycle then that cycle will be an unusually short one; and conversely, if it occurs unusually late then the cycle will be unusually long. Davies criticises this assumption, and submits that there is no conclusive evidence that the duration of activity of the corpus luteum of menstruation is rigidly constant, and that estimations of the length of the postovulatory phase of the cycle based on the above methods are unsafe. The estimation of the time of onset of the next menses in all the cases quoted by Davies is, as stated by him, purely assumption since the cycles were interrupted, generally by hysterectomy.

It is obvious that the determination of the time of ovulation can be more satisfactorily made by some other means, such as the vaginal-smear technique. The results of many years' experience of this technique, using Pasini's stain, have indicated two facts [4]: first, that while it is common for ovulation to occur about the middle of a cycle of 28 days, variations are frequent; and secondly, that in the successive cycles of any one individual the time of ovulation is remarkably constant and is even resumed with the same timing after pregnancy. One case showed extreme variation from the common condition in that ovulation was deduced to have occurred on the second day of the cycle—i.e., during the bleeding phase. That this was so was substantiated, after a long period of apparent infertility, by pregnancy based on this information. The cycle length, which had been recorded for many years, was very regular with a duration of about 25 days. During the period of investigation ovulation occurred regularly about 23 days before the onset of the succeeding menses and indicated that the functional life of the corpus luteum was of this duration. This is a wide divergence from the average of 14 days suggested by the investigators whose reports are reviewed by Davies.

A more extended survey of menstrual cycles than any yet made would seem to be necessary before deciding what may be regarded as normal and as abnormal in the time of ovulation within the cycle. At the moment, as Davies indicates, there is no certain evidence to justify the conclusion that the day of ovulation can be even approximately deduced from the time of the succeeding menstrual period.

University of Sheffield. W. S. BULLOUGH.

1. Jones, C. M., Chapman, W. P. *Arch. intern. Med.* 1944, **73**, 322.
2. Chapman, W. P., Arrowood, J. G., Beecher, H. K. *J. clin. Invest.* 1943, **22**, 871.
3. Fed. Proc. 1943, **2**, 187.
4. Bullough, W. S. *Brit. J. Obstet. Gynæc.* (in the press).

AN ALLEGED RACKET

SIR,—An ingenious journalist preparing his column for a Sunday paper some weeks ago thought up and published a method by which, he said, the public could exchange a National Health Service prescription for toilet preparations with an easy-going chemist. The chemist would not dispense it, but would be paid by the State as if he had. No-one can prove that such a thing has never happened among the millions of prescriptions dispensed under the National Health Insurance Act, but certainly I can call no case under that Act to mind during the last twenty years, and the ingenious journalist was careful to give no specific instance under the National Health Service Act.

The matter might have rested there, as no more than a titbit for Sunday readers, had not one of your Peripatetic Correspondents given the fable the authority of your columns a week ago. Like the ingenious journalist, he gave no specific instance, for there is no instance for him to give, but he started the hare again and the papers have taken it up, quoting THE LANCET as authority. I trust that on looking at the paragraph again you will agree that it is regrettable that this reflection on pharmacy should have been published, even in lighter vein. It has already hit medicine as well. One paper now alleges that some doctors "are handing out prescriptions regardlessly" as their part in this imaginary racket.

Pharmaceutical Society of Great Britain, 17, Bloomsbury Square, London, W.C.1. HUGH N. LINSTEAD Secretary.

*** Our correspondent, being assured that the abuse has happened, hoped that informal publicity might prevent its ever happening again. Neither he nor we intended any reflection on a profession which sets and maintains an exemplary standard of conduct.—ED. L.

DEADLY NIGHTSHADE POISONING

SIR,—As a pharmacist of over twenty years' experience, I followed the recent articles on this subject [1] with keen interest.

The advice given seemed to be to empty the stomach and obtain medical attention. I was very surprised to find no mention of the general antidote to alkaloids—i.e., tannic acid. As, of course, is well known, this forms an insoluble tannate of the alkaloid, and absorption is retarded.

During my professional life I have several times had a distracted mother, a child under one arm and a botanical specimen in the other hand, rush into the pharmacy. I invariably give 10–15 grains of tannic

1. *Lancet*, Sept. 11, pp. 423 and 438; *Ibid*, Sept. 25, p. 513; *Ibid*, Oct. 2, p. 546.

acid in water as a draught statim, and instruct the becalmed parent to make hot tea for herself and the child. This revives the one and supplies further tannin to the other. No untoward results have been brought to my notice.

London, N.17. ALFRED JORDAN.

APPLICATION FOR HOSPITAL POST

SIR,—Let me hasten to assure your correspondent "A.B." that he is perfectly correct in his letter last week when he says: "It would seem that more tact and consideration are applied in obtaining the services of a cook than those of a doctor"; and let me add that even more tact and consideration have to be applied in retaining those services once they are obtained. This is, of course, only one aspect of the dismal situation arising from the inexorable law of demand and supply; cooks and maids are nowadays almost unobtainable, while anything from 30 to 70 physicians and surgeons are scrambling for every precious vacancy offered in their respective specialty. When contemplating the huge pass-lists for the higher qualifications, one wonders when this oversaturation of the market for specialists will finally reach its logical conclusion, with holders of the M.R.C.P. and F.R.C.S. scrubbing the floors and washing the dishes, while the cook-generals and housemaids on the house committee dictate the treatment of the patients.

While on the subject of comparative values, let me end by asking what we are to think of the generous terms of the Spens reports while certain dentists in the N.H.S. are now earning money at the rate of £24,000 a year?

PHYSICIAN.

DOSAGE OF SULPHETRONE

SIR,—The oral dose of 'Sulphetrone' to be aimed at is that which gives a blood-level of 7·5–10 mg. per 100 ml. As Dr. Ewing indicates in his letter on Oct. 30, the oral dose which is finally administered varies considerably, but is usually 6–10 g. for adults, or 3–6 g. for children. The incidence of side-effects is reduced when the gradual scheme of dosage suggested by Madigan is employed.

It is our view that should absorption be so faulty as to necessitate daily adult doses in excess of 12 g., or children's doses in excess of 6 g., recourse should be had to the parenteral route for at least a proportion of the drug. It should be remembered that there is always a potential reservoir of drug in the gut, unabsorbed, or re-excreted by the ileum; normally this is lost to absorption by passage into the cæcum. This picture is reversed with stasis, when sudden rises in blood-concentrations have been observed. It is clearly unwise to increase unduly the concentration of drug in the gut, and adult oral doses in excess of 10 g., or sometimes 12 g., daily are not to be recommended.

Tuberculosis Chemotherapy Unit, County Hospital, Farnborough, Kent. D. G. MADIGAN

Wellcome Research Laboratories, Beckenham, Kent. GEORGE BROWNLEE.

PHARAOH FACIES

SIR,—Expressions such as "facies Hippocratica," "typhoid facies," and "adenoid facies," not to mention "risus sardonicus" and others, have long since received official sanction. I have been wondering how the expression "Pharaoh facies" would be received if suggested as an addition to the list. I believe it fully fits a very well-defined clinical entity—the preliminary phase of all forms of deafness of sudden onset. Thus it is found typically in salicylate poisoning and cinchonism.

My first observation, made over ten years ago in a hospital outpatient department, was on a patient suffering from the former condition. She was a young girl presenting a picture of almost complete indifference to any attempt at normal communication with her on the part of physician, nursing staff, and orderlies—until finally a question was put to her in writing.

This is a typical history. During this preliminary phase she was really out of touch with the world around her, having had no time to familiarise herself with lip-reading, finger-spelling, and gesture. It was this attitude of almost supreme indifference to all that was going on that recalled to me those historical notes on that government administrator in Ancient Egypt, the Pharaoh who hearkened not to Moses, the founder of public health. I feel sure that anyone who has met deafness of sudden onset, in its early phase, will agree that this simile is quite appropriate.

Pharaoh facies is not seen in patients with deafness of gradual onset, who have had ample time to adapt themselves to changing conditions—for example, those with progressive labyrinthine deafness or presbyacusis. I believe, however, that colleagues will agree that Pharaoh facies aptly describes the preliminary expression of the patient in noise deafness, concussion deafness, and shellshock deafness, before lip-reading or other devices have been learned, and occasionally in the deafness complicating epidemic cerebrospinal meningitis, measles, mumps, or typhoid fever, and the deafness found in certain forms of drug idiosyncrasy and poisoning, as described above.

London, W.1. S. HALES.

Parliament

Removal of a Mental Patient

IN the House of Commons on Nov. 1 Mr. E. McN. COOPER-KEY drew attention to an "unwarranted intrusion and abuse of power by public servants."

Mrs. Salter, he said, lived with her daughter, a mental deficient, in a basement flat in Hastings. On Oct. 8 Mrs. Salter went shopping, leaving her daughter alone in the flat suffering from gastric trouble. On her return she found two policemen and an official from the Ministry of Health had forced an entry. She ordered the men to leave. They informed her that the entry had been authorised by a high authority and she was asked for her keys. She refused again, and asked the men to leave. They then informed her that her daughter was to be removed to a mental hospital. A police surgeon arrived who produced a roughly drawn certificate to the effect that Mrs. Salter and her daughter were of unsound mind and should be removed to the local hospital. At the hospital Miss Salter was removed to a private room, a justice was summoned, and she was pronounced of unsound mind. At 7.30 P.M. Mrs. Salter was released and told that if she called next morning she would be able to see her daughter. But in fact, her daugher was removed an hour later to Hellingly Hospital.

Mr. Cooper-Key said that the local authorities sought to justify their action under section 14 (1) of the Lunacy Act as amended by the National Health Service Act.

This provided that if a duly authorised officer (*a*) had reasonable grounds for believing that a person was of unsound mind, and (*b*) was satisfied she was not under proper care, he should, not may, within 3 days give notice to a justice.

Mr. Cooper-Key did not complain of the provisions in paragraph (*a*) in this case, but was it seriously suggested that a devoted mother's attention and nursing was not proper care?

Under section 72 of the Lunacy Act, as amended by the National Health Service Act, any patient resident in an asylum should be discharged on application by the appropriate relative. On the following Tuesday Mrs. Salter accordingly went to the asylum and demanded the return of her daughter, who was at once discharged. There had been no question of course of this patient having either homicidal or suicidal tendencies. As the law stands, Mr. Cooper-Key pointed out, local authorities have the power to remove an individual against the wishes of her parent, but the asylum must release her immediately on application by the parent. He submitted this rendered nonsensical the administration of the Act.

Mr. JOHN EDWARDS, parliamentary secretary to the Ministry of Health, in reply, related how, in consequence of information received by the medical officer of health for Hastings, a duly authorised officer visited Mrs. Salter's flat.

He heard peculiar noises coming from a room, but got no response to knocks on the door. Looking through the

window he saw Miss Salter behaving like an imbecile. The official arranged with the police surgeon, the police, and the St. John Ambulance Brigade to meet him at the house, over two hours after his first visit. While preparations were being made for Miss Salter's removal Mrs. Salter returned home. She refused to open the door and became violently hysterical. The senior partner of the police surgeon on his arrival gave the certificate, on which the officer acted, that mother and daughter were of unsound mind.

The original action taken by the officer, Mr. Edwards explained, was under section 20 of the 1890 Act as amended by the 1946 Act which provides that an officer may remove, without warrant, a person of alleged unsound mind to a hospital for 3 days pending proceedings. When Miss Salter arrived at St. Helen's Hospital she was in a dirty condition and thin to the point of emaciation. She could only walk with a little support and had to be assisted with her feeding. Later in the evening Mrs. Salter and her daughter were seen by a justice of the peace and the partner of the police surgeon who did not consider Mrs. Salter then to be certifiable. She was allowed to leave the hospital, but the justice signed the order for Miss Salter, who was removed to Hellingly Mental Hospital. The medical superintendent certified that Miss Salter was suffering from chronic schizophrenic dementia, but he had no alternative but to allow her to leave the hospital in conformity with a direction given by her mother under section 72 of the 1890 Act, as he was unable to certify that she was both dangerous and unfit to be at large.

As to the forcible entry into the flat, Mr. Edwards pointed out that the authorised officer had a statutory responsibility to discharge and he would have been negligent if he had not tried to do something about it. He (Mr. Edwards) had also been asked about legal changes necessary to get rid of the inconsistencies in the administration of the Act, but he would not be in order to go into that matter.

Gifts to Hospitals

In the House of Lords on Nov. 2 Lord SALTOUN asked whether the removal of hospital collecting-boxes from railway stations was not contrary to the Government's expressed wish that private subscriptions to hospitals should continue.

Lord SHEPHERD, in reply, said that the Minister of Health and the Secretary of State for Scotland hoped and were confident that private generosity, which had done so much for the hospital service in the past, would not now come to an end. But they did not consider it proper that the new governing bodies of hospitals, which were public bodies financed from public funds and were no longer dependent upon private charity, should themselves appeal for funds. Appeals made by independent voluntary organisations on behalf of the hospital service, or of particular hospitals, for money to provide extras and amenities outside the ordinary running of the service, were, of course, a wholly different matter.

More Fats and Sugar

Mr. JOHN STRACHEY, Minister of Food, announced in the House of Commons on Nov. 2 that the weekly domestic ration of cooking fat would be increased from 1 oz. to 2 oz. from Dec. 5 to March 26, 1949, and of sugar from 8 oz. to 10 oz. from Dec. 5. The sweet ration would be 1 lb. for each four-week period from the same date. The rationing of jam and marmalade would end on Dec. 5.

QUESTION TIME

Cost of National Health and Insurance Services

Sir WALDRON SMITHERS asked the Chancellor of the Exchequer if he would state in terms of pence per £ in income-tax what was the cost to the taxpayer of the National Health Service and the National Insurance scheme, respectively.—Sir STAFFORD CRIPPS replied: The National Health Service and the National Insurance schemes will have been in force for the last nine months of the current financial year. It is estimated that during this period the cost to the taxpayer of the former will be equivalent to an income-tax of about 1*s.* 0½*d.*, and that the contributions of the Exchequer to the latter will be equivalent to one of about 8½*d.*

Health Service Registrations

Replying to a question, Mr. ANEURIN BEVAN stated that 18,165 general practitioners, 8343 dentists, and 93·1% of the population had joined the National Health Service.

Basic Salary

Mr. JOHN RANKIN asked the Minister why it had been decided that new entrants to the general practice of medicine were not to receive the basic salary as of right—Mr. BEVAN replied: To meet the wishes of the medical profession themselves.

Mr. SOMERVILLE HASTINGS asked the Minister in how many cases applications for basic salary had been received by executive councils in England and Wales; and in how many cases this had been granted—Mr. BEVAN replied: Precise figures are not available but I understand that more than 1000 applications have been granted. Mr. HASTINGS: Can the Minister give any idea of the proportion of the applications which have been granted?—Mr. BEVAN: I cannot give any details at the moment. This is primarily a matter for the executive councils. Unless appeals are made at this stage I would not have the information.

Dr. S. SEGAL: Does not the Minister agree that the attempt on the part of the medical profession to impose a means test upon doctors who apply for a basic salary is really an effort to defeat the whole object of a basic salary?—Mr. BEVAN: It would be undesirable for me to make a comment upon the representations of the medical profession. I must deal with the representatives of the profession. If doctors have individual complaints they ought to make them first to their profession, so that I may hear them through the profession.

Medical Supplies

Sir ERNEST GRAHAM-LITTLE asked the Minister whether he was aware that under the National Health Service (Scotland) Act, 1947, medical practitioners are permitted to obtain without restriction medical supplies for their personal use in their practices upon presentation of their own prescriptions; that under the National Health Service (England) Act, 1946, medical practitioners are for this purpose granted only 2*s.* 6*d.* per annum per 100 patients; and whether in the public interest he would make the same concession to English practitioners as is made to Scottish practitioners.—Mr. BEVAN replied: I see no reason to alter the arrangement; which, incidentally, was in force before, under the old National Health Insurance scheme.

Local Hospital Committees

Mr. DOUGLAS MARSHALL asked the Minister whether he was aware that the press is not now admitted to meetings of the local hospital committees west of Bristol or in Cornwall; and, in view of the fact that these local hospital committees were provided so that they would form a liaison with the public, he would take action to remedy this grievance.—Mr. BEVAN replied: The function of hospital management committees is the day-to-day control and management of their hospitals; and while I hope they will take every opportunity of keeping the closest contact with public opinion, the admission of the press to their meetings is a matter for their own decision.

Hearing-aids

Lieut.-Commander CLARK HUTCHISON asked the Minister whether, in view of the fact that the standard Medresco hearing-aid supplied under the National Health Service does not suit all deaf persons, he would allow such persons a grant to assist them to purchase alternative equipment more suited to their individual needs.—Mr. BEVAN replied: The answer is, "No, Sir." Lieut.-Commander HUTCHISON: Does not the Minister appreciate that the same type of aid does not necessarily suit every person who suffers from deafness, and will he give further consideration to this matter?—Mr. BEVAN: Further investigation is proceeding as to the proportion of deaf people who cannot be properly fitted with the instrument which we are supplying. At the moment, that percentage is unknown, and until further investigation has taken place we think it would be very unwise to extend the facilities.

Mr. A. C. M. SPEARMAN: Does not the Minister think that if free batteries are allowed to holders of Government aids and not to owners of commercial types, it is a direct encouragement to the latter to throw away their aids and unnecessarily require Government aids, thereby increasing the expenditure

which will fall upon the taxpayer?—Mr. BEVAN: It would be very difficult administratively to provide the variety of batteries required in the private sets. It is much easier administratively to provide the standardised batteries which are provided with the Government aid.

Dental Treatment

Sir WALDRON SMITHERS asked the Minister how many people had applied for free dental treatment since the setting up of the National Health Service.—Mr. BEVAN replied: About $1^3/_4$ million.

Mr. GERALD WILLIAMS asked the Minister what was the total amount paid or owing to dentists under the National Health Service up to date; and by how much this exceeded his original estimate.—Mr. BEVAN replied: The total amount paid or owing to dentists on Oct. 30 for work completed under the National Health Service is estimated to be £$4^3/_4$ million. The estimate for this service for the period July 5 to March 31 next was £7 million.

Medical Registration: the Foreign List

Replying to a question Mr. BEVAN stated that the number of medical practitioners enabled to practise in this country by virtue of registration in the foreign list of the Medical Register under the Medical Practitioners and Pharmacists Act, 1947, since Jan. 1 last was 932, of whom all but 85 had previously been temporarily registered.

Tuberculosis Treatment in Switzerland

Mr. ANTHONY GREENWOOD asked the Minister whether he was aware that regional hospital boards were unable to pay for the treatment of tuberculous cases in Switzerland as was previously the practice of some county and county-borough councils before the National Health Service Act came into operation; and whether, in view of the deficiency of beds in this country for the treatment of tuberculosis, he would make it possible for regional boards to provide treatment abroad when desirable.—Mr. BEVAN replied: I have no power to make it possible for regional boards to do this or to authorise expenditure of this kind. Mr. GREENWOOD: In order that it may not be possible to say that tuberculosis patients are worse off under the new scheme than previously, will the right hon. gentleman consider the possibility of legislation at a later stage?—Mr. BEVAN: I cannot agree that they are worse off. I think that is a gross exaggeration. If there are further forms of treatment that can be given in other countries the remedy is not to send our people to other countries, but to make that form of treatment available here.

Mr. JOHN LEWIS: Will the Minister bear in mind that the climatic conditions in Switzerland are regarded as a form of treatment?—Mr. BEVAN: That is a matter for medical opinion and not for me.

Medical Examination of Food-handlers

Mr. CHARLES TAYLOR asked the Minister whether he would introduce legislation making it compulsory for handlers of food to be examined periodically to ascertain that they were not carriers of disease such as paratyphoid.—Mr. BEVAN replied: I am afraid the very elaborate arrangements which would be needed are at present impracticable, nor am I advised that the present state of our knowledge would justify them.

Infection from Train Lavatories

Mr. SOMERVILLE HASTINGS asked the Minister of Health whether his attention had been called to the danger of the dissemination of typhoid fever, infantile paralysis, and other diseases, as the result of the lavatories of main-line trains discharging directly on to the track; and what action he proposed to take.—Mr. BEVAN replied: I am advised that there is hardly any evidence at present that disease is spread in this way: but my medical officers are keeping in close touch with current research in this field.

". . . The study of the individual patient as the principal agent of his disease is only just beginning to recover from its neglect during the ascendancy of bacteriology. We are slowly relearning that the assistance of natural recuperative powers is no less important than the development of specific treatments aimed at the 'disease entity.' No treatment can be more specific than the resistance of the individual to his disease."—Dr. IAN P. STEVENSON, *N.Y. St. J. Med.* 1948, **48**, 2156.

Obituary

JOHN PERCIVAL HELLIWELL

C.B.E., M.R.C.S., L.D.S.

Major-General Helliwell, who was director of the Army Dental Service in 1935–36 and has since been consulting dental surgeon to the London County Council, died on Nov. 7 at the age of 64. Son of the late James Helliwell, of Manchester, he was educated at Owens College and at St. Mary's Hospital, London, where he qualified in dentistry in 1908. From 1910 to 1914 he worked in India as a civilian in dental charge of British troops, and in 1915 he received one of the first dental commissions in the Royal Army Medical Corps. He was soon promoted to be inspecting dental officer, and when the Army Dental Corps was established in 1921 he became inspector of dental services at the War Office. In 1935 he was promoted major-general and first director of the service which he had done so much to bring to birth. On retirement a task of almost equal magnitude awaited him as a whole-time member of the staff of the L.C.C., which was then expanding its hospital dental service and coördinating this with the school dental service. Both in military and civilian life he showed himself an able administrator, approachable, sincere, and keen-sighted. Outside his administrative work he became a principal exponent of a policy for the dental profession which may yet prevail. Regarding dentistry as essentially a branch of medicine, he at all times opposed the separation of the two professions; he believed that if possible dental surgeons should have a basic medical qualification, and he testified to his belief by taking the M.R.C.S. in 1926 when he had already spent several years at the War Office. His reservations to the final report of the Teviot Committee in 1946 pointed out that "the one great aim of the dental surgeon should be the preservation of the natural teeth and their associated tissues and to prevent as far as possible the need for artificial dentures"; yet it was from dentures that he made his greatest profit. In Helliwell's view the provision of dentures should be entirely in the hands of trained technicians; the dental surgeon should be able to derive an adequate income from the conservative work which is his proper task; and the present large deficiencies in the dental care of the people should be reduced by delegating much of the simpler preventive and surgical work—e.g., in school and other priority services—to dental ancillaries.

General Helliwell married in 1914. Mrs. Helliwell survives him, with a son and a daughter.

ALFRED WOLFF-EISNER

M.D. TÜBINGEN

Dr. Wolff-Eisner, professor extraordinary at Berlin and later at Munich, died on March 29.

Born in 1877 in Berlin, he followed his medical studies there and at the universities of Kiel and Tübingen where he took his doctorate with highest honours in 1901. As a student he had already published work on the cutis, and in 1902 he became an assistant to Richard Pfeiffer at the Institute of Hygiene at Königsberg. Pfeiffer remained a lasting influence in his life and thought. He returned to Berlin to become director of the bacteriological department at Friederichshain Hospital, a post which he held till 1913. Promotion came to him but slowly, and it was not till 1926 that he received a professorship in Berlin University and was put at the head of his own laboratory at the Charité. He was also sub-chief of the Robert Koch Institute. It was characteristic of him that he refused a full professorship offered on condition that he "changed" his Jewish religious ties. In 1933, under the Nazi racial laws, he was removed even from the appointments he held, and in 1943 he was sent to the concentration camp at Theresienstadt. His account of the deficiency diseases observed there was reviewed in our issue of Aug. 7 (p. 228), and a letter from his widow, who shared his imprisonment, appears in our present issue. On his release he settled in Munich, where, besides his university appointment, he became medical director of the Schwabinger Hospital for Displaced Persons and director of

the serological laboratory of the university clinic for nervous diseases. The state of his health prevented his accepting appointments offered to him in Venezuela and Bolivia.

Wolff-Eisner regarded it as his life's work to prove that Pfeiffer's discoveries on lytic immunity and the endotoxins apply not only to typhus and cholera but also to many other diseases in men and animals—especially tuberculosis. His *Handbuch der experimentellen Serumtherapie* was published in 1910. He was the friend of Ehrlich and Calmette, and his relationship with the latter was unclouded by their rival claims for priority in the discovery of the cutaneous and conjunctival reaction for tuberculosis.

In the memorial printed at his death a colleague stresses as his outstanding quality—"seine unbestechliche Wahrheitsliebe, ein absolutes Gefühl für Recht, das ihn zwang, überall dort in die Schranken zu treten, wo er glaubte dass Recht bebeugt würde, auch wenn er sich . . . selbst sehr oft damit geschadet hat."

Public Health

Insurance against Industrial Diseases

EARLY last year a committee was set up by Mr. James Griffiths, Minister of National Insurance, with instructions to advise on the principles which should govern the selection of diseases insurable under the National Insurance (Industrial Injuries) Act, 1946. In its report [1] the committee expresses the opinion that the tests which the Samuel Committee of 1906 recommended for application before a disease was scheduled are no longer appropriate. The present committee recognises, that for a disease to be selected for insurance, particular cases must normally be attributable with reasonable certainty to the nature of employment. Subject to this overriding test, the primary consideration should be whether the disease is specific to an occupation, or, if not specific, whether the occupation causes special exposure to risk of the disease; incidence alone is not a conclusive test of risk. A condition which can be treated as an accidental injury should not be selected for insurance as a disease, unless it can be more suitably dealt with in this way. The committee also recommends the appointment of a small standing committee to investigate proposals for adding to the list of selected diseases, to review periodically the existing list, and to suggest subjects for research.

Diphtheria in Scotland

The capacity of inoculation to protect against diphtheria and to reduce fatality is well known. There is, however, less evidence of the difference in the characteristics of the illness in the inoculated and the uninoculated; and in Scotland a subcommittee of the Department of Health's scientific advisory committee has undertaken an investigation [2] to fill the gap.

The subcommittee, under the chairmanship of Prof. J. W. McNee, investigated the records of 4272 of the 9340 cases admitted to hospital in 1942. Of these 4272 cases 58·5% were in females, and over the age of 15 almost 75% were in females—a finding attributed to this sex's greater attachment to the home and closer contact with children.

Of the 3187 cases in which the type of organism was recorded 2219 (69·6%) were of the gravis type. Altogether 1746 (40·9%) of the patients developed some complication; and the incidence of toxic complications was appreciably higher in patients under the age of 10. The over-all fatality-rate was 2·97%—a low rate in view of the preponderance of gravis infections. Over half the deaths were in patients with circulatory complications. In uncomplicated cases the fatality-rate was 0·75%. With tonsillar diphtheria gravis infection was six times more fatal than intermedius and mitis, whereas with pharyngeal and multiple sites gravis infection was only twice as fatal.

Counting all the 1023 with a history of inoculation as "inoculated," the fatality-rate in the inoculated was 0·68%, while in the uninoculated it was 3·69%. With regard to the incidence of complications, the inoculated fared little better than the uninoculated. Of all inoculated cases, 2·16% developed nervous complications, 7·2% circulatory complications, and 0·3% a combination of these two; for the uninoculated the comparable figures are 4·05%, 4·8%, and 0·77%. However, in inoculated patients there were significantly fewer toxic complications than in the uninoculated of the same age-groups. In the inoculated who developed nervous complications there were no deaths, while in the inoculated with circulatory complications the fatality-rate was 6·4%; for the uninoculated the fatality-rates were respectively 5·26% and 27·88%. Compared with the uninoculated, the inoculated had a significantly higher proportion of gravis infection (suggesting a less solid immunity than against intermedius and miti). They also had a significantly higher proportion of tonsillar infections and significantly less pharyngeal and multiple infections. On admission toxæmia was significantly less.

1. Ministry of National Insurance: Report of the Committee on Industrial Diseases. Cmd. 7557. H.M. Stationery Office. 4*d*.
2. Department of Health for Scotland. Diphtheria: Report by the Infectious Diseases Subcommittee of the Scientific Advisory Committee. H.M. Stationery Office. Pp. 31. 6*d*.

Poliomyelitis in British Zone of Germany

The peak of the poliomyelitis outbreak in the British zone of Germany was reached between Sept. 18 and 25 with 267 cases and 34 deaths. Totals for the month of September were 937 cases and 67 deaths. A British film on early diagnosis and treatment, completed earlier this year, has been shown, "dubbed" in German, before large medical audiences in Berlin and Hamburg.

Notification of Infectious Diseases

ENGLAND AND WALES

Disease	Week ended Oct. 2	9	16	23	30
Cerebrospinal fever	28	31	36	31	22
Diphtheria	114	112	141	153	129
Dysentery	58	84	114	99	68
Encephalitis lethargica	1	1	1	1	2
Measles, excluding rubella	3546	4061	4536	5303	6211
Ophthalmia neonatorum	65	63	55	53	45
Paratyphoid fever	6	13	9	4	7
Pneumonia, primary or influenzal	402	421	479	426	418
Polioencephalitis	5	7	7	4	4
Poliomyelitis	83	79	81	76	66
Puerperal pyrexia	97	111	100	115	107
Scarlet fever	1234	1273	1519	1389	1374
Smallpox	..	..	..	..	..
Typhoid fever	40	18	12	13	10
Whooping-cough	2204	2073	1949	2163	2060

". . . In qualifying the measures of child care as mostly arbitrary, I refer to the fact that only a very few of these measures, outside the actual chemical composition of the food of children, are actually based on the welfare of the infant. They are instituted for all sorts of extraneous reasons: facilitating a normal social life for the mother by rigid adherence to a feeding schedule; making matters easier for the nursing personnel in the obstetrical hospitals by advising against nursing and for bottle-feeding infants; segregating newborn infants in a separate room without contact with their mothers, for the purpose of making the control of infections easier; and many others. The strangeness of these measures will strike you immediately if you try to apply them to the grownup."—Dr. RENÉ A. SPITZ, *Medicine in the Postwar World*. New York and London, 1948; p. 38.

Notes and News

AID TO HOSPITAL ADMINISTRATORS

FOR some time past King Edward's Hospital Fund for London has afforded information and advice to voluntary hospitals and other organisations interested in hospital work. With the aim of coördinating and extending this service the Fund has established a division of hospital facilities which comprises an information bureau, an advisory service, a library of hospital books, journals, and plans, and an index to hospital literature. The director of the division, which began work last Monday, is Captain J. E. Stone, to whom all inquiries should be directed at the fund's offices, 10, Old Jewry, London, E.C.2.

PARPANIT

IN our last issue Dr. Dunham and Dr. Edwards recorded a trial, at the National Hospital, Queen Square, of 'Parpanit,' a synthetic antispasmodic with atropine-like activity, first described two years ago in Switzerland. From Italy, V. Davini and A. Borellini [1] report using it in 10 cases of extrapyramidal or pyramidal lesions, where the dose was gradually increased to a maximum of 0·2 g. daily. In those patients who were already receiving atropine, the dose of atropine was gradually reduced to find out at what dosage symptoms began to reappear; at this point parpanit was given in increasing doses whilst the doses of atropine were still being reduced. Owing to supply difficulties, long courses of parpanit were not possible; but these workers claim that their results confirm the report of Grünthal and of Hartmann in Switzerland, that parpanit goes a long way to restore normal movement in parkinsonian spasm, but that it gives much less benefit in other forms of spasm, tics, and chorea. Untoward effects were noted in two cases: one patient had slight palpitations and giddiness; the other was so upset that he refused to continue the treatment. The drug seemed to begin to take effect 15–30 days after the start of the course, probably owing to the time taken to reach the effective dose. Two patients said that their limbs felt strangely light, as if made of rubber or immersed in water; and that they were unable to tell exactly where the end of a limb was. They also said that their muscles were not so easily tired and that active movement was made much easier.

REGIONAL ORTHOPÆDICS

To be effective the orthopædic service should be linked with other services in the region and with the doctors and hospitals of the neighbourhood. In a brochure prepared for the Central Council for the Care of Cripples, Mr. G. R. Girdlestone, F.R.C.S., has reviewed the possible arrangement of the service on lines which will allow for early discovery and prompt treatment of cases, education of crippled children, and aftercare and vocational training. He points out that in a large region there may be several orthopædic organisations, each serving a district of manageable size, and all coördinated by the regional hospital board. Arrangements for "cold" orthopædics, he thinks, must differ from those made for cases of acute disease of bone and joint. "Cold" orthopædics—such things as locomotor disorders and deformities correctable by exercise—can be managed, he finds, by staff centred in the main hospital and working through a radiating service of clinics. Acute cases and compound fractures, however, must be in the care of the orthopædic and accident staff of the region, working not only in the central orthopædic hospital but in the general hospitals of outlying towns. At each of these hospitals a surgeon should be appointed to take charge of the unit with the help of adequate resident staff—a registrar and a house-surgeon. These surgeons should not work in isolation but should be visited regularly by a senior member of the central hospital staff on clinic days, and should attend clinical conferences at the central hospital once or twice a week. If a large region offers special difficulties, this close association may not be possible; but at least frequent clinical conferences and an agreed system of records should be arranged.

Some members of the regional orthopædic team will work only in the central hospital; others, including surgeons and orthopædic physiotherapists—better called "aftercare sisters"—will work partly at the centre and partly in outlying hospitals and clinics. But the team embraces more than surgeons and sisters: it includes all who are working in the wards, theatres, workshops, and special departments of the hospital. The clinics will best be housed in local hospitals, or, failing that, in any quarters which give adequate space and equipment for removal and application of plasters, examination of patients on the couch, and study of gaits and movement. The local clinic is specially important for the diagnosis of chronic and insidious disorders, since a mother will often consent to bring her child there when she would hesitate to take him, perhaps some distance, to the central hospital. Physiotherapy at the clinics takes the form of simple remedial exercises; more elaborate physiotherapy must be undertaken at the central hospital, where such things as warm swimming-baths and other modern equipment must be provided. This hospital should be placed, if possible, in or near a university town with a teaching hospital. The senior staff in the orthopædic and accident units will also be on the staff of the orthopædic hospital. Most of their out-patient work will then come to the teaching hospital, while the orthopædic hospital will be almost entirely inpatient. Hospital workshops will enable the orthopædic hospital to supply all the splints, boots, and appliances needed in the region, and will also offer training and employment for some disabled boys and men. Vocational guidance and training during treatment can be so effective, he finds, that the vast majority of patients can go into full employment at normal rates of pay in skilled trades, even though they are badly disabled.

Mr. Girdlestone ends his little treatise with a plan for an orthopædic hospital and some practical notes on its equipment. All he says is telling and instructive, but some will feel the heart of his message is concerned with other things than buildings and tools: "This care," he says, "is indeed needed day by day, or week by week, and often year after year. . . . Only explanation and the maintenance of an obvious and lively interest by surgeon and aftercare sister all through active treatment, and far into the final stages of convalescence, can assure success. . . ."

1. *Minerva med.* 1948, **39**, 432.

LOUDSPEAKER UNDER THE PILLOW

A NEW small extension loudspeaker suitable for placing under the pillow has been introduced by Messrs. Philips Electrical Ltd., under the name 'Pillotone.' This comprises a bimorph crystal drive unit mounted flexibly in a plastic case, about 4 in. in diameter and 1 in. thick at the centre. The advantages claimed for such a unit are that it provides more comfortable listening than earphones, and, unlike the ordinary loudspeaker, does not impose noise on those who do not wish to listen.

University of Cambridge

On Oct. 30 the following degrees were conferred:

M.D.—R. A. D. Crawford,* J. N. Milnes, J. S. Heller, P. D. Samman.

* By proxy

University of Aberdeen

On Oct. 27 the degree of M.D. was conferred on H. McL. Raffan.

Royal College of Physicians of Edinburgh

At a meeting of the college held on Nov. 2, with Dr. W. D. D. Small, the president, in the chair, the following were elected to the followship:—

G. A. H. Gumley (Dunfermline), S. Thiambiah (Vepery, Madras), Ernest Bulmer (Birmingham), J. D. Ross (Kingskettle), A. W. Branwood (Edinburgh), H. J. S. Matthew (Edinburgh).

The diploma of membership was conferred upon the following:—

L. M. Comissiong, E. G. L. Mark, G. A. Rail, T. G. Wilson, H. C. Falcke, Israel Kessel, W. R. Lang, C. C. Foote, Solly Lopis, W. A. B. Campbell, J. W. Nelson, M. S. Fraser, A. F. J. Maloney, E. N. Moyes, Joan E. Spicer, J. D. T. Steele, J. C. Mehta, A. T. Macqueen, W. N. M. Lyon, P. B. Fox, J. S. Robson, Mary K. MacDonald, J. A. Loraine, Wickramaratchyge A. Karunaratne.

The Hill Pattison-Struthers bursary in clinical medicine was awarded to Dr. David Bull.

Royal Faculty of Physicians and Surgeons of Glasgow

At the annual meeting of the faculty on Nov. 1, the following office-bearers were elected: president, Dr. W. R. Snodgrass; visitor, Mr. W. W. Galbraith; treasurer, Mr. Matthew White; librarian, Dr. A. L. Goodall; representative on the General Medical Council, Mr. Andrew Allison; other councillors, Dr. Stanley Alstead, Dr. Thomas Anderson; Dr. G. B. Fleming, Dr. J. Gibson Graham, Dr. D. McKay Hart, Mr. A. B. Kerr, Mr. T. Murray Newton, Dr. E. G. Oastler, Dr. Charles Read, Mr. G. H. Stevenson, and Dr. G. M. Wishart.

Guild of St. Luke, SS. Cosmas and Damian

The following officers have been elected for the forthcoming year: Master, Dr. W. B J. Pemberton; secretary, Dr. W. J. O'Donovan; treasurer, Dr. Patrick Corridan.

University College, London

On Wednesdays, Dec. 1 and 8, at 5.15 P.M., in the physiology theatre of the college, Gower Street, W.C.1, Dr. J. W. Trevan, F.R.S., will lecture on Statistics from the Standpoint of a Pharmacologist.

Ling Physical Education Association

The association is holding a conference from Dec. 29 to Jan. 1 at Chelsea Polytechnic, Manresa Road, London, S.W.3, on health education in schools. The speakers will include Dr. Dora Cadman, Dr. J. L. Dunlop, Dr. Robert Sutherland, and Dr. Marjorie Wilson.

Empire Rheumatism Council

A weekend course will be held by the council at the Apothecaries' Hall, Black Friars Lane, London, E.C.4, on Nov. 26, 27, and 28. Further particulars may be had from the secretary of the council, Tavistock House (N), Tavistock Square, W.C.1.

Owing to unforeseen circumstances Dr. Pedro Belou will be unable to give his lectures at the Royal College of Surgeons on Nov. 12 and 17 and at the Royal Society of Medicine on Nov. 15.

Mr. J. Burke Ewing, surgeon to the Wigan Infirmary, has been appointed professor of clinical surgery at Ottawa University and surgeon-in-chief to the Ottawa General Hospital. Mr. Ewing is a graduate of Queen's University, Ontario.

Flight-Lieutenant Alexander Mather, M.B., R.A.F.V.R., has been appointed M.B.E. for distinguished service in Palestine.

The insignia of the fourth class of the Brilliant Star of Zanzibar has been conferred by the Sultan on Dr. C. E. Roberts, O.B.E., specialist officer in the health department of Zanzibar.

Appointments

ABELES, F. M., M.D. Frankfurt, F.F.R., D.M.R.: radiologist, West Middlesex Hospital, Isleworth.
BIRNIE, C. R., M.D. Lond., M.R.C.P., D.P.M.: physician superintendent, St. Bernard's Hospital, Southall, Middlesex.
CARSON, M. B., M.B. Lond.: surgical registrar, M.R.C. burns unit, Birmingham Accident Hospital and Rehabilitation Centre.
EDWARDS, T. A. W., B.A., M.B. Camb., M.R.C.P.: physician, Clare Hall Hospital, South Mimms, Herts.
LESSLIE, JANE, M.A., M.B. St. And., D.P.H.: senior asst. M.O., maternity and child welfare, Wolverhampton.
PARKIN, THOMAS, M.B. Edin., M.R.C.P.E.: registrar, department of dermatology, Royal Sheffield Infirmary and Hospital.
SWINNEY, JOHN, M.C. Durh., F.R.C.S.: surgeon i.c. urological department, Newcastle General Hospital.

Births, Marriages, and Deaths

BIRTHS

BELL.—On Oct. 30, at Claygate, the wife of Mr. A. C. Bell, F.R.C.S.—a son.
BENNETT.—On Oct. 29, the wife of Dr. N. O. Bennett—a daughter.
DORNHORST.—On Nov. 3, the wife of Dr. A. C. Dornhorst—a daughter.
HARLAND.—On Nov. 3, at Kachhwa, India, to Dr. Grace Harland, the wife of the Rev. R. P. Harland—a son.
HUMPHREY.—On Oct. 31, the wife of Dr. Leslie Humphrey—a daughter.
KAULA.—On Oct. 27, the wife of Dr. Charles Kaula—a son.
LASK.—On Nov. 3, at Ascot, the wife of Dr. J. P. Lask—a daughter.
PATON.—On Nov. 2, in London, the wife of Dr. Ian Paton—a son.
ROSE.—On Nov. 5, at Bushey Heath, to Dr. Muriel Rose, the wife of Mr. Frederic Campbell Rose—a son.
SMITH.—On Oct. 31, at Wiggington, near Banbury, the wife of Dr. T. H. S. Smith—a son.
STEPHENS.—On Nov. 3, in London, the wife of Dr. F. D. Stephens, D.S.O.—a daughter.
TAYLOR.—On Oct. 30, at Woking, the wife of Mr. Lionel Taylor, F.R.C.S.—a daughter.

MARRIAGES

BARLAS—COUTANCHE.—On Oct. 30, at Hildenborough, Kent, John Alexander Barlas, M.B., to Pamela Honor Coutanche.
CAHILL—SHERRY.—On Oct. 9, at Esh Laude, Durham, John Cahill, M.R.C.S., to Kathleen Sherry.
PILCHER—SMEDLEY.—On Oct. 30, at Crich, Derbyshire, Richard Pilcher, M.C., M.R.C.S., to Elizabeth Margaret Smedley.

DEATHS

HEALEY.—On Nov. 4, at Lower Hellesdon, Norwich, Frederick Henry Healey, M.D., B.SC. Birm., D.P.M.
HELLIWELL.—On Nov. 7, John Percival Helliwell, C.B.E., M.R.C.S., L.D.S. R.C.S., major-general, retd. aged 64.

Diary of the Week

NOV. 14 TO 20

Monday, 15th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Prof. Robert Platt: Ætiology and Surgical Treatment of Hypertension. (Part I.)
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. A. Schweitzer: Reflex Control of Blood-pressure and Heart-rate.
5 P.M. Dr. B. D. Pullinger: Cell Multiplication in Adult Tissues.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS, 58, Queen Anne Street, W.1
NOON. Prof. A. M. Claye: Use of Analgesic Drugs in Labour.
5. P.M. Mr. H. H. Evers: Postmenopausal Hæmorrhage.
HUNTERIAN SOCIETY
8.30 P.M. (Apothecaries' Hall, Black Friars Lane, E.C.4.) Dr. W. J. O'Donovan, Miss Arnot Robertson, Dr. Charles Hill, Miss Bronwen Lloyd-Williams: That the Practice of Instructing the Layman in the Nature and Treatment of Disease is being Carried to Excess.

Tuesday, 16th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Professor Platt: Ætiology and Surgical Treatment of Hypertension. (Part II.)
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. Schweitzer: Measurement of Cardiac Output and Factors Influencing It.
5 P.M. Dr. Pullinger: Cell Multiplication in Adult Tissues.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Prof. H. J. D. Smythe: Induction of Labour.
5 P.M. Dr. E. Rohan Williams: X-ray Pelvimetry.
UNIVERSITY OF LONDON
5 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Dr. Charles Swan: Rubella in Pregnancy as an Ætiological Factor in Congenital Malformations and Stillbirth.
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

Wednesday, 17th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. D. H. Brinton: Intracranial Aneurysm. (Part I.)
ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Geoffrey Keynes: Portraiture of William Harvey.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Prof. R. A. Lennie: Obstetric Operations in Difficult Labour.
5 P.M. Dr. J. E. Morison: Establishment of Extra-uterine Respiration.
HARVEIAN SOCIETY OF LONDON
8.15 P.M. (26, Portland Place, W.1.) Prof. Ian Aird: Value of a Tumour Clinic in a General Hospital.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. C. W. McKenny: X-ray Technique.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
Dr. P. G. H. Gell: Food and Resistance to Disease.

Thursday, 18th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Robert Coope: Tuberculous Enlargement of Intrathoracic Lymph-nodes, and its Aftermath. (Mitchell).
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. Henry Barcroft: Blood-flow in the Limbs.
5 P.M. Dr. C. Keith Simpson: Blunt Head Injury.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Mr. J. E. Stacey: Obstetrical Damage and Repair.
5 P.M. Mr. S. G. Clayton: Endometriosis.
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
5 P.M. Mr. J. Johnston Abraham: Victorian Doctor.
HONYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Prof. W. C. Wilson: Blood-volume in Surgical Disorders.
BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. F. Gardner: Angiocardiography as an Aid to Diagnosis of Cardiac Abnormalities. Dr. J. M. Weston Wells: Cardiac Anatomy as Demonstrated by Angiocardiography.

Friday, 19th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. E. B. Strauss: Affective Psychoses, including Cyclophrenia.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Professor Barcroft: Blood-flow in the Limbs.
5 P.M. Dr. Keith Simpson: Death from Vagal Inhibition.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Dr. A. G. Wrigley: Dysmenorrhœa.
5 P.M. Dr. A. W. Spain: Symphysiotomy.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
4.30 P.M. Mr. Walter Howarth: The End of an Era.
FACULTY OF RADIOLOGISTS
2.15 P.M. *Diagnosis Section.* (Royal College of Surgeons.) Dr. T. H. Hills: Angiocardiography in Congenital Heart Disease.
BRITISH TUBERCULOSIS ASSOCIATION
3.30 P.M. (Royal Empire Society, Northumberland Avenue, W.C.2.) Dr. Percy Stocks: Tuberculosis—Some Statistical Problems. Prof. B. W. Windeyer: Radiosensitive Thoracic Tumours.
LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. J. R. B. Hern: Asthma.
ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh
8 P.M. Sir Francis Fraser: Medicine in the New Social Order.

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CONTENTS

PARENTHOOD AND SOCIAL CHANGE*

RICHARD M. TITMUSS

I

IT is precisely one hundred and fifty years since Malthus published the first edition of his *Essay on the Principle of Population.*[7] There was nothing particularly original in his hypothesis concerning the relationship of people to food resources; his most important argument, as he took pains to state, had already been expounded in part by Hume and Adam Smith and by other writers in the past. His place in history is due, not to originality, but to the fact that he was the first to elaborate and document the argument, and the first to have any real influence on public opinion.

Malthus addressed himself to philosophers like Godwin and Condorcet who believed that poverty and disease were eradicable nuisances. He did so in an age—not so dissimilar after all from the present century—when the air of Europe was heavy with a sense of wrong, when custom, with its magic that takes the sting out of injustice, was in retreat, and when the future of man appeared to depend on (in Malthus's words) "that tremendous phenomenon the French revolution, which, like a blazing comet, seems destined either to inspire with fresh life and vigour, or to scorch up and destroy the shrinking inhabitants of the earth."

Malthus, in 1798, saw one great obstacle to an improvement in the condition of society. Beginning with two simple postulates, which he came to regard as immutable laws, "that food is necessary to the existence of man," and "that the passion between the sexes is necessary, and will remain nearly in its present state," he arrived at the following thesis: that population is necessarily limited by the means of subsistence, and that population always increases when the means of subsistence increase unless it is prevented by such checks as famine, war, plague, or moral restraint. In short, the theory was that the fecundity of humanity was sufficient, if unchecked, at least to double the population every twenty-five years, and that an increase in food-supplies could not possibly keep pace with such an increase in the number of people to be fed.

This pessimistic doctrine, and the fears of economists like Ricardo who had been profoundly moved by the brooding menace of overpopulation and famine, were not borne out in the Western world. The first reply to Malthus came in dramatic fashion. In 1825 Parliament passed a Bill enabling locomotives to be used on the Stockton and Darlington railway, and two years later the first steamboat crossed the Atlantic. The development of steam transport by land and sea opened up the granaries of the New World, and allowed the means of subsistence to increase much more rapidly than the increase of population in Britain. Yet the rate of population growth was phenomenal; in England and Wales numbers doubled between 1801 and 1851—from 9 to 18 million—despite the filth, the cholera, and the "low and grovelling mode of living" which accompanied the unrestricted growth of an industrial society.

Godwin had pointed out that the answer to the problem of more food lay in calling in the resources of the new world. "Three-fourths of the habitable globe is now uncultivated. The parts already cultivated are capable of immeasurable improvement."[4] Malthus scorned these possibilities, and rejected the idea that Godwin's "beautiful system of equality" could be realised from the products of the plains of the new world. He refused to believe because he did not wish to believe. He was intent on controverting the idea that social justice was either possible or desirable, and he was successful in proving his case to the satisfaction of the great majority of the governing and middle classes. His teaching fell upon willing pupils; it was delivered at a receptive moment in history; it was the response to the challenge of the new philosophies.

Fifty years later it was not the answer to the revolutionary ferment of 1848. The idea that human fecundity would outrun food-supplies had withered away. But, in England at least, it long exercised a powerful influence on economic and political thought. From this doctrine the inference was drawn that charity and social services were futile, tending only to increase the numbers of destitute by increasing births and postponing deaths. One practical effect of the diffusion of this belief was to assist the movement for repressive administration of the poor-law, and to prepare the way for one of the harshest Acts ever placed on the statute-book—the Poor Law Amendment Act of 1834. This Act, which inaugurated the famous doctrine of less eligibility, a theory that throughout the 19th and into the 20th century controlled the approach of English Government to the relief of destitution, "announced to the World," said Disraeli, "that in England poverty is now a crime."[9] It did more than that, according to a Conservative candidate at Bradford who denounced it as a Bill which "separates those whom God had joined together."[5]

In applying a penal discipline, the new poor-law broke up the family, assigning its members to different parts of institutions, it separated husbands from their wives and mothers from their children, and implicitly condemned procreation. Although it was vigorously attacked by John Walter of the *Times*, by Thomas Wakley of the *Lancet*, and by a large body of opinion in the country, the influence of Malthus was dominant and the Bill became law. If poverty was a personal and public crime, then the failure to save was likewise evidence of wrong. As children increasingly became a financial burden instead of a financial advantage, it was only a short step from this precept to the realisation that smaller families were not only socially respectable but were the means of avoiding poverty.

This is only a fragment of the story of the fate of the family under the impact of the industrial system; a system which led in the course of time to the disappearance of the family as the main unit of economic production, to a transformation in the protective and educative functions of the family, and, ultimately, to the liberation of marriage from the authority of childbearing. The Malthusian doctrines cannot be held responsible for these changes; many social, economic, and psychological forces were combining in the 19th century to elevate the individual and modify the characteristics of parenthood. The reasons for the emergence of the small-family habit have to be sought in the nature of the civilisation and culture which accompanied the growth of modern industrial society. But these doctrines did shape the form and they did influence the administration of the first, and in longevity the greatest, of England's social services for the relief of distress. Therein lies their particular relevance to the argument of this paper, for we see that the first intellectual approach in Britain to the problems of population policy had consequences which were detrimental to the family. Basically, these consequences sprang from a fear of overpopulation; from too many, rather than too few, births.

II

The past hundred years have witnessed a profound change in the problems affecting parenthood and family

* From the Lloyd Roberts lecture for 1948 delivered at Manchester on Oct. 28.

life. Children are no longer the inevitable accompaniment to marriage. This check to population growth—a check which has banished a vast amount of distress and which represents one of the major blessings of the 20th century—has followed from the collective decisions of men and women to limit the size of their families. Stimulated by neo-Malthusian propaganda, aided and abetted by an emulative culture born of economic individualism, strengthened by the emancipation of women from the 19th century authority of men, and impelled by the growth of a new sense of values in which the material has been dominant, the practice of birth control has found favour among an increasing number of married couples. This voluntary process, this apparently rational act based on a host of often irrational hopes and fears, has led for seventy years in one direction only—in the direction of smaller families. Between the 1870s and the outbreak of war in 1939 the birth-rate for England and Wales fell by nearly 60%. The average number of children born to married women which, in the 19th century, was over five, with many mothers bearing ten or more, had fallen by the 1930s to about two.

In 1923 the net reproduction-rate—an index which shows the number of potentially fertile women who, in the succeeding generation, will replace a woman now passing through the fertile period—fell for England and Wales below the point necessary for replacing the population. It continued to be insufficient for twenty-three years until 1946, the first year to gather in the post-war babies of the second world war. Expressed more simply the change appears more striking. Thus, $4^1/_4$ million women aged fifteen to forty-five in the 1850s produced more babies each year than 10 million women of similar age during the 1930s. This has had far-reaching effects on living standards, for it is probably true to say that the rise in the approved cost of living for children at most income levels has been much greater than that for adults and higher still than the rise in real wages. Nevertheless, these are effects which from time to time we forget. When we congratulate medicine, ourselves, and the Government on the good health of our children during the recent war, we do well to remember that the country had 2 million fewer of them (a number larger than the total child population of Australia) to feed, clothe, and house in 1939 than in 1914. Had this not been so we might all have been desperately short of milk.

Three observations can be made about this change in the reproductive habits of the British people. First, the strength and consistency of the trend towards the smaller family, regardless of prosperity or slump, war or peace, and seemingly unaffected throughout this period by the rise of the modern social service State. Secondly, the speed at which this revolution in attitudes to childbearing has been accomplished. Thirdly—and what is important to the theme of this paper—the fact that these changes have taken place without producing any demand insistent enough to influence social policy in favour of counter-measures. Nothing resembling in power the effects of the Malthusian doctrine in moulding opinion and legislative action can be discerned among all the forces which have determined social values and guided national policies during the last seventy years. On the contrary, in many respects the social environment, reflecting and informing the conscious and unconscious motives that underlie thought and behaviour, has become increasingly inimical to the family. We may well ask why the fear of too many people is so much more powerful than the fear of the consequences of a population declining in numbers, ageing in composition, and disinclined to replace itself.

Many decades passed before much notice was taken in this country of the possible effects of a declining birth-rate. And when they did begin to attract discussion the essential problems of family life were obscured by other issues. An insular preoccupation with questions of the different birth-rates of different social groups, their levels of intelligence, and their inherited qualities, came naturally to a country with a strong caste system steeped in traditional values and accustomed to assessing social merit by social position. This preoccupation confused the problem. It did so by suggesting that assistance to the family—for instance in the form of child allowances—would encourage the breeding of the unfit. No such concern about the differential birth-rate arose in Australia, New Zealand, the United States, or in Sweden and other countries faced with similar questions of a declining birth-rate.

Attention was thus diverted in this country away from the fundamental problems to associated, but subsidiary, questions about the reproductive habits and social worth of two relatively small groups in society. Concern about the 10% at rest at the foot of the contemporary scale of economic and cultural values and —by contrast—about the 10% poised at the top, distracted attention from the 80% who determine the future of the birth-rate and the quality of family life. In this controversy, at all events, the ends have dominated the mean.

Other events during the past thirty years have likewise prevented us from thinking clearly and asking the right questions. We have continually shifted our gaze at the bidding of recurring national crises. The first signs of concern about the birth-rate during 1914–18, which arose as a result of war losses and a man-power shortage, soon evaporated in the immediate post-war years. Some half a million extra babies in two to three years were sufficient to make many people think that they had been mistaken about the population trend. They led the late Lord Keynes, for instance, to suggest in 1922 that the devil of Malthus had once again been unchained, and they contributed to the planning of grandiose schemes for moving millions of British people to the Dominions.

These schemes soon foundered on the rocks of unemployment and economic depression. The Australians, whatever they may think now, only wanted immigrants when trade was good and not when it was bad. And as unemployment rose and the depression deepened, it became increasingly unrealistic in Britain to talk about too few babies. Such talk did not make sense to the man in the street when the allowance for the children of the unemployed was less than 2*d.* a day.

The population question certainly attracted more attention from economists and social scientists during the 1930s than at any time since the beginning of the 19th century. Nevertheless the debate made little impression on the public mind. The individual—in contrast to the family—continued to dominate the values and the morality of the period. The social problem of this period, the problem of mass unemployment, was seen as a problem of the economically dispossessed individual, and not as a crisis in the lives of families. And with the growth of autocracy in Europe, all controversy centred round two governing poles of interest —the State and the individual. For these and other reasons, many deeply rooted in the history of political philosophies, the trade unions and the Labour Party in Britain took no interest in the problems of population. The demand for child allowances, led by independent radicals like Eleanor Rathbone, increasingly acquired the character of a plea for the relief of distress.

It was against this background that a Royal Commission on Population was unexpectedly appointed by the Coalition Government in 1944. Few Royal Commissions can have come to life with so little public stimulus, and few can have found themselves, after the

lapse of over four years, with so many social and economic problems which were not envisaged when they were born.

Throughout this period of fifteen years, during which the birth-rate theoretically constituted an important national question, the status of the family did not improve. The accent in social policy did not shift in its favour. In the hierarchy of values displayed by society parenthood continued to give place in choice and esteem to other goals, other pursuits, and alternative modes of living.

Some of these generalisations must now be supported with facts and figures. I wish, in particular, to direct attention to certain economic matters which illustrate the broad trend of public opinion and policy during the last decade or so. Although these examples relate to material standards their real importance lies in the light they throw on contemporary attitudes to the family.

III

First, there is the central fact that the industrial system of reward for labour, which pays no regard to family responsibilities, continues to command approval. Repeatedly, during the inter-war years, one after another social survey, in York, in Bristol, in Birmingham, and in many other cities, was forced to draw attention to the consequences of this system. Children were shown to be the primary cause of poverty, and few families, at most income levels, escaped relative degrees of hardship in some shape or form. In any economic group, the level of living of a family is seen in relation to other families in the same group, and equality is lost when children are born. For most people, the level of living today is more dependent on size of family than on income. The introduction of family allowances for all but the first child has done something to alleviate this disability. So, too, has the great extension in the provision of milk and meals at school. It needs to be remembered, however, that the child allowance has not the value it had when the demand for 5*s*. a week developed thirty years ago. In terms of the price level of the 1930s it is doubtful whether the allowance is, today, worth much more than about 2*s*. a week, less income-tax. It is significant that all the pressure for more money during the last few years to meet the rising cost of living has concentrated exclusively on wage-rates and salary scales. It is tacitly assumed that the controversy about children and poverty is at an end; the gesture has been made, the 5*s*. granted.

How widespread and unquestioned is this assumption can be judged by the reception given to the Government's change of policy in 1945 concerning the pay and allowances for officers and men of the Armed Forces. All the tax-free allowances and special grants for children and other dependants which, by 1945, had reached standards generally appropriate to a wide diversity of family circumstances in comparison with those ruling in 1939, were swept away.† In their stead, the industrial system of reward was adopted. "The Government," it was said, "regard the present system as unsatisfactory in that the resulting family allowances, particularly in the case of large families, constitutes an unduly large proportion of the emoluments of the married man, by comparison with the pay of the batchelor." "The new arrangement will avoid the present disparities between one married man and another of the same rank."[11] A study of the results of the change in pay suggests that all Servicemen (officers and other ranks) with two or more children experienced a reduction in income after allowance is made for the improvements in basic pay, and the addition of the allowance of 5*s*. a week for second and subsequent children. Those who gained, and gained substantially in comparison with their fellows, were bachelors and married men without children. Childlessness was rewarded, and disapproval was shown to those with more than two children. The system now works as an economic device for discouraging parenthood among the fit.

There may well be strong reasons for adjusting Service pay to industrial conditions; it is so much simpler to ignore the family, the complications of dependency, the immense variety of circumstances, the economic crises which beset most families on the occasion of birth, illness, and death. The primary object, however, of this incursion into the question of Service pay is to make certain observations on the theme of parenthood. While on the one hand, we still shower respect on the family, with, as Alva Myrdal has said, "a whole system of verbal generalities, taboos and moralities,"[10] we continue, on the other hand, to act as though it was not in need of constant reinforcement. The anthropologists tell us that "the persistence of customs depends upon their rewarding value."[3] They are neither self-perpetuating nor self-destroying; they are not arbitrarily accepted or rejected; rather, they are habits strengthened by social rewards or weakened by a lack of them. What, in fact, is remarkable about this particular story of Service pay is the entire absence of public protest about a policy detrimental to family life.

IV

A second example of the trend of public policy in running against the interests of the family relates to the problem of income-tax and the cost of living. The Oxford Institute of Statistics recently estimated that the weekly cost of Seebohm Rowntree's "human needs" diet for a family of five persons was 83% higher in March, 1948, than at the end of 1936.‡ For families on a less austere standard the increase is probably greater. Nevertheless, it must be noted that the income-tax allowances for a child (£60) and for a married couple (£180) are precisely the same today as they were before the war. On the other hand, the allowance for a single person has risen from £100 to £110. Greater disparities in the incidence of taxation between those with and without children have been created by the rise in the allowance on the earned income of married women. The maximum has grown from £45 in 1938 to £110 in 1948 plus reduced rate relief.

The effect of these changes can be shown quite simply. On a total earned income of £500 a year, the married man with a wife at home and two children now pays £22 in tax, or nearly as much as the childless married couple who are both working, whose tax (if the wife earns £3 a week) is £25. If we take instead an income of £1000, the man with a wife and two children pays £180 against £184 for the childless couple who are both working. And if the wife earns £8 a week instead of £3 the tax falls to £145. The man with £1000 a year and three children is now paying £30 more tax than before the war, whereas the working couple without any children are paying less. This man with a wife and three children to keep pays only £112 a year less tax than the single man or woman earning the same amount. These four dependants are thus allowed only about 11*s*. a week a head, or in terms of pre-war purchasing power about 6*s*.

These illustrations relate, of course, to middle-class families. The economic struggle today of those below the taxable line to maintain two or more children on an income of less than £7 a week must be very hard. The estimated rise since before 1939 of about 80% in

† In 1939 the allowances for children of men in the ranks ranged from 2*s*. to 4*s*. a week; by the end of the war the allowance was 12*s*. 6*d*. a week, tax-free, for each child.

‡ See *Bulletin* of the institute, May, 1948. This broadly agrees with the estimate by Prof. R. G. D. Allen that the price rise for food, clothing, rent, fuel and light, and other items was about 60–65% for the period 1938 to mid-1947. *Bulletin* of the London and Cambridge Economic Service, 1947, no. 111.

their cost of living may indeed understate the real change, for these families can no longer buy the cheap alternatives, the secondhand clothes, and the cut-price articles. Rationing, by standardising price and quality and by largely abolishing the cheaper substitutes, has in one sense worked against those who have need to count every penny every week.

Does it not seem, in face of all this, that the causes of inflation in recent years—of too much money pursuing too few goods—have been misunderstood? Is it not possible that the demands for luxury and semi-luxury goods and services—for holidays abroad, for beer, cigarettes, cinema seats, wireless sets, and so on—have largely come, at all income levels, from single people and married couples without children or without dependent children? If this is so, and if the different circumstances of those with and without dependent children have not been appreciated because the economists have forgotten the family, then it follows that measures taken to counter inflation will penalise parenthood at all income levels, and will not effectively remove purchasing power. Food subsidies, said the *Economist* without distinguishing between these differently placed groups, "are the main source of the colossal sums spent by working people on beer and tobacco." [2]

V

The situation today can now be more easily misunderstood because of the introduction in June, 1947, of a new cost-of-living index based on expenditure by an "average" working-class family or household containing only one child under 14 years of age.[6] This index was constructed on the Ministry of Labour's cost-of-living inquiry in 1937–38 relating to average expenditure by a family of $3^3/_4$ persons of whom $1^3/_4$ earned wage or salary. It was an elderly family, and one which, in biological terms, was not replacing itself. It was a family which, out of its weekly expenditure of £4 6*s*. 3d. spent not much more than one-third on food. Nearly as much was spent on tobacco, drink, entertainment, newspapers, household equipment, and other miscellaneous items. The whole budget reflected adult patterns of spending and social habits.

This new index, now to govern many plans and policies on economic matters, wage and price levels, replaced an index modelled on working-class budgets collected in 1904.[1] In most respects this index was out of date, but it had the grace and reality to give prominence to the costs of children. It related to an average family of 5·6 persons, of whom 3·6 were under fourteen years old.

The sociologist will observe that while the first inquiry approached the problem of the cost of living in terms of the family, the second, although using scientific method such as random sampling and taking advice from expert economists and statisticians, was based on the concept of the average household—a concept which has not been defined and is largely an economic abstraction. This change, adopted, it seems, without conscious thought, is of fundamental importance.

The detail of these indices differs in the following ways. Of total expenditure, the old index gave a proportionate weight of 72% to food and clothing. The new index gives only 44%. Children's clothing and footwear accounts for only one-fifth of all clothing expenditure in the new index. It is astonishing to find that the "average" working-class family of today is expected to spend more on its weekly butter ration of 3 oz. a head than on children's clothing and footwear, and twice as much on wines and spirits (excluding beer) as on children's shoes. This is, indeed, a remarkable British working-class family.

In terms of economic policy, the inference to be drawn from all this is reasonably clear. Price controls, for example, can be removed, and the cost of children's clothing and footwear can soar to unparalleled heights, but the nation's cost-of-living index will remain unmoved and insensitive. Similarly, changes in the cost of food will now have much less effect on the index than formerly. Conversely, increases or decreases in the price of beer, cigarettes, cinema seats, and other miscellaneous items, will now exert a powerful influence. If food subsidies were cut, and simultaneously the tax on beer or cigarettes was appropriately reduced, the index might well remain at about the same point. The pressure for wage increases might thus be damped down, the individual worker—as an isolated individual—would not be much worse off; the single person or childless couple would be better off; but the family—the family with several children—would be heavily punished.

VI

It is not my purpose to discuss here the relationship between the cost of living, the level of wages and salaries, and the economics of home-making. It is a big problem, requiring much research, and I hope the Royal Commission on Population will provide us in its report with up-to-date information. For the truth is that, in comparison with the 1930s—the period of the Social Survey and the family budget inquiry—we know today very little about the reality of economic life as it affects the family. That, to me, is symptomatic of an all too prevalent contemporary attitude. We see around us evidence of inflation, of high expenditure on tobacco, entertainment, and so on, and we assume that all is well with economic standards. We do so, I suggest, because we are acquiring the habit of considering the nation as a collection of individuals and not of families.

We have not, in the attitudes we adopt and in the policies we sanction, deliberately set out to attack the family. We have not agreed that this institution—"a device well suited to its purpose through countless ages of trial and error" [14]—has failed. Some of the developments in our social and economic life are the result of acts of policy aimed at other objectives. We have manipulated the instrument of taxation, for instance, to induce more married women to work. Whether it has produced the desired result I do not know, but what I do suggest is that this policy has been pursued without conscious thought for the interests of the family. It need not have involved harming the family.

My purpose in discussing the problems of Service pay and the cost-of-living index was to give force and precision to the general argument of this paper. These examples show that the debate about the population question during the last fifteen years has made little impression on public policy. They demonstrate how some of the characteristic ideas of our age still revolve round the individual. And we note the absence of strong protesting voices. This must mean approval; at least unconscious approval by that section of the community who play such a large part in focusing and influencing public opinion. By contrast, the profound effects of the first intellectual approach to the population problem in the age of Malthus and his followers is striking.

I do not think that the relatively high birth-rate of the last few years—a rate which is now declining again—has been responsible for the lack of interest in the subject of population, or in the wider aspects of the situation of the family in modern society. While the trend of the birth-rate since about 1943 may have confused some people—as it did in the early 1920s—we must remember that this is not a trend in favour of larger families. By and large, it is the result of more and earlier marriages and the birth of more first and second children. The number of large and medium families has continued to decline. Between 1939 and 1945, for

instance, the number of fourth and subsequent births in Scotland fell by 18%.[12] I believe that the report of the Royal Commission on Population will record a continuing diminution in family size—particularly among working-class families—for the whole of Britain.

The population question for this country today is not one of deciding whether it would be better to have a larger or a smaller population. We can rule out the possibility of a future of expanding numbers. The choice lies between a population of about the present size, not too over-weighted with old people, or (in the words of the Royal Commission) "the ultimate threat of a gradual fading out of the British people."[13] Sir John Orr has spoken of the problem of world food resources and a world population continually growing in size. This country can be of no service to the world, and particularly the Eastern world, by allowing its population to enter a phase of decline, by growing steadily older, and by being less equipped for productive work. A few million less people in Britain will not solve the world food problem, but such a change could confront us with serious social and economic consequences. We should then be less able and less willing to make our contribution to the work of international coöperation. Nor will it help anyone to move a substantial section of our young people to Australia or elsewhere. We cannot solve the problem of not enough food by shifting people about the world, or by approving a process whereby the family slowly disintegrates for want of encouragement and the nation grows steadily older in years and in mental outlook.

Thus, the situation of the British people today is not similar to that which confronted Malthus one hundred and fifty years ago. The wheels of a revolutionary process which began to affect the institution of the family in the 19th century are still turning.

It is now time that we recognised in our social policies that the family is not what it used to be. Although it is smaller in size, its responsibilities and its anxieties are greater. "We now expect," said Margaret Mead, "a family to achieve alone what no society has ever expected an individual family to accomplish unaided."[8] We call upon it to be responsible for the personality development of children; for their socialisation and acculteration. We expect their nutritional needs to be met; it is no longer sufficient to simply provide them with enough food. We expect the working of their minds and their bodies to be understood today to a greater extent than at any time in the past. And we expect all this from an inexperienced family which has largely lost or has been deprived of the support and the security formerly bestowed by custom, by religion, and by community life.

In medicine, and in education too, the trend of thought today is looking away from egocentricity and towards sociality; towards considering the individual as a social being; to thinking of him as a member of a family, a group, living in a particular environment, and working in a particular setting. It is in this way that the family, still happily a tough institution, can be helped to discharge its heavy responsibilities. We require that this attitude should penetrate and inform all social policy. Already we have a part of the framework to hand. If the National Health Service, the Education Act, and the housing programme are consciously guided, administered, and inspired by this philosophy, family life will be strengthened, providing—and this is the core of the matter—there are no fundamental contradictions in social policy as a whole. I have attempted to show in this paper that the area of contradiction and conflict stretches over much of our social and economic policy, not because we do not care about the family but because we do not think about the family.

References at foot of next column

CLINICAL ASSESSMENT OF PERIPHERAL NERVE INJURIES

TINEL'S TEST

W. R. HENDERSON
M.B. Edin., F.R.C.S.
NEUROLOGICAL SURGEON, GENERAL INFIRMARY, LEEDS

THIS paper is concerned with two aspects of diagnosis in peripheral nerve injuries: (1) the value of Tinel's test, when it is interpreted according to his original description, which differs from present-day usage, in helping to decide whether to resect established lesions; and (2) the simplicity of routine quick exclusion of damage to nerve-trunks at any time after injury. It is based upon experiences in treating over 400 nerve injuries in prisoner-of-war hospitals in Germany during 1940–45 About 60 nerve sutures were performed. In some hospitals operations could not be done, for reasons outside British control, until after two years, and sometimes not at all; but in others there was no such hindrance. This enforced delay afforded an opportunity of studying all degrees of spontaneous recovery and of correlating it, and the appearance of the lesion at operation, with Tinel's test, the value of which was first appreciated in cases operated on at a late stage. Histological examinations could not be made. Detailed observations cannot be given, because the notes were lost in Germany.

Tinel's Test

After a nerve injury each axon that was damaged sufficiently to break its continuity degenerates distally, whether or not its individual sheath (endoneurium) was also broken. Axons sustaining milder trauma, without being broken, do not degenerate, though there may be temporary loss of function which, however, recovers quickly and completely within a few days or weeks (neurapraxia). The distal segments of broken axons undergo Wallerian degeneration, whereas the proximal ends regenerate and may re-establish peripheral connexions after a few months. This outgrowing of the proximal ends begins after a latent interval of perhaps two or three weeks, and those fibrils which are inside endoneural sheaths advance along the nerve at a rate of about 3 in. a month, whereas others that cannot find distal sheaths remain coiled up inside the neuroma.

The first few inches of the advancing young sensory axons are unmyelinated and sensitive to mechanical stimulation. Hence their position along the nerve can be detected clinically by percussion, which produces a tingling sensation referred to the cutaneous distribution of the nerve (and not to the region percussed). This tingling response disappears in a few months after the fibres, in the process of maturation, have become covered and insulated with myelin. This fact has long been used for demonstrating the presence of growing fibres and their rate of advance, either after suture or during spontaneous recovery, and it formed the basis of Tinel's

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test. It appears to have been generally assumed, after Tinel (1917) had described the test, that any response at all from the distal segment could be regarded as a good prognostic sign; but it was soon found that, though some cases with a (presumably strong) response subsequently had good functional recovery, others with a (presumably weak) response had none. The test consequently fell into disrepute and was neglected as being unreliable in prognosis, which it undoubtedly is when interpreted solely on the presence or absence of response from the distal segment alone (usually referred to as Tinel's sign), because it seems that very few stray fibres—too few for useful recovery—can produce tingling. But all regenerating sensory axons are sensitive, whether they are advancing along the nerve or are held up in the neuroma; hence the situation of most of the fibres can be determined by comparing the strength of the sensations induced by percussing the distal segment and the neuroma. If the test is interpreted in this manner it is believed to be more helpful than any other method of assessing the amount of regeneration that is taking place before motor or sensory recovery appears, and of determining the absence of satisfactory spontaneous regeneration. It was relied on almost entirely in deciding whether to operate (and resect) after about the fourth month, and it is believed that the test is sufficiently useful and important to warrant an account of its application which, as has been discovered, is similar to that described by Tinel.

PATHOLOGICAL TYPES OF FIBRE DAMAGE

The test is concerned only with regenerating sensory axons, and it is the damage to individual fibres and their sheaths that matters; the naked-eye lesion, whether complete division of the nerve or lesion-in-continuity, is unimportant. Three degrees of fibre damage may be recognised as regards its effect on recovery.

Type I.—Both the axon and its sheath are broken, and the sprouting axon is prevented by scar or wide separation from entering the distal segment of the nerve. All such axons coil about inside the neuroma and make it increasingly tender (as happens in amputation stumps).

Type II.—Both axon and sheath are broken, but the young fibre succeeds in entering a distal channel. The fibre may enter its own sheath if the ends remain together but, if they are displaced, as must usually happen, it is more likely to find another channel. Greater displacement or obstruction causes a further delay of weeks or months before the fibre finds a Schwann tube (or it may never do so as in type I); hence there is likely to be a continuous small stream of delayed fibres passing down the distal segment of the nerve for a long time after the first wave. This type of lesion, which probably occurs in its purest form after a good suture, inevitably leads to much axonal confusion and wastage through fibres entering wrong channels, and the degree of recovery is influenced by the similarity or diversity of functions subserved by the nerve (cf. radial and median). For clinical convenience each sprouting axon is referred to as a single fibre, though it actually divides into many thin branches or fibrils which may enter many sheaths; each sheath at first contains up to a dozen branches, probably from different fibres, but only one survives and matures (Young 1942).

Type III.—The fibre sheath remains intact, with the result that the broken axon regenerates inside it and must reach its own end-organ. If all fibres are thus affected (axonotmesis), functional recovery is complete.

As regards the nerve lesion as a whole, the types I, II, and III of individual fibre damage, followed respectively by no recovery, partial recovery, and complete recovery of nerve function, may occur alone or together, though a pure type II is hardly possible, because some axons inevitably remain stranded in the neuroma. In mixed lesions, therefore, some fibres may be permanently held up, others find channels of any kind after various delays, and the remainder regenerate quickly and correctly. Pure types I and III lesions can be distinguished clinically (groups I and IV below) by Tinel's test after three or four months, but mixed lesions show such well-marked variation in functional recovery that they have been subdivided into two clinical groups (groups II and III).

These three pathological types differ slightly from the classification (Seddon 1944) of nerve injuries into neurotmesis (which includes types I and II), axonotmesis (type III), and neurapraxia (in which there is no axonal degeneration, and, being of no importance in relation to Tinel's test and operation, is not considered here).

CLINICAL GROUPS

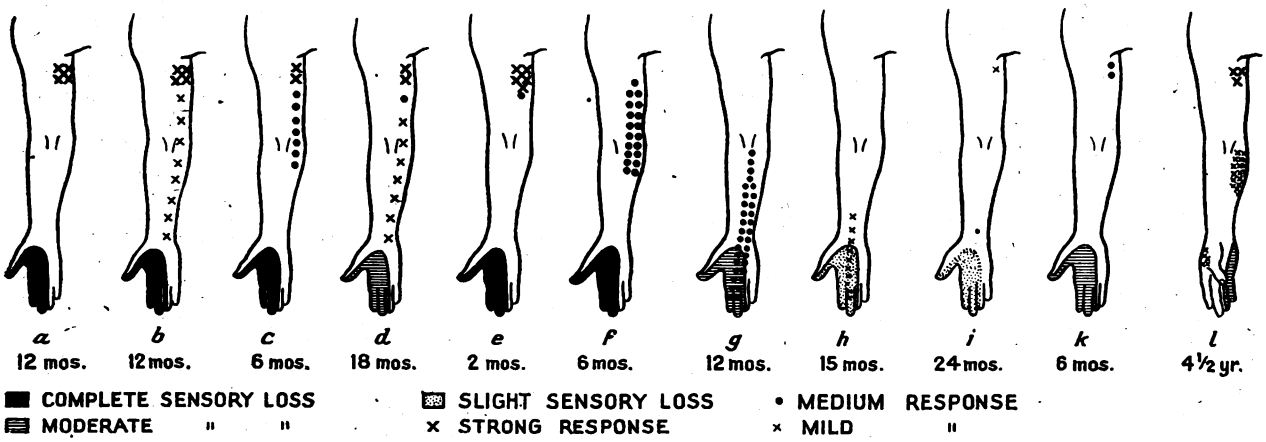
On the basis of Tinel's test, nerve injuries fall into four clinical groups. It is assumed in the following description that there has been sufficient time for fibres to grow at least several inches along the distal segment.

Group I: No Regeneration.—Tapping on the nerve lesion (pathological type I) produces tingling which is mild during the first few weeks and then becomes stronger when the sprouting axons are more exposed inside the neuroma. (The reverse of this is seen in the almost complete disappearance of response at the suture line immediately after resection of a tender neuroma.) In striking contrast, and of equal importance, is the absence of tingling on percussing the distal segment (fig. *a*). This response does not differentiate between complete division of the nerve and a complete lesion-in-continuity, nor does it matter; it shows that all fibres are held up at the lesion and it is an absolute indication for resection.

Group II: Negligible Regeneration.—In many severe (mixed) lesions, which to the naked eye resemble those in group I, a few stray fibres succeed in passing the obstruction in a lesion-in-continuity, or in bridging a gap of several inches. The sensation from the neuroma is virtually as strong as in group I, but tingling can also be obtained from the distal segment, though it is weak. Some fibres are therefore regenerating along the nerve, but the well-marked difference in the strength of the sensations shows they are few and insufficient for useful recovery (fig. *b*). There is never more than slight improvement of sensibility on the palm or sole, resulting mainly from the encroachment of fibres from neighbouring normal nerves, but none on the digits, and only rarely slight action in the proximal muscles, principally those of the tendo Achillis. The persistently strong neuroma response is a more important prognostic sign than is the weak tingling from the peripheral segment. This response also is an absolute indication for resection.

These cases might well be included in the next group, but they have been segregated to emphasise the fact that a weak nerve response, which is sometimes referred to as a false Tinel's sign, has no significance for recovery. It was, no doubt, this group that brought the test into disfavour. The importance of differentiating groups II and III was first appreciated in cases operated on at a late stage.

Group III: Partial Regeneration.—These intermediate cases show a wide range of partial recovery, varying from slight to good. All three types of fibre damage may be present (and perhaps also fibres undamaged or originally affected by neurapraxia). There is likely to be a preponderance of type III (axonotmesis) after a slight injury, whereas more severe lesions contain only types I and II, as after suture. The advancing wave may therefore be strong or weak, and long after it has reached the digits the nerve remains sensitive, showing that other fibres are continually leaving the



Tinel's test: *a* no regeneration; *b* negligible regeneration; *c* and *d*, stages during partial regeneration; *e*, *f*, *g*, *h*, stages during complete regeneration; *i*, almost complete regeneration; *k* partial lesion without regeneration; *l*, severe lesion with poor recovery, axonal confusion and sensory fibres ending in the long flexor and interossei muscles.

neuroma; these later fibres produce only slight further recovery of the more simple muscle actions or cutaneous sensibility (figs. *c* and *d*). There is less disproportion between the neuroma and nerve responses than in the other groups, which sometimes makes the test difficult to assess, especially when the lesion is deep. The decision whether or not to resect depends broadly on (1) the estimated proportion of fibres in the first wave—i.e., whether they represent the majority, half, or a minority of all fibres in the nerve—and (2) how much recovery, especially in distal functions, the surgeon thinks would take place after suture. If it is accepted that axonal confusion is, in general, less after a lesion in continuity than after suture, few cases in this group require operation.

Group IV: Complete Regeneration.—When all the fibre sheaths are intact, percussion of the dense wave of unmyelinated axon tips advancing simultaneously along the nerve produces as strong a sensation as the neuroma response does in groups I and II. There is a delay of one or two months before this advance is detectable, and then it progresses about 3 in. a month (figs. *e–h*). The sensation from the lesion is for a time similar to, but not stronger than, that from the nerve; next it becomes weaker and finally disappears within six months of injury, after the zone of response has passed completely into the distal segment (fig. *f*). This zone advances like a wave some 6–12 in. long, and behind it the nerve no longer responds to percussion. It is thus assumed that not more than 12 in. of a regenerating fibre, and possibly much less, is sensitive to mechanical stimulation before it is effectively insulated by myelin, though maturation is not necessarily yet complete. The advancing wave from an upper-arm lesion, for example, reaches the distal forearm before the long flexor muscles begin to contract; when it reaches the skin area, sensibility returns rapidly (fig. *g*), and recovery is well advanced as its tail disappears (fig. *h*). If recovery is not quite perfect, the tail of the wave may be lengthened by a few straggling fibres; and, after it has disappeared, slight tingling may persist from the neuroma, showing that a few fibres are permanently held up—this is reflected in slight residual sensory impairment, probably confined to the digits, and perhaps distal muscular weakness, though this is more difficult to detect (fig. *i*). In such cases a permanent fusiform thickening of the nerve can sometimes be palpated, or seen during late operation on neighbouring nerves.

COMMENTS

The *peripheral reference* of the tingling to the cutaneous distribution must be verified, especially when several injured nerves lie together, since it indicates which is responding—e.g., whether ulnar, median, or internal cutaneous in an upper-arm injury.

Transmission of stimulus is negligible, except sometimes through an extensive thick scar or from a percussed insensitive nerve to a nearby sensitive one—e.g., between median and ulnar in the forearm—but this is recognised from the peripheral reference of the tingling.

The *strength of response* is modified by the depth of the nerve and whether it lies on firm or soft structures. Stronger percussion or deep pressure is required in muscular regions, especially when a fracture has distorted the anatomy. Tendons covering the nerve should be relaxed as in the distal forearm; it is always difficult to obtain a response from the peroneal nerve behind the biceps tendon. The ulnar nerve should be percussed close to the dorsal border of the ulna and not on the anterior aspect of the forearm. Before percussion is repeated, tingling must be allowed to subside, which may take 10–15 sec.; and percussion should begin on the distal insensitive portion of the nerve. With experience it soon becomes possible to assess the strong disagreeable and the weaker not unpleasant sensations, and to estimate good or poor regeneration from examination of the peripheral segment alone when the lesion is inaccessible, as in the axilla. The test is generally easier in the upper extremity.

Interval after Injury.—Tinel's test has no value during the first two months. After that one quickly suspects which cases must have resection (groups I and II) and which are showing good spontaneous regeneration (group IV). This can be confirmed at the latest by three or four months when the lesion is superficial, and from four to six months when it is deep, because by then fibres held up in the neuroma have made it more sensitive, while those in the nerve have advanced several inches. Group III cases, in which the nerve tingling is not so strong, and that from the neuroma not so weak, as it should be for good recovery, may require another month or two for the wave to travel further and facilitate comparison of the responses.

The *rate of advance* could not be observed at sufficiently regular intervals for obtaining accurate data. It seemed, however, that, as others have stated, the initial latent period before axons begin advancing down their own intact sheaths is shorter, perhaps by several weeks, than when they must find new channels; but that, once they have started, there is little, if any, difference in the rate of advance. There is not sufficient difference in distances covered in a given time after injury to indicate the type of damage, more especially as the wave may be mixed. For this reason we assess Tinel's test entirely from the relative strengths of the sensations and not from the rate of advance nor, as already stated,

simply from the presence or absence of tingling from the distal segment.

Partial Lesions.—A third factor, in addition to the sensations from the lesion and the peripheral segment, must be taken into account—i.e., any cutaneous sensibility which remains after injury, because it represents undamaged fibres in a partial lesion and the greatest obtainable tingling is correspondingly less. When the residual sensibility is considered adequate, or not likely to be improved by operation, absence of regenerating fibres is not then an indication for operation (fig. *k*). The test cannot distinguish between a diffuse partial lesion and a clean partial division of the nerve.

The Significance of the Advancing Wave.—A strong advancing wave in group III, or after suture, does not, by itself, have the same good prognostic significance as in group IV, in which all the fibres are going to correct end-organs. In the latter all fibres are in the peripheral segment and the tingling is of maximal intensity, which it cannot be in group III, since some axons are held up. It is impossible to say from the strength of the tingling whether or not it is maximal; a strong wave merely indicates that many fibres are regenerating, without any clue about whether they are in right or wrong channels, for, before becoming myelinated, they appear to be sensitive in either. It is the persistence after a few months of some response from the lesion that shows the damage is not purely axonotmesis, if at all, thus making incomplete recovery a certainty, and its strength is a measure of the deficiency. A strong peripheral response merely proves that many fibres are growing distally, probably as many as there would be after suture; and there is always the possibility that some are in their own unbroken sheaths, which should not be sacrificed by resecting the lesion unless recovery is likely to be improved.

Multiple Lesions of One Nerve.—When a nerve-trunk is injured in several places, the test demonstrates, after sufficient interval, the situation of a complete block and of partial injuries proximal to it, but it does not exclude more distal injuries which might prevent recovery after resection of the complete lesion.

Brachial-plexus Injuries.—Many plexus injuries, mostly of the traction variety caused by parachute, were seen. A strong response was often obtained at the posterior border of sternomastoid muscle, which was assumed to indicate the site of the lesion. In some cases the response zone progressed downwards across the axilla and along the nerves in the arm, where the sensation was strong and was referred to the correct skin areas; unfortunately, the patients could not be kept long enough for distal function to return, but good recovery was already taking place in proximal muscles and sensation. In others there was no extension of response to the arm and no recovery. After a few severe injuries, percussion did not elicit tingling anywhere and there was no recovery (but the cases were not observed for longer than twelve months); the lesions may have been very high, near the intervertebral foramina and inaccessible to percussion, but the important prognostic sign is the absence of response above and below the clavicle. These observations are incomplete, but it is believed that Tinel's test can be of great value in assessing the prognosis of brachial-plexus injuries after a few months.

Axonal confusion can be demonstrated by Tinel's test after severe injuries. It was first noted about $1^1/_2$–2 years after upper-arm lesions with only slight spontaneous recovery. Weak tingling from the peripheral segment showed that a few axons were still growing distally, but it was considerably stronger in the proximal half of the forearm, where if should be weaker because of the overlying muscle, than elsewhere. This stronger sensation was obtained from a wide area corresponding to the bellies of the muscles supplied by the nerve, and was therefore regarded as evidence of sensory fibres having regenerated along motor channels into the muscle where they remained excitable. The same effect was observed after severe sciatic injuries.

A clearer demonstration was seen, for example, in a man with a severe unoperated lesion-in-continuity of the ulnar nerve near the axilla, $4^1/_2$ years after being wounded in May, 1940. There had been only a little spontaneous recovery, as shown by slight action of the flexor carpi ulnaris and flexor profundus muscles, much wasting and paralysis of the intrinsic muscles, a little poor-quality sensibility in the ulnar area, and a tender neuroma indicating a large hold up of fibres. Percussion along the nerve to the elbow and in the distal forearm elicited no sensation, but over the flexor carpi ulnaris muscle and on the dorsal interosseous spaces, especially the first, it produced considerable tingling referred always to the little finger (fig. *l*); this tingling disappeared during procaine block of the ulnar nerve at the elbow. It was concluded that the sensory fibres, including those in motor channels, had become myelinated, except their ends, which remained sensitive within the muscles.

This late response from the muscles can hardly be confused with a strong advancing wave preceding good recovery, because it appears some months later, is associated with signs of a severe lesion, and persists.

This observation seems to show that fibres in wrong channels do not atrophy in spite of failing to establish a functional connexion, important though that appears to be for full maturation (Sanders and Young 1945); neither do sensory fibres ending blindly in a neuroma atrophy. In rabbits the terminal ramifications of misdirected sensory axons have been demonstrated in the connective tissue between muscle-fibres at least twelve months after their arrival (Gutmann 1945), but it is not clear where the myelin ends.

Relationship between Sensory and Motor Recovery.—Since there is no method of demonstrating regenerating motor axons, it is necessary to consider the relative damage sustained by sensory and motor fibres and their recovery. Motor fibres are more vulnerable to injury than cutaneous sensory fibres and may be the only fibres affected (by axonotmesis which recovers completely), but injuries that tear the fibre sheaths seem to affect both kinds of fibres more or less equally. Therefore the end-result, whether good or bad, to be expected from spontaneous regeneration, as indicated by Tinel's test for sensory fibres, may also be inferred for the motor fibres; it is impossible to have an abundant correct regeneration of sensory fibres and none of motor fibres, or vice versa.

In conclusion, nerve recovery should be thought of not as the recovery of one nerve but of innumerable nerves within it. The aim in treatment is to obtain maximal regeneration of axons in the hope that as many as possible will reach correct or reasonably appropriate end-organs. It is believed that Tinel's test, which is a quantitative test, is the best available method of assessing the volume of down-growing axons. The decision about resection is easy when the test shows clearly either good or poor regeneration, but in borderline cases the surgeon's attitude will be influenced by which nerve is concerned and whether the lesion is high—i.e., above the proximal muscles, which are the only ones likely to recover—or low. The tendency should be towards conservatism, and even a minority of intact fibres should not be sacrificed, especially when sensation is important. Tinel's test entails waiting for several months after injury, which is often necessary for other reasons; and it will be interesting to learn, when the final follow-up results appear from the nerve-injury centres, what effect delayed suture, within a reasonable time, say, six months, has on recovery, especially of proximal as compared with distal muscles.

Quick Exclusion of Nerve Injuries

Excellent descriptions of the essential minimal examination for quick routine exclusion of damage to nerve-trunks are available (Russell and Harrington 1944). They rightly include an account of trick movements, but some are difficult to identify without careful examination, which may be prevented by an extensive wound, fracture, or covering plaster. Further, the possibility of abnormal innervation of intrinsic hand muscle or of damage to muscular branches may cause uncertainty. Cutaneous sensory fibres are on the whole less vulnerable to trauma than are motor fibres. Pain sensibility is therefore relied on for the three principal mixed nerves, because it gives a better indication of the minimum of serious damage than does muscular paralysis; also it is more easily tested in ill patients, in whom reflex movement of a limb in response to pain is more readily elicited than voluntary movement.

The main nerves to the limbs are concerned chiefly with sensation and movement of the digits, which are always affected as much or more than proximal functions. The integrity of the nerve-trunk can therefore be verified by examining the digits. Additional information that other muscles are paralysed is of no immediate importance; for, if there is an isolated muscle paralysis, it means damage either to the muscle or to its nerve branch, the repair of which is rarely practicable.

The tests recommended, no matter how trivial or how severe the wound or injury to the limb, are (1) if pinprick sensibility on the ends of the index and little fingers and the great toe is normal or nearly so (in comparison with the corresponding area on the opposite limb), there is no serious damage to the median, ulnar, and tibial nerves; and (2) extension of the thumb, metacarpophalangeal extension of the fingers (the chief function of the radial nerve is to open widely the hand), and extension of the great toe exclude damage to the radial and peroneal nerves, the sensory functions of which are unimportant.

These simple tests are not hindered by a properly applied limb plaster. They supply essential early information that the nerves are functioning either normally, partially, or not at all, which is valuable for others who may have to consider operation later. The last two groups require constant attention to the mobility of digital joints, repeated examinations at weekly intervals to exclude possible neurapraxia, and full neurological examination when conditions allow. Useful additional information may be obtained even when the limb is in plaster—e.g., the strength of the long muscles to the digits and of the intrinsic muscles.

The following tests must also be made at the first opportunity: (1) biceps action by *palpating* the muscle during elbow flexion—musculocutaneous paralysis is easily missed, since the elbow can still be flexed (similarly, with high sciatic lesions the hamstring tendons must be palpated, because the knee can be flexed by gracilis); (2) deltoid contraction to exclude injury to the upper brachial plexus or to the axillary nerve—damage to the lower roots would have shown in the digital examination—a partial brachial-plexus traction lesion (usually C5-6) may be present in addition to more obvious gunshot-wound nerve injuries; and (3) quadriceps femoris action in extending the knee.

SUMMARY

Attention is drawn to the great value of Tinel's test in assessing the amount of regeneration after about the fourth month following injury or suture, provided it is interpreted by comparing the sensations from the lesion and the distal segment. The occurrence of tingling from the distal segment alone is unreliable, because it may result from the presence of too few regenerating fibres for useful recovery.

The simplicity of routine quick exclusion of damage to nerve-trunks immediately after injury or later is emphasised.

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SAFETY OF INTRAPERITONEAL AND INTRATUBAL PENICILLIN

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Frisk and Westman,[1] investigating the absorption of penicillin instilled into the fallopian tubes, recovered 51% from the urine as against 61% of intramuscular penicillin. From the fallopian tubes and the pelvic peritoneum, however, penicillin was less rapidly absorbed than when it was injected intramuscularly. Consequently, its concentration in the blood was lower, and a longer time elapsed before it was excreted in the urine. This has also been found to be the case with intrapleural penicillin.

If 20,000 units of penicillin or more is instilled every twelve hours into the fallopian tubes, a stable bacteriostatic concentration is maintained for a considerable time in both the fallopian tubes and the pelvic peritoneum. This must be of great practical value not only in combating salpingitis and pelvic peritonitis but also in preventing infection after salpingography. But it is important to ascertain whether or not penicillin has an irritant effect on the pelvic peritoneum or on the tubal mucosa; for such an effect might bring about adhesions or the agglutination of the mucosal folds in the oviducts, and the treatment would then do more harm than good.

This question does not seem to have been studied previously. This is not surprising, because penicillin is usually administered when inflammation is already present which will mask any possible irritant effect of the penicillin. To determine this question we made experiments on animals and on women.

EXPERIMENTS ON ANIMALS

The experiments were made on rabbits. Earlier experience has shown that peritoneal adhesions often form after abdominal operations on rabbits. These animals are therefore particularly suitable for the experiments to be described. In all cases a small incision was made through the skin, muscles, and peritoneum in the midline immediately below the xiphoid process. Through this opening a predetermined dose of penicillin was introduced with a cannula fixed to a syringe and gently worked into the pelvic cavity. The rabbit was held upright so that the penicillin solution remained fairly long in the lower part of the abdominal cavity.

The effect of the penicillin was assessed by the macroscopical and microscopical findings in the pelvic organs and the peritoneum, and by function tests made by mating the animals after the administration of penicillin and observing the migration of the ovum. (In rabbits the follicles rupture after coitus.)

Experiment 1.—Penicillin 20,000 units in 20 ml. of solution was given by intraperitoneal injections to each of two rabbits. Necropsy three days later showed that a small quantity of the penicillin solution was still in the pelvic cavity; there was no redness or other sign of irritation either in the pelvic peritoneum or in the reproductive organs. Microscopically the tubal peritoneum and mucosa were normal.

Experiment 2.—Penicillin 20,000 units in 20 ml. of solution was given by intraperitoneal injection to each of

1. Frisk, A. R., Westman, A. *Lancet*, 1946, ii, 118.

two rabbits. Necropsy two weeks later showed nothing abnormal either macroscopically or microscopically.

Experiment 3.—Penicillin 200,000 units in 30 ml. of solution was given by intraperitoneal injection to each of two rabbits. Necropsy two weeks later showed no change.

Experiment 4.—Penicillin 20,000 units in 20 ml. of solution was given by intraperitoneal injection to each of two rabbits. Necropsy ten months later showed no change.

Experiment 5.—Penicillin 20,000 units in 20 ml. of solution was given by intraperitoneal injection to each of two rabbits six hours before coitus. A normal pregnancy ensued.

Experiment 6.—Penicillin 20,000 units in 20 ml. of solution was given by intraperitoneal injection to each of two rabbits twenty-four hours before coitus. A normal pregnancy ensued.

Experiment 7.—Penicillin 20,000 units in 20 ml. of solution was given by intraperitoneal injection to each of two rabbits seven days before coitus. A normal pregnancy ensued.

STUDIES IN WOMEN

Penicillin was instilled via the fallopian tubes into the pelvic cavity with the instruments used in salpingography at different times before a predetermined laparotomy. Patients were selected whose past history and condition warranted the assumption that neither old nor fresh pelvic inflammation was present. The material obtained at operation was examined microscopically, special attention being given to the fimbriæ of the tubes, which are particularly sensitive and respond readily to the slightest irritation. The mucosa also was carefully examined. In none of the following cases were there any microscopical evidence of a reaction.

Case 1.—Operative sterilisation. Penicillin 20,000 units in 15 ml. of solution was instilled on the day before operation. At operation a small amount of bloodstained fluid was found in the pouch of Douglas. There was no microscopical evidence of changes either in the peritoneal covering or in the mucosa of the tubes.

Case 2.—Myomectomy. Penicillin 20,000 units in 20 ml. of solution was instilled two days before operation. At operation a small amount of bloodstained fluid was found in the pouch of Douglas.

Case 3.—Operative sterilisation. Penicillin 20,000 units in 20 ml. of solution was instilled three days before operation.

Case 4.—Operative sterilisation. Penicillin 200,000 units in 60 ml. of solution was instilled daily for four successive days before the day preceding operation. At operation a moderate amount of bloodstained fluid was found in the pouch of Douglas.

Case 5.—Operation for ovarian cyst. Penicillin 40,000 units in 40 ml. of solution was instilled six and five days before operation.

Case 6.—Myomectomy. Penicillin 20,000 units in 20 ml. of solution was instilled daily eleven and ten days before operation. At operation a small amount of slightly bloodstained fluid was found in the pouch of Douglas.

Case 7.—Operative sterilisation. Penicillin 200,000 units in 60 ml. of solution was instilled thirteen and twelve days before operation.

DISCUSSION

In the experiments on animals penicillin was directly injected into the pelvic cavity. The powerful suction which takes place in the fallopian tubes, particularly in connexion with the rupture of the follicles [2] justifies the assumption that a fairly large amount of penicillin is thereby introduced into the oviducts.

In the experiments on women penicillin was instilled via the fallopian tubes and thus came directly into contact with their mucosa.

In some cases a comparatively large dose of penicillin was given. In most of the experiments on animals 20,000 units of penicillin in 20 ml. of solution was administered (in the third experiment 200,000 units of penicillin was given). The average weight of the rabbits being about 3000 g., this dose was comparatively large. Some of the women were given a larger dose than has hitherto been administered by instillation into the fallopian tubes. In the fourth case 800,000, and in the seventh case 400,000, units of penicillin was given in 4 and 2 days respectively. In all these cases the microscopical examination was made fairly soon after the treatment with penicillin, the longest interval being 13 days (case 7). For practical reasons it was impossible to lengthen the interval between the treatment with penicillin and the operation. On the other hand, I have observed several cases where the patients became pregnant one or several years after an operation for occlusion of the tubes and postoperative treatment with penicillin. These observations strongly suggest that the possibility of penicillin therapy having side-effects may be ruled out. In experiment 4 there was no evidence of changes either in the pelvic cavity or in the tubes despite the fact that 10 months elapsed between the penicillin treatment and necropsy.

The experiments on animals and on women have yielded identical results. Microscopically, there was no evidence of changes in the pelvic peritoneum or in the peritoneal covering or in the mucosa of the fallopian tubes attributable, to an irritant effect of penicillin, irrespective of whether the microscopical examination was made soon or long after its administration. The function tests in rabbits have shown that penicillin does not interfere with the mechanism controlling migration of the ovum.

This study has produced evidence that penicillin does not cause either toxic or chemical damage interfering with migration of the ovum, and that it can be safely used in the local treatment of inflammation in the reproductive organs. This opens up new therapeutic possibilities of combating salpingitis and its sequelæ.

SUMMARY

Before using penicillin in the prophylactic and therapeutic treatment of the fallopian tubes and the pelvic cavity it was important to ascertain whether penicillin causes any irritation which might bring about adhesions or any other damage interfering with migration of the ovum.

Experiments on animals and observations in women have shown that penicillin does not cause any such change.

2. Westman, A. *J. Obstet. Gynæc.* 1937, **44**, 821.

ANTHISAN IN PERENNIAL VASOMOTOR RHINORRHŒA

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IT is generally agreed that the administration of anti-histamine drugs improves some cases of perennial vasomotor rhinorrhœa (allergic coryza), but published reports show that there is considerable variation in the response to treatment with different preparations. Feinberg [1] found that only 15% of cases responded to treatment with 'Benadryl,' whereas 64% were improved with 'Pyribenzamine,' some of the cases which did not respond to benadryl being much benefited by pyribenzamine. Calder [2] treated 38 cases of vasomotor rhinorrhœa with 'Anthisan' and found that 76% of them were improved.

For the purpose of experimental work we consider that perennial vasomotor rhinorrhœa can only be

1. Feinberg, S. M. *J. Amer. med. Ass.* 1946, **132**, 702.
2. Calder, A. G. S. *Lancet*, 1948, **1**, 863.

diagnosed definitely if nasal biopsy shows a typically allergic mucosa with its characteristic feature of eosinophil infiltration, and cure can only be claimed if this mucosal pattern returns to normal as the result of treatment. It is well known that many non-specific influences may play a part in the aggravation of this disorder, not the least of which is the psychological one. Because of this any study designed to estimate the potency of a new preparation in chronic rhinorrhœa must be carefully controlled.

Conditions of the Experiment.—We used anthisan because it is the most specific anti-histamine drug. We chose 37 patients all of whom had had the typical symptoms of rhinorrhœa, sneezing, and nasal blockage for at least six months and on nasal biopsy showed the characteristic histology. Cases with sepsis and large polypi were excluded. The series consisted of 16 males and 21 females aged 10–53 years. Before treatment with anthisan was begun, every patient was given dummy tablets of similar appearance for two weeks. This was done to assess, if possible, the emotional factor in the condition, and it also trained the patient to take the tablets regularly. During this period we rejected cases in which nasal biopsy did not show an eosinophilia sufficient to warrant the diagnosis of allergy.

The results were as follows:

	Inactive tablets (*cases treated* = 37)	*Anthisan* (*cases treated* = 35)
Complete relief, with reversion of mucosa to normal	2 = 5%	19 = 54%
"Some relief"	13 = 35%	12 = 34%
No relief	22 = 60%	4 = 12%

During the control period 35% of patients had "some relief," though the appearances of the nasal mucosa were unaltered on inspection. Such are the vagaries of vasomotor rhinorrhœa that 2 patients, both females, experienced complete relief of symptoms while taking inactive tablets and subsequent biopsy revealed a normal nasal mucosa. The remaining 35 patients were then given anthisan 0·6 g. in the day in divided dosage. In some there was improvement with as small a dose as 0·2 g. in the day, whereas 4 patients required 0·8 g. daily for complete relief. The treatment was continued for four weeks. Two control biopsies were done, one immediately after completion of treatment and one a month later. The tabulated results show that 54% of patients obtained complete relief of symptoms, with reversion of the nasal mucosa to normal, and that 34% had "some relief," without significant alteration in the nasal histology. It is considered that these latter cases must be disregarded in the therapeutic assessment of this preparation because of our experiences with "dummy" tablets. Only 4 cases obtained no benefit.

None of the patients who obtained complete symptomatic relief and histological "cure" have reported in the past six months for further treatment, though it was impressed on them to do so if symptoms recurred. Most of those who experienced "some relief" continue to attend the department.

Side-effects developed in the same frequency as reported by Hunter and Dunlop.[3] In no case were they severe enough to interfere with treatment.

Conclusion.—This experiment establishes that over half the cases of perennial vasomotor rhinorrhœa may be at least temporarily cured with anthisan. Some 35% of patients in our series experienced "some relief" with anthisan, but the use of control periods and nasal biopsy both suggest that this effect may be psychological.

We are indebted to Dr. R. F. Ogilvie and Dr. A. C. P. Campbell for their reports on the nasal sections; and to Prof. D. M. Dunlop and Dr. I. Simson Hall for advice and criticism. Anthisan tablets and control tablets were provided by Messrs. May & Baker Ltd.

3. Hunter, R. B., Dunlop, D. M. *Quart. J. Med.* (in the press).

MYANESIN IN TETANUS

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THE favourable effects of 'Myanesin' in two cases of tetanus reported by Belfrage (1947) prompts us to publish a third case of tetanus in which myanesin apparently gave much benefit.

On May 8, 1948, a man, aged 62, was working in a garden shed when a glass jar fell from a shelf and made a cut about 1/2 in. long on the left occipitoparietal region of his bald head. Bleeding was insignificant, and a dressing was applied without any cleansing. It is noteworthy that the patient's 5-year-old grand-daughter had played with this jar in the garden, where horse manure had been piled the previous year.

On May 12, while shaving, the patient noted that the left side of his face felt tight, and on looking in the mirror he saw that that side of his mouth seemed to be drawn up, and his left eye was watering and difficult to open. Next day he developed prickling sensations lasting a few seconds, starting in the lumbar region and spreading to the abdomen and waist. They occurred every hour or so and were so unpleasant that he was afraid to touch the skin during them. In the next few days these symptoms became more severe, and his mouth became difficult to open, so that he could not wear his false teeth or eat comfortably. By the 19th his mouth was so difficult to open that he could not eat at all, and his left eye was almost completely closed, so he attended a hospital.

On May 23, eleven days after the first symptoms, he began to have spasms of pain. At first the pain was not very severe; it started in the lumbar region and spread to the abdomen, and then up to the chest and armpits and down to the hips and feet. He described it as like a severe cramp; it came about every hour at the start and lasted only a few seconds, during which his body tended to straighten out. These paroxysms became gradually longer, more severe, and more frequent, and he found that they were induced by a slight cough, so that he became afraid to drink lest he should choke and so precipitate a spasm. On the 27th he was admitted to the West Middlesex County Hospital as an abdominal emergency.

On admission he was having obvious attacks of pain. The sheet on which he was lying was soaked with sweat. In every spasm beads of sweat broke out on his body, his face was contorted, the muscles of the neck stood out, his limbs stiffened, especially his legs which flexed at the hips and knees, and his abdominal muscles became rigid, showing clearly the intersections of the recti. These attacks came on every 5 min. if he were not disturbed, but they were precipitated by the slightest movement or the gentlest examination. His temperature was 99°F, respirations 20 and pulse-rate 92 per min., weight 123 lb. The left eye was partially closed in repose but could be opened fully; there was presumably spasm of the orbicularis oculi. His left cheek felt stiff, and his mouth was drawn up on that side from spasm of the facial muscles; he could open his mouth only about 3/4 in. There was no neck-rigidity. His bald head showed a small completely healed scar in the left occipitoparietal area, which was not tender. The abdominal muscles were tense. All four limbs were stiff, the legs more so than the arms. Reflexes were all brisk, especially in the legs, which showed bilateral unsustained ankle clonus and right patellar clonus. The plantar reflexes were flexor. No other abnormality was found in the central nervous system. The heart showed a triple rhythm, the blood-pressure was 230/100 mm. Hg, and the vessels were arteriosclerotic. Tetanus was diagnosed.

Treatment.—During the first night the patient was given two injections of morphine gr. 1/3. Next morning, May 28, to enable a lumbar puncture to be done, anæsthesia, or at least relaxation, was necessary; so myanesin, 1 g. in 10 ml. of water, was diluted with an equal quantity of water, and was injected intravenously. This dilution was used in all subsequent intravenous injections except one. The immediate effect was complete relaxation from all spasms, and it was decided to

continue myanesin as a therapeutic agent. An initial intramuscular injection of 200,000 units of antitetanic serum was given, and penicillin 30,000 units was injected four-hourly from May 28 to June 8. The full sedative treatment was as follows:

Date	*Time*	*Sedatives*
May 27 ..	10 P.M. ..	Morphine gr. $^1/_2$
May 28 ..	6 A.M. ..	Morphine gr. $^1/_2$
	11 A.M. ..	Myanesin 1 g. I.V.
	8.45 P.M. ..	Myanesin 1 g. I.V.
May 29 ..	4.30 A.M. ..	Myanesin 1 g. I.V.
	5.30 P.M. ..	Myanesin 0·5 g. I.V., and 0·5 g. I.M.
	9 P.M. ..	Myanesin 1 g. I.V.
	10 P.M. ..	Pentobarbital sodium gr. $1^1/_2$
May 30 ..	2 A.M. ..	Myanesin 1 g. I.M.
	4.30 A.M. ..	Morphine gr. $^1/_4$
	2 P.M. ..	Myanesin 1 g. I.M.
	9 P.M. ..	Myanesin 1 g. I.V.
	10 P.M. ..	Pentobarbital sodium gr. $1^1/_2$
May 31 ..	2 A.M. ..	Morphine gr. $^1/_4$
	3 P.M. ..	Myanesin 0·5 g. I.V., and 0·5 g. I.M.
	11 P.M. ..	Pentobarbital sodium gr. $1^1/_2$
	11.45 P.M. ..	Myanesin 1 g. I.M.
June 1 ..	6 A.M. ..	Myanesin 1 g. I.M.
	11.30 A.M. ..	Myanesin 1 g. I.M.
	8.15 P.M. ..	Myanesin 1 g. I.M.
June 2 ..	1.30 A.M. ..	Myanesin 1 g. I.M.
	5.15 A.M. ..	Myanesin 1 g. I.M.
	1.45 P.M. ..	Myanesin 1 g. I.M.
	11 P.M. ..	'Sodium amytal' gr. 3
	11.05 P.M. ..	Myanesin 1 g. I.M.
June 3 ..	8 A.M. ..	Myanesin 1 g. I.M.
	4.30 P.M. ..	Myanesin 1 g. I.M.
	11 P.M. ..	Sodium amytal gr. 3
June 4 ..	12.45 A.M. ..	Myanesin 1 g. I.M.
	2.30 A.M. ..	Myanesin 1 g. I.V.
	10.30 P.M. ..	Sodium amytal gr. 3
June 5 ..	10 P.M. ..	Myanesin 1 g. I.M.
June 6 ..	2.50 A.M. ..	Sodium amytal gr. 3

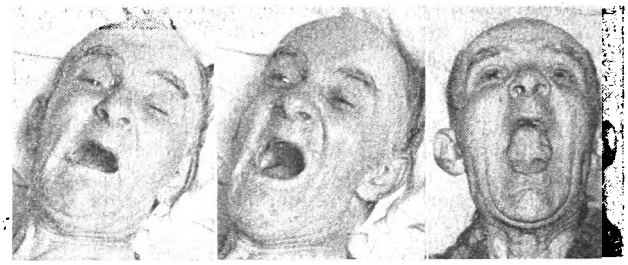
The total amount of myanesin given in nine days was 22 g. (7 g. intravenously and 15 g. intramuscularly.)

Progress.—After the last injection of myanesin on June 5 recovery was uninterrupted. There were no further spasms, and the patient could open his mouth wide enough to insert his false teeth and take a solid diet. Previously he had been fed entirely on fluids, and after the first day, when he drank little, his intake was always more than double his output. The tone of his limbs appeared normal, though that of his abdominal muscles was still a little increased and remained so for a further week. His reflexes were still brisk, but the clonus had gone. His general condition was good, his blood-pressure had fallen to 200/104 mm. Hg, and his triple rhythm had vanished. The last sign to disappear was the spasm of the orbicularis oculi on the left, which was still present until June 23, more than six weeks after it had first developed.

EFFECTS OF MYANESIN

The injections of myanesin caused no objective sensory change, but there was a feeling of a hot and pleasant flush sweeping over the body. There was no loss of voluntary power. The rigidity of the muscles was greatly reduced, and the abdomen could be palpated comfortably. The patient could open his mouth twice as wide (see figure) and he could drink in comfort and without fear. The spasm of the left side of the face became much less, and his left eye was more opened. The reflexes remained brisk, and the ankle clonus persisted. The only mental change was an emotional lability shown by two attacks of weeping, one 2 min. and one 10 min. after an injection of myanesin. Myanesin relieved the spasms and made feeding and nursing easy. Its effect lasted for about twelve hours when it was given intravenously; when it was given intramuscularly its effect lasted for only half the time. The result of giving half the dose intravenously and the other half intramuscularly was also less successful.

Hæmoglobinuria was looked for both microscopically and macroscopically but not seen, and a red-cell fragility curve done on June 1, after a total of 12 g. of myanesin had been given, was completely normal, in contradiction to the findings of Wilson and Gordon (1948). A total of 8 g. of myanesin was given intravenously in eight days and no intravascular thrombosis occurred until, unfortunately, in the early morning of June 4 myanesin was given undiluted in error, and, after some difficulty had been experienced in getting into a vein, a local venous thrombosis developed.



(*a*) (*b*) (*c*)

Effect of myanesin on lockjaw in tetanus: (*a*) fullest extent to which patient could open his mouth at 11.30 a.m. on June 1 before injection of myanesin; (*b*) same three minutes later, immediately after intravenous injection of myanesin 1 g.; (*c*) same on June 18 after recovery.

DISCUSSION

Severity of Tetanus.—In considering the efficiency of myanesin it is necessary to assess the severity of the tetanus in this case. The early conception that the prognosis depended on the time between the infection and the first symptom, which in this case was only four days, suggested that this would be a severe illness. Later, however, Cole (1938) stated that the time between the first symptom and the first spasm was more important. This was long (eleven days) and, but for the clinical picture, would place the case in the relatively mild category. Vener and Bower (1941) put the mortality for patients over the age of 40 at 50%, and stated that it was the exception for anyone over the age of 60 to survive. Not only was this patient over the age of 60 but also he had hypertension and an impaired coronary circulation, as shown by electrocardiography.

Sedation.—After the first night myanesin was the only drug used to control the spasms, other sedation being insignificant. The patient was freed from pain for long periods and yet remained fully conscious and able to drink, owing to the relaxation of the masseter muscles. Nursing was made easy and was carried out without trouble in a busy general ward.

Advantages of Myanesin over Curarine.—Cases treated with curarine have been described by Mitchell (1935) and West (1936). Mitchell gave curarine by intramuscular injection, West by continuous intravenous drip. With curarine, however, there is the danger of respiratory paralysis, since the margin between the dose causing freedom from the muscular contractions and that causing respiratory failure is small. Myanesin in the doses given has no effect on respiration, and Mallinson (1947) stated that the dose affecting the vital centres in animals was ten times that causing muscular relaxation. Further, patients given curarine are paralysed and therefore more difficult to nurse, and the difficulties of maintaining an intravenous drip for nine days are great.

Complications.—It is interesting to note the complete absence of complications from the use of myanesin so long as it was diluted; no signs of intravascular hæmolysis were seen, and the fragility of the red cells was unaffected. The accidental giving of an undiluted injection was followed by thrombosis. Pugh and Enderby (1947) suggested that this complication depended entirely on the concentration.

Site of Action.—Berger and Bradley (1946) supposed that myanesin acted on the synapses of the cord, but Stephen and Chandy (1947) produced evidence to show its action was on the basal ganglia, since it relieved pain of thalamic origin and reduced parkinsonian tremor and rigidity. Hunter and Waterfall (1948) stopped epileptic attacks in 30 sec. by injecting myanesin. In our case, too, there is some evidence that there was a central effect, in view of the spontaneous weeping and the fact that the spasms ceased though the reflex activity remained brisk and clonus persisted.

CONCLUSION

The beneficial effect of myanesin in this case was so obvious that it is hoped that it may be given an extended trial in further cases, including its exhibition by mouth as well as by intramuscular and intravenous injection.

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ACUTE TOXIC ENCEPHALOPATHY OF UNKNOWN ÆTIOLOGY IN TWO BROTHERS

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ACUTE toxic encephalopathy of unknown ætiology is rare, and I have not been able to find any other report of the simultaneous affection of two members of a household.

CASE-REPORTS

The brothers, A.B. and C.B., aged 17 and 12, had not previously had any serious illness. On Dec. 13, 1947, A.B. developed acute tonsillitis and was confined to bed. His diet consisted of fluids only until the 16th, when he had a cereal with milk in the morning and in the afternoon felt well enough to want solid food. At this time C.B. was in his usual good health. Their mother prepared a soup from stock made two days previously, and a stew from meat which had also been cooked two days previously and had contributed to the stock, with potatoes, onion, carrots, and a proprietary flavouring and colouring agent. This meal was eaten at 5.30 P.M. The parents and both boys had the soup, but the stew, apart from a taste taken by the mother, was eaten only by the boys, each of whom had a large helping. C.B. then went out, returning in a few minutes with some sweets, which he shared with his brother.

About an hour after the meal the father felt dizzy—"as if drunk"—for about 5 minutes. The mother felt no ill effects. At this time A.B. complained of headache and nausea and a little later went to bed. He did not actually vomit. At 8 P.M. C.B. returned home and said he had vomited at a friend's home, and felt "rotten." He went straight to bed.

The boys' illness was so fulminating that at no time after this could the parents communicate with them. During the succeeding hours the boys were restless and groaning. Their parents visited them several times and noted that each boy was clasping his abdomen as if in pain; but since they did not reply to questions they were assumed to be asleep and to be restless owing to some simple abdominal upset.

At about 3 A.M. on Dec. 17, however, the parents heard a disturbance in the boys' room and found both boys out of bed, standing stiffly erect with jaw dropped, frothing at the mouth, and with arms held flexed at the elbows and pronated. They resented interference, and much difficulty was experienced in removing them to the Manchester Royal Infirmary, which they reached at 6 A.M. on the 17th.

On admission, A.B. was comatose and lay quietly unless disturbed. Temperature 97·6°F, pulse-rate 106, and respirations 26 per min. Examination was violently resented and led to screaming and vigorous movements. The eyes were closed; trismus, photophobia, and neck-rigidity were present, and attempts to open the eyes or mouth or to flex the neck forwards again produced screams and violent movements. The pupils were moderately dilated but reacted to light; the eyes spontaneously moved freely in all directions. No defect was detected in the remaining cranial nerves, so far as they could be tested. Power in all limbs was good, reflexes were brisk, and plantar responses flexor. Kernig's sign was negative. No abnormalities were detected in the heart. After sedation with thiopentone 0·5 g. intramuscularly the fundi were examined and found to be normal, and relaxation of trismus allowed inspection of the tonsils, which were large and hyperæmic but no exudate was present. Lumbar puncture was then performed. It was impossible to estimate the pressure owing to continuing restlessness. The fluid was clear and colourless and flowed freely: it contained 10 leucocytes per c.mm. (6 lymphocytes and 4 polymorphs) and protein 30 mg. per 100 ml. Unfortunately the fluid was not examined in more detail. A blood-count showed red cells 5,350,000 per c.mm., Hb 104%, and white cells 17,400 per c.mm. (polymorphs 91%, lymphocytes 6·5%, large mononuclears 2%, eosinophils nil, basophils 0·5%).

C.B. on admission also lay quietly unless disturbed and was apparently comatose. Temperature 97°F, pulse-rate 100, and respirations 20 per min. During examination, however, he opened his eyes and said "I can't see anything." Neck-rigidity, trismus, and photophobia were present, and he resented interference like his brother. The pupils were not dilated and reacted to light; spontaneous ocular movements were full in each direction. Power in all limbs was good; reflexes were brisk, and plantar responses flexor. Kernig's sign was weakly positive. The throat appeared healthy, and no abnormality was detected in the heart, lungs, or abdomen. Lumbar puncture after sedation revealed a clear colourless fluid containing 3 lymphocytes per c.mm. and protein 25 mg. per 100 ml. A blood-count showed red cells 4,450,000 per c.mm., Hb 86%, and white cells 14,200 per c.mm. (polymorphs 86·5%, lymphocytes 11·5%, large mononuclears 2%).

The patients presented a strikingly similar picture of meningeal and cerebral irritation, though C.B. was not so deeply unconscious as A.B., the moderate dilatation of the pupils was present in A.B. only, and C.B. had a weakly positive Kernig's sign. It was thought likely that the cause was some exogenous poison, and the findings indicated that A.B. was the more seriously affected. The signs did not suggest poisoning with belladonna or other alkaloid, and the early onset of unconsciousness ruled out botulism. There had been little vomiting and no diarrhœa, but abdominal pain had apparently been present, and heavy-metal encephalopathy appeared to be a possibility. Treatment was therefore begun with dimercaprol (B.A.L.), A.B. receiving 120 mg. four-hourly, and C.B. 80 mg. four-hourly. Penicillin 30,000 units three-hourly was given to A.B. because of the throat infection, and both patients were given rectal saline. Sedation was continued with small doses of paraldehyde per rectum.

Progress

The illness developed in the two patients along almost identical lines. Throughout the day of admission cerebral irritability remained the dominant feature. Both boys showed an increasing neck-retraction, which became extreme towards the end. During the morning of admission clonic jerking of the arms and legs and nystagmus were present at rest and with vertical and horizontal ocular deviation.

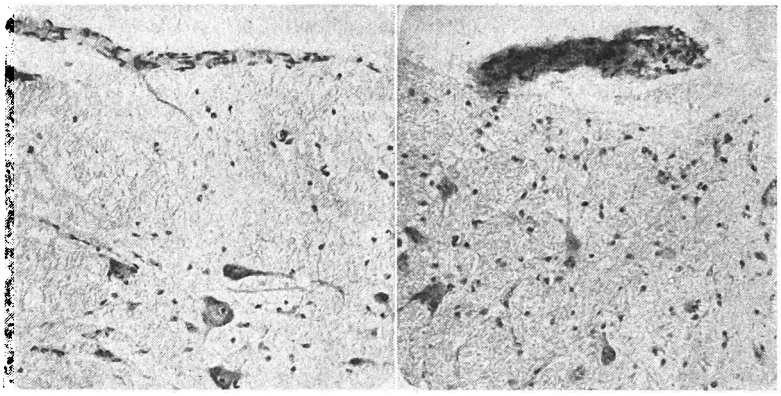
Dr. Fergus R. Ferguson, who saw the patients, could not recollect having seen two similar cases at the same time, and he thought that the presumptive diagnosis was acute toxic encephalopathy probably due to an exogenous toxin.

On the day after admission both boys were quieter and no longer responded excessively to stimuli. Trismus was not now in evidence, but A.B. had developed a right-sided facial paralysis. Conjugate upward deviation of the eyes was present in both cases, and the pupils were moderately dilated and reacted sluggishly to light. C.B. showed rhythmical movements of his head and opening and closing of his lower jaw. The reflexes remained equal, and the plantar responses flexor. Both boys were incontinent of urine, but the bowels were not opened. A further lumbar puncture did not reveal any change in the findings.

Respiration became shallow, but the rate was not increased, and cyanosis appeared. Oxygen was given by B.L.B. mask, and electrical suction was used to aspirate mucus from the upper respiratory tracts. After progressive deterioration A.B. died at 5.15 P.M., and C.B. at 10.50 P.M. There was a rise in temperature before death, in A.B. to 103°, and in C.B. to 100·4°F.

Necropsy Findings (Dr. William Susman)

In A.B. both lungs were distended and showed hypostatic congestion and œdema. The mucosa of the œsophagus, stomach, duodenum, jejunum, and upper ileum was acutely congested, with a large amount of adherent catarrhal exudate. There was a brownish tinting of the gastric mucosa, suggesting breakdown of blood pigment, and there were scattered hæmorrhagic erosions on its surface. Six ulcers about 3 mm. in diameter were present in the first part of the duodenum. The remainder of the small intestine and the large intestine showed patchy acute congestion and passive congestion. The liver



(a) (b)

Sections through reticulate substance of medulla, showing increased vascular cellularity, cerebral œdema, and degeneration of nerve-cells: (a) in patient A.B., and (b) in patient C.B. (× 125.)

was passively congested with scattered areas of fatty degeneration. The spleen showed passive congestion and the malpighian bodies were prominent. The pia-arachnoid was acutely congested. The cerebral convolutions were flattened, and cerebellar and tentorial pressure cones were present. The brain was extremely œdematous. The grey matter was acutely congested, except the basal ganglia.

In C.B. large purpuric hæmorrhages were present over the lower lobes of both lungs; otherwise the post-mortem findings were identical.

Neurohistological Report (Dr. Eugen Pollak)

The neurohistological findings were the same in the two cases. There were no signs of an inflammatory lesion. Some of the blood-vessels in the cerebral cortex showed an increase of endothelial and adventitial cells. There was no perivascular cuffing; nor were any hæmorrhages seen. The most prominent feature was severe affection of the nerve-cells, which were swollen, with disorganised cytoplasm. Nissl bodies were only occasionally and faintly seen. There were signs of fatty infiltration of the nerve-cells, some of which were mere shadows. These changes were present throughout the brain, but the large cells in the reticulate substance of the medulla oblongata were most severely affected. There was a slight pericellular glial reaction.

Public Analyst's Report (Mr. Harri Heap)

Examination of the stomach and intestinal contents and of the liver in both cases revealed no evidence of barbiturate, chloral, sulphonal, alkaloid, or any poisonous metal.

Bacteriological Report (Dr. H. R. Cayton)

The material submitted for examination consisted of a bowl of meat and vegetable hash and a packet of "gravy maker." From both of these, samples were subjected to bacteriological examination, aerobic and anaerobic methods of cultivation being used. From the sample of hash bacteria were isolated only after enrichment methods, and those isolated were common air-borne saprophytes.

In an attempt to incriminate the hash as the poisonous vehicle, feeding experiments were tried, but the results were inconclusive, since only small portions of the food were eaten, and one animal died of starvation. A representative sample was then minced and a crude filtrate prepared. Four guinea-pigs were inoculated intraperitoneally with the extract, one pair receiving 1 ml. and one pair 5 ml. All the animals survived.

DISCUSSION

The simultaneous onset in two brothers of this acute illness and its identical progress suggested exogenous poisoning. The signs were not those of any alkaloidal poisoning, but the view that a heavy metal might have been responsible was strengthened by the finding of severe gastro-enteritis at necropsy. The restricted diet of A.B. before the onset of symptoms facilitated investigation of this point, since it appeared that the meal of hash was the only food which could have contained a poison. However, neither the remains of the hash nor the contents of the patients' gastro-intestinal tracts contained any poisonous substance. A month after their death it became known that the boys had eaten sweets after the hash, but investigation of the sweets did not seem likely to be profitable after such a delay, since no-one else appeared to have been affected.

A.B. had a throat infection when he was taken ill, but C.B. was in good health, so an endogenous bacterial toxin could not have been to blame.

The cases occurred at the end of an epidemic of poliomyelitis, but the simultaneous onset of poliomyelitis in two brothers was thought improbable; nor were the findings in the cerebrospinal fluid in favour of this diagnosis. Fulminating polioencephalitis could not, however, be excluded clinically, and it is worth noting that a clinically similar case which occurred at another hospital in this area during the same week was proved histologically to have been a typical case of polioencephalitis.

There remains for discussion the acute toxic encephalopathy of unknown ætiology first described by Anderson (1923) and later by Brown and Symmers (1925), Brain and Hunter (1929), and Baker (1935). This diagnosis can only be finally established histologically. The histological differentiation of non-suppurative encephalitis of infectious origin and of toxic encephalopathy is discussed by Hassin (1921), Grinker and Stone (1928), and Low (1930), and the following criteria are laid down:

(1) In infective cases there is infiltration with mesodermal elements, producing perivascular cuffing and perhaps parenchymatous infiltration, whereas in toxic cases there is no such infiltration.

(2) In toxic cases there is a proliferative reaction of the local vascular system. There is new vessel formation and stimulation of endothelium, with obliteration of many capillaries—the so-called endarteritis productiva.

(3) In toxic cases there is particularly severe affection of the ganglion cells which commonly takes the form of acute liquefaction. Severe neuronal change may, however, be seen in polioencephalitis, but it is then accompanied by mesodermal infiltration.

The changes in toxic encephalopathy are similar whether the condition is caused by bacterial toxins, as in diphtheria, pneumonia, septicæmia, erysipelas, scarlet fever, and dysentery (Ford 1937), by heavy metals, such as lead, arsenic, and manganese, or by unknown toxins.

The essential neurohistological findings in the present cases are the absence of mesodermal infiltration and the presence of cellular liquefaction and slight vascular proliferation. These findings exclude polioencephalitis or any other form of non-suppurative encephalitis. Since the analytical and bacteriological reports did not reveal any known neurotoxin, the diagnosis is acute toxic encephalopathy of unknown ætiology.

SUMMARY

An acute cerebral illness developed simultaneously in two brothers, aged 17 and 12, who died within forty-eight hours.

Histological examination showed features characteristic of acute toxic encephalopathy.

The responsible toxin was not traced.

It seems that no report has previously been published of acute toxic encephalopathy of unknown ætiology occurring in one family or in one household.

I wish to thank Prof. Crighton Bramwell, under whose care the patients were admitted, for his help and guidance in the preparation of this report; Dr. Fergus R. Ferguson, who examined the patients in consultation; Dr. W. Susman, for the necropsy; Dr. Eugen Pollak for neurohistological, Dr. H. R. Cayton for bacteriological, and Mr. Harri Heap for analytical reports.

References at foot of next page

THROMBOSIS OF THE ABDOMINAL AORTA

APPARENTLY CAUSED BY PRESSURE FROM A VERTEBRAL OSTEOPHYTE

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SINCE the condition was first discussed by Graham (1814), many cases of thrombosis and embolism of the aorta have been reported. Greenfield (1943) collected 161 cases, including 5 of his own. Banowitch and Ira (1928), who give an extensive bibliography, emphasise that most of the cases are associated with chronic cardiac and arterial disease, and that in fully half of these there is a history of mitral stenosis and auricular fibrillation. Thrombosis due to syphilitic infection is described by Greenfield (1943) and by Ronald and Leslie (1940), and aortic occlusion is a very rare complication of specific fever such as typhoid and influenza.

Abdominal aorta opened to show clot in portion distorted by vertebral osteophyte.

Of 73 cases of thrombosis of the abdominal aorta reviewed by Hesse (1921) 3 were due to external pressure—from a uterine fibroid, a uterine carcinoma, and a neoplasm of the 2nd and 3rd lumbar vertebræ. In the last case the aortic wall was invaded by the tumour.

In the case described below the cause appeared to be pressure on and distortion of the wall of the abdominal aorta by a large osteophytic outgrowth from the 2nd and 3rd lumbar vertebral bodies.

A man, aged 81, was admitted to the Royal Masonic Hospital with a severe pain in the left calf of sudden onset six hours before admission. Two weeks previously he had had an attack of bronchitis, and a week before admission a "heart attack."

On examination the left leg below the knee was cold and pallid; and, though the femoral pulse was easily palpable, no pulsation could be felt distally. The right leg was normal. The heart rhythm was regular, and there were no signs of cardiac failure, but in view of the history it was thought probable that the popliteal embolus had come from the heart.

Operation.—The patient was seen by Sir Heneage Ogilvie, who decided to attempt embolectomy. After administration of intravenous heparin the left popliteal artery was opened; but, though a length of soft clot was removed, no circulation could be established in the artery. The incision was closed and the patient returned to the ward, where he died some sixteen hours later.

Necropsy Findings.—Heart normal; no mural thrombi. When the abdominal aorta was exposed, a large osteophyte was seen projecting forward from the junction of the 2nd and 3rd lumbar vertebræ compressing the vessel from the left side. When the aorta was opened it was found to contain a thrombus which about half-filled the lumen, and over the indentation caused by the osteophyte there were small tags of organised clot from which masses had clearly broken away. At the aortic bifurcation a saddle-shaped thrombus lay, with prolongations extending a short way down the common iliac arteries on each side: the tail of that on the left side had broken off. There was moderate atheroma of the aortic wall but no calcification. No evidence was found of any occlusion of the mesenteric and renal vessels, which were clear of the thrombotic process. The left femoral artery was obstructed from 3 in. below the inguinal ligament, the clot becoming increasingly solid down to the adductor canal.

In view of these findings the doctor who had sent the patient to hospital was asked for further details of the "heart attack," which proved to have been one of complete heart-block. It thus seems probable that slowing of the blood-flow through the distorted aorta had led to the deposition of the thrombus within it.

It is interesting to compare these cases of aortic thrombosis due to external pressure with those of brachial occlusion due to cervical rib or crutch pressure described by Lewis (1936).

I am indebted to Sir Heneage Ogilvie for permission to publish this case. The drawing is by Miss Barbara Nicholson.

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New Inventions

A WALKING-CHAIR FOR SPASTIC CHILDREN

TEACHING spastic children to walk is difficult and slow. Those who can do exercises with fair coördination while lying on their backs regain their spasticity as soon as the leg muscles take the weight of the body. The children need hours of walking practice, but neither nurses nor physiotherapists can be spared to support these children and lead them slowly round the ward for so long. The apparatus described here helps to overcome this difficulty. It consists of a walking-machine in which the child is suspended by a harness and counterbalancing springs adjusted to take any desired proportion of the child's weight.

The machine is improvised from standard hospital equipment; a more elaborate model is being designed. The post of a bed-gallows is lashed to the front of a standard walking-chair, and the lower end fixed to a wooden crossbar. A spreader to which the patient's harness is attached is hung from the gallows by a cord passing over a pulley. The cord is attached to two springs. By using different springs at different extensions the "lift" on the patient is adjusted. At first a "lift"

of about two-thirds of the body-weight is used; this is lessened as coördination improves. The harness is made of 1 in. lamp-wick, the joins being sewn with linen thread, and buttons and holes being used for fitting. Three bands pass round the body—at the chest, waist, and hips—and are joined by two vertical ones at the front and two at the back, prolonged below to make groin straps and above to fasten to the spreader. This harness is buttoned over the clothes and can be worn for a long time with comfort.

Experience suggests that the device is of most value in the first walking exercises and in the more severe cases; in the milder cases the only advantage is that the child is more confident, since he cannot fall and hurt himself. The very severe cases, which would otherwise be bedridden (the child in the photograph was one), can use the device to walk about unattended, visit other children, and take the air in the hospital grounds. The difference which this makes to such a child can well be imagined.

I am grateful to the medical superintendent, Cherry Knowle Emergency Hospital, and Mr. D. G. W. Brown, visiting orthopædic surgeon at this hospital, for encouragement in developing the device, and to Sister D. Armin, who made the harnesses and spends many hours a day teaching the children to walk.

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Reviews of Books

Textbook of the Rheumatic Diseases

Editor: W. S. C. COPEMAN, O.B.E., M.D., F.R.C.P., physician to the rheumatism department, West London Hospital. Edinburgh: E. & S. Livingstone. 1948. Pp. 600. 50*s*.

NOW that the rheumatic diseases are increasingly recognised as a suitable basis for special practice, and also as a subject urgently needing more special study, the appearance of a new and authoritative textbook is welcome. As editor of this volume, Dr. Copeman set out "to collect and collate modern knowledge of the rheumatic diseases from the best sources," and the resulting symposium, representing as it does the combined efforts of 24 contributors, can be regarded as a success. Modestly restricting his own contribution to chapters on non-articular rheumatism and chorea, the editor sets a high standard which is well maintained by his collaborators. The chapter on rheumatoid arthritis by Prof. L. S. P. Davidson, those on gout and the rarer arthritic syndromes by Prof. Henry Cohen, and Dr. Ernest Fletcher's account of osteo-arthritis, are in themselves sufficient to justify the book. The two chapters by Dr. J. H. Kellgren on pain, and that by Dr. Percy Stocks on statistics, although primarily for research-workers, are of general interest, while the essay on rheumatic fever by Lord Horder is a model of graceful writing. It is much to the credit of the editor that in a book that includes contributions from specialists in neurology, psychiatry, physical medicine, orthopædic surgery, and pædiatrics, as well as from general physicians, there is hardly any overlapping. There is, moreover, a striking uniformity of approach: large gaps in our knowledge of the ætiology of almost all the rheumatic diseases are frankly admitted, while the current empirical treatments are critically assessed. The book is well printed and lavishly illustrated, and its value as a work of reference is enhanced by an excellent index.

Congenital Malformations

(2nd ed.) DOUGLAS P. MURPHY, M.D., F.A.C.S., assistant professor of obstetrics and gynecology, University of Pennsylvania. Philadelphia and London: J. B. Lippincott. 1947. Pp. 127. 30*s*.

A SURPRISINGLY high proportion of pregnancies terminate in malformed offspring. Gynæcologists have become more interested in the subject since more has been learnt about some of the fœtal pathological states—such as icterus neonatorum, and the effects of maternal rubella. But a large proportion of fœtal abnormalities remain unaccountable. Professor Murphy was one of the pioneers in this field, in the early 1930s, and a summary of the results of his Philadelphia surveys on the incidence of causes of malformations was first published in 1940. This enlarged edition, now easily available to British readers, is welcome. He finds that the frequency of gross malformation is 0·5% of all births, being higher in white than in coloured populations; and his analysis of the incidence in relation to maternal age and parity reveals a significant excess among the later births—though the description of the statistical methods used is far from clear. No relationship was found between maternal ill health or nutrition and fœtal disease, though the data are remarkably abundant. The juxtaposition of cases of known recessive diseases with malformations of quite different origin, and the crude treatment of the problems of familial incidence, may trouble genetically minded students; and the failure to discriminate between these different groups makes some of the generalisations unsound, especially those relating to prognosis for subsequent pregnancies. But the somewhat dogmatic approach may have the effect of stimulating readers to make further inquiries in this hitherto neglected field; for Professor Murphy's account is not so much a textbook as a concise account of pioneer researches. Two brief new chapters on maternal pelvic irradiation and on maternal rubella add to its usefulness.

Reid's Practical Sanitation

(24th ed.) Revised and rewritten by JOHN J. BUCHAN, M.D., D.P.H. London: Charles Griffin. 1948. Pp. 300. 18*s*.

"Reid" appeared first in 1892, and between that date and 1937 achieved 23 editions. This new one has been entirely rewritten by Dr. J. J. Buchan, formerly medical officer of health for Bradford. Reid wrote his book for sanitary inspectors; but it was, and is, also pre-eminently suitable for medical students of hygiene, since two-thirds of it deals with practical sanitation and the remaining third with sanitary law. This edition contains little of what Reid said 56 years ago, but justly retains his name because it retains his object—to provide an introduction to the study of sanitary science.

Principles and Practice of Modern Cosmetics (Vol. 2: Cosmetic Materials. London: Leonard Hill. 1948. Pp. 479. 35*s*.).—Mr. Ralph G. Harry, dealing with the substances employed in pharmaceutical and toilet preparations, considers a wide range of drugs and inorganic and organic materials, giving synonyms, formulæ, molecular weights, occurrence in nature or method of manufacture, physical and chemical properties, *B.P.* standards, method of use in toilet preparations, and dermatological action. He has a comprehensive knowledge both of chemistry and of modern literature on dermatological topics, and his opinions are stated without ambiguity or confusion. The book can be strongly recommended as a work of reference for those interested in cosmetics.

Vaccination par le B.C.G. par scarifications cutanées (2nd ed. Paris: Masson. 1947. Pp. 115. Fr. 180).—This monograph, by Dr. L. Nègre and Dr. J. Bretey, of the Pasteur Institute, Paris, opens with a short historical review of Calmette's earliest work on B.C.G. vaccination from 1921 onwards; and this is followed by an experimental laboratory study, on guineapigs, rabbits, calves, and a chimpanzee, of modern methods of application of the vaccine by the multiple-puncture and skin-scarification techniques, as introduced by Rosenthal and as studied in detail by Birkhaug and others in Scandinavia. These techniques avoid, to a great extent, the annoying cold-abscesses which resulted from subcutaneous inoculation. The book ends with a short clinical review of prophylaxis in man, including a summary of the well-known work of Heimbeck and others. The microscopical study of sections of the skin of animals after the application of the puncture and scarification techniques is instructive; these show agglutination of the bacilli in the subcutaneous tissues within a few hours, followed by exudation of plasma and phagocytic reaction. In laboratory animals these reactions resulted in positive Mantoux reactions in 1–4 weeks. There is little new in the monograph; indeed, it would be difficult to be very original nowadays on this subject; but it is a clear presentation written with the usual French lucidity, and is a tribute to the work of the authors' late colleague and teacher, Albert Calmette.

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THE LANCET

LONDON: SATURDAY, NOV. 20, 1948

A Symbol Reborn

THE intrinsic instability of human society is so alarming that every community is obliged to develop some means whereby the forces of cohesion are brought to a focus. In this country the focal point, which has taken centuries to evolve, is a constitutional monarchy. We in England may take pride both in our Royal Family and in our attitude towards it. In our King we have a representative of a father, a father of a grown-up family, who receives the affection we bestowed on our own father in childhood and the respect we pay him in our adult years—a father who grows up with his children. With us he is no distant figure in shining armour, nor is he cut off from us by police cordons and armour-plate glass as other leaders in recent years have been. Both he and we live within one framework; we are constitutional subjects as he is a constitutional monarch. Both he and we are tied by bonds of family relationship: and a family is not only a group which can give the highest expression and satisfaction to the sentiments of affection; it is also a bridge over the generations—a bridge that spans the chasm of the grave and thus performs a social function no less important than the biological.

In the Royal Family we find a nucleus for our national sentiments; being in an equal relation to it we can all identify ourselves with each other in the common direction given to our good regard. That family is also a model we can copy, and in its human completeness we can find some compensation for our failures. It is refreshing that in a world split into ideological camps, divided by forceful though usually shallow doctrinal views on the pre-eminence of the economic basis of human associations, we can without denying the importance of these issues discern their limited relevance, and feel our way to a wider understanding of our personal and social life. Party factions may go on to the end of time; by the wisdom or petulance of the people, Governments will continue to fall and be replaced by others, destined in their turn to be dismissed; and a healthy discontent will thus find outlet for our divided feelings towards the central authority. But always we have in our Throne an outlet for affection, which, while untouched by party strife, touches our profoundest feelings.

With our King and our Princess we rejoice in the arrival of a new generation in Our Family. Four generations now span the slowly changing customs of our time, and a new arch has been added to the bridge that joins our past to our future.

Maternity

A SURVEY of the social and economic aspects of pregnancy and childbirth, produced jointly by the Royal College of Obstetricians and Gynæcologists and the Population Investigation Committee,[1] draws attention to the uneven working of our maternity services—to variations in antenatal care and in care during confinement, to shortcomings in some nursing-homes and hospitals, to the cost of attendance and of baby-clothes and equipment, and to unnecessary and unrelieved pain. It is based on an inquiry made by the health visitors of 424 maternity and child-welfare authorities (92% of all such authorities in England, Wales, and Scotland). The mothers of all babies born during the week March 3–9, 1946, were visited eight weeks after delivery, and interviews were completed with 90% of them. In all, 13,687 mothers helped by answering questionaries, 7287 of them on the availability and use of the maternity services, and 6400 on the medical and other costs associated with the birth of their children.

All sections of the community, it seems, make use of antenatal clinics, and the pregnancies of no less than 73% of women were supervised under local-authority schemes—54% at clinics, 5% by general practitioners working for local authorities, and 14% by municipal midwives. But "even in the most favourable conditions" less than half the mothers attend during the first three months of pregnancy, when antenatal supervision should begin if it is to have its best chance of preventing premature births and neonatal deaths, and of promoting breast-feeding. The committee regret that few local authorities take much trouble about advertising their antenatal services or encouraging women to attend early; and women may be actively discouraged by unsuitable premises for the clinic, and by the lack of an appointments system, which makes a visit awkward for multigravidæ who have to find someone to mind their children in their absence. Further, the standard of antenatal care is by no means always high. The committee points out that, if a doctor is consulted at every visit, the abnormal side of pregnancy may be emphasised; moreover, the midwife is deprived of the interesting part of her work at the clinic and loses authority when she comes to deliver the mother. But a more serious objection is that the doctor's examination—doubtless because he has other things waiting to be done—is apt to be hurried and inadequate. At one clinic visited the doctor had seen 29 women in 80 minutes, and at another he was over an hour late. In this second clinic the waiting-room was small and overcrowded and equipped with wooden benches. One mother complained that it is very trying, towards the end of a pregnancy, "to sit on a hard chair in an antenatal clinic for $2^1/_2$ hours waiting to be seen."

The difficulty of finding someone to look after the older children may prevent a mother from going to hospital to have her baby, even though her own home is unsuited to the purpose. "Many confinements," the committee found, "take place in appalling conditions of overcrowding." This does not appear to increase the actual risks of delivery, and

1. Maternity in Great Britain, London: Oxford University Press. 1948. Pp. 252. 12*s*. 6*d*.

indeed home delivery carries a low risk of stillbirth and neonatal death; but appearances are here deceptive, for about half of those originally booked for home delivery are finally admitted as unbooked cases to hospital, and among these the rates for stillbirth and neonatal death are very high. It seems that many women would prefer to have their babies at home, if they could have better homes and some help in them; but the majority would probably be glad to take the chance of getting away from their household cares for a week or two if they knew that all was well at home. At present, of course, there are not nearly enough beds, and many of those that exist are badly understaffed. The result is that women are often left alone for long periods during labour—a frightening experience which they would almost certainly avoid at home. The committee urge the need for more hospital staff, more domestic help, and better housing—agreeable commodities, but remote. It would be more constructive perhaps to consider in detail ways of using our present staff and accommodation to better advantage.

Many will be surprised to hear that only 5% of mothers confined at home, and only about half those confined in hospital, were given analgesia. Midwives are now allowed to give gas-and-oxygen with the Minnitt apparatus provided another person, acceptable to the patient, is present; but only since 1946 has their course included training in this method. During the preceding ten years practising midwives were so few that it was impossible to release many of them for such training, and in 1946 only one practising midwife in five held a certificate of proficiency. Fortunately the position has now improved; for the Central Midwives Board's latest report shows that, up to March 31 last, 6137 midwives had taken the board's certificate, while a further 4725 held certificates from other bodies. In addition to the Minnitt apparatus, midwives are nowadays trained to use the Walton-Minnitt, the Amwell, the Jecta, and the Talley gas-air apparatuses, and the board is anxious to make them proficient in the use of as many methods of relieving pain as the Royal College of Obstetricians and Gynæcologists approve. The great drawback to gas-and-air methods is the weight of the apparatus. It is too heavy to be carried conveniently on a bicycle, and some local authorities will neither provide a midwife with a car nor allow her a mileage or maintenance allowance if she uses her own. Some which will not provide a car arrange to have the apparatus delivered by ambulance at the mother's house, but others refuse even this service on the ground that it would encourage the midwives to ask to be taken to the confinement in the ambulance themselves! Also the Minnitt machines are still scarce, though supplies are improving; and even those in hospitals may be out of order and hence never used. To provide analgesia means a little extra trouble, which midwives may be unwilling to take unless the mother insists; and in some hospitals this difficulty has been overcome by requiring the midwife to state the reason why she has *not* given analgesia.

As might be expected, analysis of cases shows that certain groups of women are much more likely than others to have their pain relieved. Thus 48% of the women attended by doctors had some form of relief, compared with only 7·6% of those attended by midwives. Again, the wives of salaried and professional workers are almost twice as likely to be given analgesia as the wives of agricultural workers. Primiparæ are more likely to be relieved than multiparæ; but, even so, only 31% of manual workers' wives were given analgesia for their first confinement, compared with 63% of the wives of salaried and professional workers; while unmarried mothers come off particularly badly, only 20% of those confined at home getting analgesia. (This is largely because they seldom engage a doctor, and often book a midwife only a few days before the confinement.) In view of these findings it is not surprising that among complaints made by women dissatisfied with their treatment during labour lack of analgesia was the commonest. Yet here is a form of pain which can be predicted with certainty, and diminished with very little trouble. It serves no useful purpose, and may even deter some women from childbearing. King EDWARD's "if preventable why not prevented" applies here with uncomplicated force. The National Health Service gives all authorities the chance to raise their maternity services to the standard of the best, and here is a straightforward issue which they could tackle without delay. At present the woman who happens to be better off is getting preferential treatment.

Nurses and Their Pay

IT is good to see that less emphasis is now being put on the "shortage" of nurses and more on their proper use and proper training. In his lucid contribution to the Lords' debate reported on another page, Lord CROOK dwelt on the steady increase in the number of nurses: 7000 more are employed than a year ago, and 31,000 more than in 1938. "What the public fail to realise," he said, "is that over the last half of a century the nursing service has grown right out of its former relation with the growth of the population . . . but the greater part of the growth has been due rather to the new conception of social care and welfare upon which Parliament and the State as a whole has embarked." Today there are 2500 school nurses, and we are faced with a demand for some 8000 health visitors; there are the district nurses, and also the nurses in industry, whose number rose to a peak of 7000 during the war. If hospitals are to secure enough nurses to serve their increasing purposes they will have to alter some of the older ideas about the abnegation of personal freedom; they will have to reduce the domestic duties now devolving on the nurse; and they will have to introduce a shift system—wisely commended to hospital management committees in the latest red-book issued by the Ministry of Health. From the many suggested remedies for our present difficulties Lord CROOK made a perspicacious selection.

The debate also gave an inkling of what the Government have in mind for their promised Bill. Their evident intention is to separate responsibility for training nurses, on the one hand, and for providing nursing services on the other. The wisdom of this policy is already being challenged, and the South-East Metropolitan regional hospital board, supported

by others, has strongly deprecated the introduction of regional training councils to look after the training of nurses, and the removal from regional boards and management committees of all direct responsibility, administrative or financial, for such training. Nevertheless the advantages of separate financing of education have long been obvious,[1] and we welcome the Government's move in this direction, which is undoubtedly wiser than any attempt at sudden reform of the nursing curriculum. It must be recognised, however, that the whole conception of student status, which has so long dominated serious discussion, depends on the hospitals being able to recruit and retain enough trained staff; for otherwise the students' training is likely to be modified to meet other needs. The facts about loss of trained staff which King Edward's Hospital Fund has collected, and which we lately published,[2] show that much more attention will have to be given to this part of the problem.

Their Lordships were right in thinking that insufficient remuneration is not a primary cause of the present difficulties. Nevertheless the pay of the trained nurse is still on the agenda, and the recent revision of the arrangements for student nurses underlines the necessity for a new approach to the arrangements for those whose training is complete. Will the nurses state their own case with enough vigour? The Royal College of Nursing has been consulting its branches; and the salary it now suggests for the newly qualified staff nurse, says the *Nursing Times* of Nov. 6, "is £260 per annum, rising by £15 to £320, while the newly appointed ward sister starts at £310 per annum and rises by £20 annually to £430, and can by subsequent long-service increments, reach £470." At first glance this may seem reasonably satisfactory; but it appears that, after residence and other statutory deductions have been taken into account, the staff nurse's initial net income will be but £115, and that of the ward sister £150. The *Nursing Times* optimistically hopes that this "will enable them to enjoy those cultural and leisure pursuits so necessary for the balanced and valuable citizen of today, and will help to lessen the fear of financial anxiety on retirement." Of course, if the nurses do not ask for more, it is improbable that they will get it; but those in other professions will surely wonder whether it is enough. As a correspondent argued in these columns some time ago,[3] even the student nurse needs £100 a year, over and above residence, to meet her current outgoings on clothes, a modest allowance for holidays, and so on. The Government have since advanced towards this view: an allowance of about £200 per annum is now made to the student nurse as to various other categories of resident trainees, and after the deduction of residence, superannuation, income-tax, and other obligatory payments, she has about £75 a year for her personal expenditure. The question arises whether, if the trainee is recognised to need £75 for this purpose, it is sufficient to start the qualified staff nurse at a figure that will give her only £40 more. She is now a qualified and skilled worker, earning her own living, who ought to be in a position to give a little help at home if necessary and put a few pounds in the savings bank. True, her salary will slowly rise; but if she continues to work as a staff nurse, is she never to get more than £320 gross, which is £10 less than the newly qualified almoner who starts at £330? Something has surely gone wrong with the way in which these figures have been worked out: perhaps the picture has been confused by an attempt to keep the hospital nurse in relation with the non-resident health visitor or industrial nurse. The outsider would suppose that the staff nurse should receive at least £100 a year more than the trainee, and the ward sister more in proportion. It would be a pity if the prospect of getting and keeping more trained nurses were to be seriously prejudiced by too conservative and too self-effacing an approach on the part of the nurses themselves.

1. *Lancet*, 1947, i, 803, 835.
2. *Ibid*, Aug. 14, p. 266.
3. *Ibid*, 1947, i, 190.

Annotations

THE PLACE OF ELECTRO-ENCEPHALOGRAPHY

As soon as the electro-encephalograph was accepted as a useful tool in the hands of the clinician, it was introduced into departments of neurology and psychiatry throughout the United States. Now, with a lag determined by our conservatism, lack of opportunity, and the war, the same thing is happening here. Of course, every neurological or pyschiatric unit in this and every other country should have access to an electro-encephalograph, and, if it can employ it fully, should have its own; for there is no doubt that the apparatus can give information which is not to be had otherwise. With it, for instance, the different forms of epilepsy can be recognised, and treatment consequently determined. With it, also, the area of abnormal brain can be assessed, and even the severity of brain damage judged in patients who have local brain lesions. A final answer may be given to the suspicion that a brain abscess is present, or that late epilepsy is due to a tumour which has not yet caused any other symptoms or any signs.

But the trouble is that an electro-encephalograph is worse than useless without trained people to interpret its results, however many channels it may have and whatever its fidelity in recording. Two kinds of people must serve it—the recording technician who transfers the electrical activity of the brain to paper, and the physician who interprets the record and integrates the results with the other clinical evidence. This physician should be a trained neurologist or psychiatrist and he should also have considerable knowledge of electro-encephalography—its physics, physiology, and clinical application. A factual description of a record given by a technician, physicist, or physiologist rarely helps the clinician at all, and a clinical opinion upon the record given by a physiologist may mislead him, for he is impressed by the spurious objectivity of the report, which seems to him more securely based than his own opinion. It is quite essential, therefore, that an interested clinician should be available and trained before any institution sets up a department of electro-encephalography.

Jasper,[1] in his presidential address to the American Electro-encephalographic Society, outlines the development of the subject and draws attention to the present trend towards mediocre departments of routine investigation, from which little original work comes. Most of the work has been dull descriptive stuff, far removed from the fundamental investigation needed in so young a branch of physiology. He points to the limited extent of our knowledge of the physics of "brain waves" and of the physiological processes that determine their

1. Jasper, H. H. *Science*, Oct. 1, 1948, p. 343.

presence, and then he goes on to suggest many ways in which this knowledge could be increased. There are now societies of electro-encephalography in several countries and a journal will appear next year. But Jasper has found—and others in the States and in England will agree with him—that the volume and quality of original work has been disappointing. "Instead of representing a stimulus to more intense fundamental investigation, clinical applications have drawn us away from basic research. . . . The outcome has been a number of pseudo-scientific clinical investigations which have served only to burden editors and readers of scientific journals without providing a great attraction to more serious minded investigators concerned with the fundamental aspects of brain function." There appears, therefore, to be danger of criticism from two sides—the clinical and the physiological—presumably because the subject has a difficult position within both fields of work. The solution may lie in the use of a team, consisting of physicist, physiologist, and clinician, as well as the group of technicians. Such a unit would be far beyond the needs of most institutions, but it is necessary if the standard of work is to be maintained at a high level and if knowledge is to be increased. Even if most units are necessarily smaller than this, each should include a well-trained clinical worker who has knowledge of physiological method and who at least can work in close touch with academic physiologists.

CEREBROVASCULAR ACCIDENTS IN HYPERTENSION

THE precise nature of vascular accidents to the brain in hypertension is sometimes certain and at other times obscure. With the classical cerebral hæmorrhage or thrombosis the clinical picture is usually unmistakable, and the pathogenesis beyond question. A larger group of cases is characterised by transient paralysis, paresis, aphasia, or amaurosis. Such a syndrome, now known by the generic title of hypertensive encephalopathy,[1] may take an acute or chronic form. Acute encephalopathy occurs with the hypertension of acute nephritis and of toxæmia of pregnancy, and with acute exacerbations of chronic hypertension. The attacks, consisting of severe headache, drowsiness, vomiting, and convulsions, may be preceded or followed by focal cerebral signs which usually leave no stigmata in those who survive. Volhard's original suggestion that the immediate cause is acute œdema of the brain is now generally accepted; but it is still undecided whether this œdema is due to excessive or defective arteriolar constriction. The principal features of encephalopathy in chronic hypertension are its brief duration and the completeness of recovery from motor or sensory disturbances; there is, as a rule, no loss of consciousness. It has long been held that the disturbance is due to localised spasm of the cerebral arterioles. Pickering,[2] however, now postulates that it is the outcome of embolism or thrombosis. Cerebral arteries, he points out, have exceptionally thin walls, and the media of cerebral arterioles contain relatively little muscle tissue. This anatomical evidence against contractility is supported by physiological evidence of difficulty in producing vasoconstriction by either adrenaline or stimulation of the cervical sympathetic fibres. Pickering draws attention to the similarity of the cerebral syndrome in hypertensive encephalopathy with that in cerebral embolism due to mitral stenosis and auricular fibrillation. In both, he suggests, the mechanism is the same—namely, sudden organic occlusion. In hypertensive encephalopathy the eventual state varies between complete recovery and persistent paralysis. At the latter end of the scale thrombosis or embolism has always been acknowledged as the cause. He believes that the termination of transient disturbances is due to dislodgement of the embolus from a main artery; where the disturbance, though still temporary, is more protracted the embolus or thrombus may become canalised or collateral circulation develop.

Pickering's explanation—like others—is still largely based on hypothesis. But he is on firm ground in claiming that his suggestion "violates no cardinal principle in vascular physiology and is in harmony with the pathology of hypertensive disease."

1. Oppenheimer, B. B., Fishberg, A. N. *Arch. int. Med.* 1928, **41**, 264.
2. Pickering, G. W. *J. Amer. med. Ass.* 1948, **137**, 423.

THE CRIMINAL AND THE BENCH

"WRITE and tell him what you think of him, by all means," was the advice of an editor to a junior, and angry, member of his staff; "but don't send the letter." The same principle might be followed in courts of justice. Mr. Claud Mullins, giving the Maudsley lecture of the Royal Medico-Psychological Association on Nov. 12, considered it a weakness of our judicial system that sentences are usually passed within a very few minutes of the verdict being reached. Judges should be beyond emotion, yet some crimes, notably sexual offences, excite unreasonable anger in many people; and though it is unforgiveable, he said, to pass a sentence in anger, some criminals appear so unrepentant and defiant that magistrates, recorders, and even judges may be forgiven if they find them hateful. With even a smattering of psychiatric knowledge, however, judges could recognise such behaviour as a defensive reaction. The judge who forms his opinion of a prisoner by watching his conduct at the trial could hardly engage, Mr. Mullins suggested, in a more dangerous practice; and the lawyer who says "I can tell a rogue as soon as I see him" is deceiving himself: it simply cannot be done. The rule of passing sentence directly after the verdict has another drawback: it gives the magistrate no opportunity of getting further information about the prisoner—unless, indeed, such information is obtained before the trial starts. Since the prisoner is presumed innocent until he is proved guilty this too presents difficulties. Children and young people convicted of crimes are remanded while inquiries are made; and it might be wise to remand adult prisoners in the same way.

Early in his career as a magistrate, Mr. Mullins began to have doubts about our traditional methods of dealing with criminals; and he took the trouble to learn something of abnormal psychology, and to arrange for psychiatric treatment of convicted criminals who were willing to accept it. He has even managed to persuade some who had been acquitted for lack of evidence to accept treatment. The results were encouraging, especially with some sexual offenders, notably exhibitionists. He realises that such patients are not necessarily cured by psychiatric treatment: but they often give up behaving in a manner which is dangerous or annoying to others and so brings them into conflict with the law. Psychiatric treatment is not necessarily an alternative to punishment, he considers; indeed, wise punishment can satisfy a criminal's unconscious needs, and should have his approval. Unfortunately in a high proportion of cases the punishment is related to the crime, not the criminal. The new Criminal Justice Act gives express powers to the courts to arrange for a medical inquiry into the prisoner's case, provided he consents; but this is a practice which has been followed in enlightened courts for a long time. Whether or not the Act will bring better conditions depends on the willingness of the courts to use their powers. Psychiatrists, he suggested, must do what they can to form a body of public opinion favouring methods more likely to induce a change of attitude in the prisoner, and hence greater protection for the public. He quoted the case of a child sent to an

approved school for stealing, who later went to a borstal institution for the same offence, and still later was repeatedly imprisoned for stealing, getting longer and longer sentences, adding violence to theft as time went on, and at last being dubbed in the archaic legal phrase "an incorrigible rogue." Surely such a case may be considered a failure for legal methods of treatment; and if this is what such methods can do, surely psychiatrists are entitled to demand the right to help. A body of psychiatrists investigating legal procedure might consider better methods of selecting magistrates, the ways in which the laws of evidence are used to suppress facts, the ability of juries to decide on expert points, and the anomalous position in which experts giving evidence are sometimes placed. It would be better, he suggested, if experts were called by the court, and cross-examined by the advocates for both sides, instead of being called by one side and attacked by the other. Psychiatrists who offered to investigate criminal procedure would naturally be much criticised by the lawyers; but the large numbers of the recidivists produced under our present system would put them in a strong position. British legal procedure has a high reputation for justice, but he believes it places too high a value on advocacy. "A trial is too much like a sporting contest, both sides observing the Queensberry rules, with the bench as referee."

ANTICONVULSANT ACTION OF INTRAVENOUS PARALDEHYDE

PARALDEHYDE has long been used as a soporific and as an anæsthetic, but its use as an anticonvulsant is not so widely known. In 1919 Wechsler, of New York, after trying without success many known remedies to control convulsions in a hyperkinetic case of epidemic encephalitis, had recourse in desperation to intravenous paraldehyde, the effect of rectal paraldehyde having proved merely transient, never lasting more than a quarter of an hour. The intravenous dose was 1 ml., and "by the time the last drop was injected, literally before the needle was withdrawn, the patient quieted down and promptly fell asleep."[1] The first injection having proved successful, other injections of 1 ml. were given at various intervals each day for several days, and the patient recovered without sequelæ. The outcome led Wechsler to adopt this treatment in other cases of protracted convulsions, including status epilepticus. His results were various, but he concluded that intravenous paraldehyde was valuable in generalised epileptic seizures though liable to fail in convulsions due to gross organic change in the brain—e.g., tumour, subdural hæmatoma, and dementia paralytica.

The next uses of intravenous paraldehyde seem to have been as a 2–5% solution as an anæsthetic for short operations[2] and in a dose of 0·1–0·2 ml. per kg. of body-weight to induce anæsthesia for longer operations in which anæsthesia was subsequently maintained with ether.[3] No further work seems to have been described until the experiments on animals and clinical trials made by de Elío and his colleagues in Madrid, which were reported at the Dublin meeting of the Society of British Neurological Surgeons this year and have now been published.[4] They found by electro-encephalography that both in the cat and in man intravenous paraldehyde in doses of 0·2 ml. per kg. of body-weight either much reduced or abolished the motor activity of the cerebral cortex. Convulsions caused by neurosurgery stimulating the cortex and convulsions induced with leptazol were immediately abolished. Intravenous paraldehyde also protected animals against the effect of large doses of strychnine. This anticonvulsant action was observed even in decerebrate animals, spinal preparations, ganglionic synapses, and peripheral nerves, but its main action was on the cerebral cortex. In patients undergoing electric convulsion therapy intravenous paraldehyde raised the threshold of stimulation. No toxicity was observed with intravenous paraldehyde given in the recommended dosage.

1. Wechsler, I. S. *J. Amer. med. Ass.* 1940, **114**, 2198.
2. Bastedo, W. A. Materia Medica, Pharmacology, Therapeutics and Prescription Writing for Students and Practitioners. Philadelphia, 1932.
3. Nitzescu, I. I., Iacobovici, I. *Pr. méd.* 1934, **42**, 331.
4. de Elío, F. J., de Jalón, P. G., Obrador, S. *Rev. clin. esp.* 1948, **30**, 289.

INSTITUTE OF OPHTHALMOLOGY

AT the formal opening of the Institute of Ophthalmology on Nov. 4, a distinguished gathering, presided over by the Earl of Rothes, chairman of the board of management, listened to addresses by Sir John Parsons, F.R.S., the doyen of British ophthalmology, and by representatives of the New and Old World—Prof. Alan Woods, of the Wilmer institute of the Johns Hopkins University, and Prof. H. J. M. Weve, of the University of Utrecht. Under the direction of Sir Stewart Duke-Elder, the institute has been formed by pooling the resources of three London eye hospitals—Moorfields, the Royal Westminster, and the Central London. The last-named now forms the institute itself, and the beds so lost will be made up by increasing those in the other two hospitals. The institute will have the twofold function of research and teaching. Full-time research-workers are housed there in well-equipped laboratories, while clinical research will be carried on by the segregation of special types of eye disease and their routine examination by ophthalmic surgeons within the building. Courses are held for the D.O.M.S., and for the F.R.C.S. in ophthalmology, including practical instruction in operative techniques and laboratory methods.

On the same day, at an inaugural dinner, Sir Stewart Duke-Elder said that while the institute was not everything to be desired it marked a half-way house, or at least the end of the beginning. At last there was a place in London, away from the rush of hospital outpatients, where original work in ophthalmology could be done and where the scientific method could be practised.

SPECIALIST APPOINTMENTS

STATEMENTS about the shortage of specialists are heard with exasperation by the many young men who have trained for specialist employment but cannot find it. They complain that very few appointments are now being offered, and that meanwhile they and their families can hardly make ends meet. Under the National Health Service, they feel, this state of affairs should have ended: the hospital boards should be advertising a great many new posts to fill obvious deficiencies in their service to the public; or at least they should make temporary appointments. But the truth is that the boards can do nothing effective of this kind until they have reviewed their existing staff and have decided what their new establishment ought to be. The review has to be completed before April 1 next, since the new contracts are to run from that date.

The Ministry of Health advises[1] the boards to begin by considering the proper establishment of non-specialists (house-officers, registrars, &c.). "They should then consider how far the services given by the present specialist staff need modification to provide an adequate hospital service—e.g., whether further part-time service or additional whole-time posts are required, whether duties should be continued or redistributed."

> "In the same way boards should consider and determine the requirements for other medical and dental staff—e.g., consultant advisers to regional boards; general practitioners acting as medical officers of convalescent homes, &c., or as clinical assistants; general dental practitioners acting

1. Ministry of Health Memorandum RH 13 (48) 83, BG (48) 71.

as dental officers of hospitals; senior medical staff engaged on clinical work but not of specialist status."

Having determined the needs of their service in terms of whole-time and part-time posts, the boards must then decide which members of the existing staffs are of specialist status.

"In many instances the specialist status of the practitioner will be clear, deriving from the possession of academic qualifications, diplomas, &c., gained after postgraduate study, and from experience and practice as a consultant. In others—e.g., where a practitioner is engaged in general practice or in administrative work as well as in the clinical practice of a specialty—it will be necessary to have regard to length and nature of experience and to the practitioner's standing as a consultant amongst his colleagues. It is clear, however, that the determination of status cannot depend solely on the possession of postgraduate qualification, but must take account of experience, which may of itself suffice to warrant acceptance as a specialist; and that practice exclusively as a consultant or specialist cannot be applied as a criterion, since a number of practitioners engaging in other medical work may be qualified as specialists by experience or otherwise, and their services will be essential for the adequate staffing of the hospitals."

In assessing the status of their existing staffs a board of governors will be guided by its medical and dental committee, and a regional board by a special committee constituted as follows:

(*a*) Two general physicians, two general surgeons, and one obstetrician and gynæcologist practising (or retired from practice) in the area of the board;

(*b*) Two specialists of the branch under review, one of whom should be nominated by the appropriate university.

When these decisions have been made, and the terms of service and remuneration have been announced, the boards will be in a position to offer long-term contracts to their staffs, taking into account as far as possible the circumstances and preferences of the person concerned. "Only after posts have been offered to suitable existing staff on the new basis should any vacancies or additional posts be advertised for open competition."

PERCUSSION OF THE HEART

In this mechanical age some of the older methods of physical examination are lapsing into disuse. As long ago as 1923 Cabot [1] declared: "The longer I have tried to percuss the heart area, and the more I have watched others attempt to do so, correlating the results with post-mortem records and Röntgen findings, the less I believe in the value of cardiac percussion. I rarely attempt it." Such a view was naturally popular, for it was in keeping with the spirit of the times; and it simplified the physician's work, for learning to percuss accurately takes time, care, and thought. Radiography impresses the patient, and it has the real advantage of providing a permanent record. Thus despite occasional protests, such as that of Kurtz and White,[2] who showed that percussion compared favourably with fluoroscopy, the denigration of percussion continued, and it looked as if it had received the coup-de-grâce in the Lumleian lecture of 1936 [3]:

"As a final effort to resuscitate a dying method which is packed with fallacies and imperfections, there have been attempts to square the results of percussion with those of radiology, but they have led to nothing. . . . The tokens of sterility are upon it . . . in the light of X rays it will shrink into obsolescence."

A very different conclusion might be drawn from a report by Stroud and his associates,[4] who have compared measurements of the total transverse diameter of the heart by percussion and by radiography. With the chest vertical, the right border of the heart was percussed in the fourth intercostal space, and the left in the fifth space. Percussion was direct—"the stroke was made lightly and evenly by the pad of the middle finger of the right hand against the chest wall." In 305 males 74% of the measurements made in this way were within 10% of those obtained by radiology, whilst 88% were within 15%. Further analysis showed that 58% of the measurements from percussion were within 1 cm. of the X-ray measurement, while 89% were within 2 cm. In the 45 females examined 58% of the estimations by percussion were within 1 cm. of the X-ray measurement, and 90% were within 2 cm.

The X-ray enthusiast may protest that the total transverse diameter of the heart is a crude guide to cardiac enlargement; and both Kurtz and White and Stroud admit that by percussion the measurement for the left border tends to be greater, and for the right border less, than that obtained with X rays. On the other hand, except to the expert, X-ray estimation has its own mathematical hazards. The importance of radiography is no excuse for letting percussion become a forgotten art.

THE MIND IN ITS SETTING

In an old pantomime trick, the comedian undertakes to prove that the little man is as tall as the giant. And so he does, in terms of inches; but his tape-measure is made of elastic. Science, which has the duty of making exact measurements, also has the task of scrutinising its tape-measures, especially when these are relatively new and stretchable.

Tests for measuring intelligence, though convenient—more convenient, indeed, than is altogether convenient—should not be accepted too firmly as measuring a factor which we cannot even define. As a child grows, environment interacts with heredity to establish his intelligence. (If we doubt this, we need only consider those cases of children lost in infancy and reared by animals, whose abnormal environment brings them to a state indistinguishable from mental defect.) Hence an intelligence test, to be effective, must test the subject within the frame of his environmental experience. Or conversely, as Mr. Julian Blackburn, PH.D.,[1] puts it:

"the more unfamiliar an individual is with the kind of material embodied in a given test, the more he is unfamiliar with the kinds of techniques it is necessary to use in order to answer the test questions satisfactorily, the smaller his degree of sophistication about the tests, the less will the score he obtains be likely to represent his innate level of intelligence."

An extreme example, Dr. Blackburn suggests, would be to give a test designed for English school-children to an uneducated Nigerian boy: his innate intelligence would have little chance of revealing itself in such a situation. Similar, though less extreme, factors may account for differences in test scores between urban and rural children, northerners and southerners, and people in different social classes. In short, the tests are not the direct measure of innate intelligence they are meant to be: they measure, instead, a resultant of the forces of heredity and environment. Nor is the intelligence quotient a fixed star: it seems that negroes who migrate from the southern to the northern States of America show a rise in test scores; and, within limits, the longer the time a negro has spent in the north since his migration, the greater the rise in his I.Q. No doubt we all suffer some deprivations: we have abilities which are never given the chance to develop and which atrophy from lack of use; and we have no means of knowing, at present, how such local stunting

1. Cabot, R. C. Physicial Diagnosis. 8th ed., New York, 1923; p. 135.
2. Kurtz, C. M., White, P. D. *Amer. J. med. Sci.* 1928, **176**, 181.
3. Parkinson, J. *Lancet*, 1936, i, 1337.
4. Stroud, W. D., Stroud, M. W., Marshall, D. S. *Amer. Heart. J.* 1948, **35**, 780.

1. Influence of the Social Environment on Intelligence Test Scores. From the British Social Hygiene Council, Tavistock House North, Tavistock Square, London, W.C.1. 1948. Pp. 14. 1s.

affects mental growth as a whole, or whether it limits general intelligence.

Even the accepted behaviour of a group, Dr. Blackburn finds, influences test results. Tests based on language are done better, other things being equal, by those with a family tradition of literacy than by those whose interests are directed elsewhere. English-American children are used to competing for success, and come to the test prepared to do their best. North American Indians have no tradition of trying to do better than other people, and in some tribes no opinion is given on any question until a unanimous decision has been reached. In another tribe it is bad manners to reply to a question to which someone else in the company does not know the answer. Sometimes there is a rule that a member of the tribe should never reply unless he can be certain of his facts. Such high standards of manners and accuracy defeat the test situation, and rule out all chance of scoring on the lucky guess.

Again, people who take large numbers of tests, like those who make a hobby of crossword puzzles, develop insight into the way the setter's mind works, and score accordingly. Intelligence scores of recruits in the American army in the 1914–18 war showed a high positive correlation with the educational efficiency in the States from which the men came.

Nor are results uniform with different tests: the same group may differ by as much as 12 points in two different tests. If two groups give different results when tested with the *same* test, then it may be that one group was brighter than the other; but, as Dr. Blackburn points out, it may equally be that the test was better suited to the successful group. Finally, the I.Q. in identical twins brought up in the same environment differs on an average by 6 points: but who can say whether this reveals a difference in the twins or a flaw in the measuring-tape? The twins, with shared genes and experience, are perhaps a better measure of the test than the test is of the twins.

Dr. Blackburn suggests that comparisons between the scores of different groups are unreliable, and that much more experiment is needed before tests should be used on any wide scale for job selection.

FACTS ABOUT THE TSETSE

IT has been justly observed that the tsetse still governs large areas of Africa; in Nigeria, with a population of 20 million, half a million cases of trypanosomiasis have been treated during the past fifteen years. Some time ago the Colonial Office's trypanosomiasis committee appointed three investigators—Mr. T. A. M. Nash, D.SC., Prof. T. H. Davey, M.D., and Prof. P. A. Buxton, F.R.S.—to report on the incidence, and effects, of the tsetse fly in East and West Africa. Of their reports three[1] are obtainable now, and a fourth[2] will be on sale soon.

Action has already been taken on these reports, which were completed in 1946 and 1947. Thus in West Africa a research institute is being set up, while in East Africa a director of research and reclamation has been appointed. Perhaps the chief value of these accounts is in providing a comparative picture of conditions in the various colonies. This picture is certainly grim enough. In Nigeria, for example, only a fifth of the country is really safe for man and his cattle, and a third is an endemic sleeping-sickness area. The tsetse is found throughout the Gold Coast, where it prevents the people from keeping the large-humped Zebu cattle which might add enormously to the meat supply; sleeping-sickness is endemic in 37% of the country. Again, the whole of Sierra Leone is subject to the fly, and sleeping-sickness is endemic in a tenth of the country. No one method of tsetse eradication is consistently effective. In the north of Nigeria one species was destroyed by complete clearing of the undergrowth: in the south removal of the undergrowth encourages it. Jungle clearance—the chief method of combating the fly—has its problems. In some areas the sleeping-sickness service is recommending cutting trees, whereas the forestry service is recommending planting.

1. Nash, T. A. M. Anchau Rural Development and Settlement Scheme (3s. 6d.); Davey, T. H. Trypanosomiasis in British West Africa, 1947 (2s.). Buxton, P. A. Trypanosomiasis in Eastern Africa, 1947 (3s.). H.M. Stationery Office.
2. Nash, T. A. M. Tsetse Flies in British West Africa (30s.).

WORLD MENTAL HEALTH

WHEN it met in London last August the International Congress for Mental Health drew attention to the mental aspects of the main programmes of the World Health Organisation and urged that these aspects should have full attention. The executive board of W.H.O. has now approved this recommendation, and Dr. Brock Chisholm, the director-general, has announced that a mental-health programme for W.H.O. will be submitted next January to the board's third session. The World Health Assembly will be recommended to raise the low degree of priority hitherto accorded to this part of its work.

The World Federation for Mental Health, formed at the time of the international congress, is among the voluntary bodies now officially recognised for consultative purposes by the World Health Organisation and by UNESCO. The federation already comprises 21 mental-health associations of different nations, and others are likely to be admitted shortly. Dr. André Repond, of Switzerland, now vice-president, will succeed Dr. J. R. Rees as president next year. Prof. H. C. Rümke, of Holland, is chairman of the executive board, which will meet in Amsterdam in January. Arrangements are also now being made for the assembly of the federation to be held in Geneva next August.

VACCINIA AFTER BOXING

A SMALLPOX scare in Norway last September arose from a case presenting several curious features. The story begins with a young Norwegian soldier who had been vaccinated against smallpox in childhood and who came to England on Sept. 8 as a member of an Army athletic team. On the 15th and 17th he took part in a boxing competition. On the 20th he noticed a rash on his face, but he did not feel ill: indeed, he felt so well that before returning to Norway he indulged in much sight-seeing, visiting among other places the House of Commons. On his return to Norway his rash had developed into a pustular eruption and he was admitted to the Ullevaal Hospital on Sept. 25. The pustular eruption on his head, neck, and right upper arm must, it was thought, be due to one of two things—vaccinia or variola. If the cause was variola a large crop of secondary cases might be expected both in England and in Norway; but this aid to differential diagnosis would come too late for effective action. Material from the eruption was therefore sent by air to London for laboratory tests, and these tests showed the infection to be vaccinial. But how was it incurred? The patient was not aware of any contact with anyone who had recently been vaccinated.

Reporting the case to the Norwegian Medical Society on Nov. 3, Dr. Per Hanssen suggested that there may have been vaccinia pus on the boxing gloves of one or other of the three men with whom the patient boxed in London a few days before the first appearance of the rash. The length of the interval between the boxing and the appearance of the rash, and its limitation to just those parts of the body which are most exposed to abrasions during boxing, supported this explanation.

THE second World Health Assembly will be held next year in Rome, probably beginning on June 20. Britain's invitation to the assembly to meet in this country was withdrawn for economic reasons.

Special Articles

EDUCATING THE LAYMAN

HUNTERIAN SOCIETY'S DEBATE

LAST Monday the Hunterian Society met at the Apothecaries' Hall, London, under the chairmanship of Dr. G. R. MATHER CORDINER, their president, to debate the motion That the Practice of Instructing the Layman in the Nature and Treatment of Disease is being Carried to Excess.

Proposing the motion, Dr. W. J. O'DONOVAN pointed out that the public is instructed through all sorts of books, journals, and pamphlets. Who, he asked, were the people who were being thus taught? He himself had learned the right use of English by the classics; words had some meaning to him. Then he learned chemistry, anatomy, and other sciences, and only after that had he studied the mysteries of borborygmi. The public, on the other hand, was receiving medical instruction without any preliminary discipline; and doctors who took on this task were conveying the unknown to the unteachable.

The effect of teaching internal disease to the untaught and the interested was disastrous. Dr. O'Donovan mentioned as an instance of the way knowledge is gained and used by some lay people, soldiers who in the late war convinced presidents of medical boards that they had a "gastric stomach" and were therefore unfit to serve in dangerous places. There were, moreover, many unstable people among the public; and so potent was the effect on them of instruction that young patients would come and confidently assure their doctor that they had maternal fixation or an inferiority complex.

There was nothing sadder in our civilised life than the burden of consumption. Osler was persuaded that with the spread of knowledge incidence would diminish. The public now had knowledge; yet their fear of the disease had increased, and the consumptive had become almost an outcast. Where should the spread of knowledge be stopped? The answer was pragmatic. Knowledge should be imparted only if it was put to good use. Furthermore, was it good that the public should be aware of the occasional grave mishaps of medicine, and if aware would they trust the profession? In this connexion, could the truth ever be recognised by interested people, to whom mishaps loomed too large? As to informing the politician, Dr. O'Donovan asked: "Does he learn from us to aid the sick or to circumvent his opponent?" Was it good that doctors should teach medicine to their masters? It was not wise to expose the profession's weakness to those who might be its undoing and thus harm the public good.

Dr. O'Donovan denied that doctors have the necessary gifts of diction, argument, and logic with which to carry on teaching. How many, he asked, could teach medicine in such a way that their hearers understood and were not made more frightened? Instruction of the public should stop now; for they had not digested what they had already heard. Their indifference to the claims of Medicine when its body lay on the floor of Parliament showed him how uneducable they are. And what pathology were they most avid to learn? Murder most foul, arsenic, and old lace. A public avid for medical knowledge was a public to be pitied; and preoccupation with man's complexes and motives was not associated with stability and the pursuit of the pious virtues.

Opposing the motion, Dr. CHARLES HILL agreed that instruction should proceed only to the extent that it was useful; but by this he meant useful, not to the profession, but to the public. The work of health education demanded an explanation of medical knowledge. Moreover, "people demand to be relieved of the ex-cathedra pronouncements of the medical profession. They demand to have their intelligences appealed to by explanation."

In diphtheria and tuberculosis much had been done by explanation to dissipate fear; in fact no field of health education was more rewarding than tuberculosis. As for the encouragement of neurosis, the neurosis was already there; and medical instruction simply provided the neurotic with new material. Dr. O'Donovan had spoken as if the effect of instruction were to promote fear. This Dr. Hill denied; and he gave as an example instruction in the processes of cancer which, he claimed, could reduce the fear that lurked in many adult minds. Fear could, in fact, be dispersed by understanding of what actually happened in disease. As a profession doctors were apt to assume that medical knowledge was incapable of explanation to laymen. The attitude was that "only we can understand the mysteries of the human body."

Apart from health education, was it useful for the public to know about disease? Most people were interested in disease. They enjoyed ill health; it provided a conversational opportunity never to be missed, and some divided their lives into two parts—before and since their operation. To offer no explanation was to leave the public open to patent-medicine sellers, who were coining money from fear. The coated tongue, the heavy feeling behind the eyes—which were open to a very simple explanation—were built up by advertisements into elaborate syndromes. The doctor's duty was to counter such misinstruction.

Acknowledging the fact of public interest in disease, doctors should try to secure that information was based on physiology. The profession should also explain more about diagnosis and about treatment. Indeed patients had the right to know, though he conceded that regard must be had to the patient's mentality. In any event the old mystery surrounding the practice of medicine was dead; and silence was now interpreted gravely. Knowledge of health and disease was not the doctor's sole preserve.

By being more forthcoming, the doctor would foster a warmer and closer relationship with his patient. The feeling that the profession was a closed corporation with a secret corpus of knowledge had promoted misunderstanding in the last few years. Patients were not nearly so fearful with as without knowledge. "We lose sight of the fact that there are fascinating and romantic stories in the human body. Let us ring up the curtain. Let us assume that the public are as intelligent as we are."

Miss ARNOT ROBERTSON, seconding the motion, questioned the value of the instruction which had already gone out to the public. She quoted the case of a woman whose baby had lately been vaccinated at a famous hospital. According to the mother's account, this baby "came out in a black rash. I got all the doctors in front of me," and they admitted they had vaccinated the child with lymph from a black man's baby.

Visiting other houses, Miss Robertson was amazed at the little she had known and at the brave comportment of her friends; for their bathrooms were filled with medicine bottles. Some of the bottles were half full, indicating perhaps that the contents were being preserved against a return of a particular illness. These people were either bearing up wonderfully under a great load of disease, or they were hypochondriacs as a result of the barrage of suggestion in radio and press.

As a doctor's daughter, Miss Robertson expressed a healthy contempt for coloured mixtures; and she was pleased to have been reared at a time when no knowledge of medicine filtered through to the nursery. Her opinion was that the present flow of instruction simply increased suspicion. Doctors, by telling too much, promoted fear

and delayed treatment. The profession had been able to do much more good when the public had unquestioning confidence.

Miss BRONWEN LLOYD-WILLIAMS, who opposed the motion, pointed out that biology was taught in schools to give some understanding of positive health. The public needed also to learn something of disease. Likening the body to a machine, she claimed that people should be enabled to deal with minor repairs, and should know enough to recognise the moment when an expert mechanic should be called in.

There were, she suggested, four classes of people: the wilfully ignorant, the malades imaginaires, the know-alls, and the untaught. Doctors were inclined to frighten people by using technical terms. They still suffered from the power-complex cum high-priest attitude which had terrified an earlier generation. In this enlightened age, the spread of knowledge was inevitable, and among the benefits to be derived from it were: earlier diagnosis and treatment; the prompt recognition of serious disease by the patient, who would then have time to put his affairs in order; and improved coöperation between patient and doctor. No health service could work effectively without such coöperation. "I want to learn how to live—not just to be kept alive." Education could help the public to deal with the routine ills of everyday life. Miss Lloyd-Williams concluded with an appeal to doctors to come down from their aloof pedestal: "You want to help us: we want your help."

Of the subsequent speakers, one made the point that fear born of ignorance is worse than fear born of knowledge. Dr. KENNETH MCFADYEAN quoted one of the more famous sulpha drugs and radium as examples of how, with some knowledge, the purpose and effects of remedies might be misunderstood and cause alarm. To some minds, he said, the application of radium meant only one thing—cancer.

Mr. A. DICKSON WRIGHT gave eloquent support to the motion. The hardest patients to deal with, in his experience, were those who knew most about themselves; it was much easier to gain the confidence of the ignorant. In two countries which were far ahead of Britain in health education, he had been impressed by the prevalence of quackery and by the amount of patent medicines in the homes. People from one of these countries reported to the hospital outpatient department with lists of questions; these were, in Charcot's words, *malades du petit papier*. Instruction in the first signs of cancer brought to the hospital more cancerophobes than early cases of malignant disease. On the other hand, he had repeatedly seen people in the nursing and medical professions who, having malignant disease, had let their condition drift until too late. The less people knew, the happier they were. In support of this contention he mentioned medical students who, even after training in the basic sciences, were commonly gross hypochondriacs.

Nevertheless, the motion was lost by 56 to 41 votes.

REPRESENTATION OF SPECIALISTS

AN exploratory committee [1] met in September, under the chairmanship of Sir Lionel Whitby, and put forward suggestions for the formation of a joint committee to represent consultants and specialists. Discussion of these suggestions by the Royal Colleges has been private, but the gist of them now appears in a report of the central consultants and specialists committee of the British Medical Association, held on Nov. 4. [2] This announces the composition of the joint committee, on which seats are allocated as follows: Royal College of Physicians, 3; Royal College of Surgeons, 3; Royal College of Obstetricians and Gynæcologists, 2; Royal College of Physicians of Edinburgh, 1; Royal College of Surgeons of Edinburgh, 1; Royal Faculty of Physicians and Surgeons of Glasgow, 1; British Medical Association, 6. There are to be two secretaries, one appointed by the colleges and corporations and the other by the B.M.A. consultants and specialists committee. The B.M.A. committee accepted these proposals.

1. See *Lancet*, Aug. 7, pp. 221 and 233.
2. *Brit. med. J.* Nov. 13, suppl. p. 173.

FREEDOM IN MEDICINE

NEW ORGANISATION FOUNDED

SOME seven hundred doctors, meeting at Caxton Hall, London, last Saturday, voted for the establishment of a new body, to be known as the Fellowship for Freedom in Medicine. Lord HORDER was elected chairman. The following resolution, put by Dr. A. V. RUSSELL (Wolverhampton) was passed:

> That the fellowship is not in opposition to any existing medical organisations, but is prepared to strengthen their hands in so far as they are prepared to work for the maintenance of medical freedom.

STATEMENT BY LORD HORDER

Lord HORDER traced the origin of the meeting from the time, last June, when the medical press published a letter [1] by him "inviting the views of any who were concerned about the practice of medicine in this country as the result of the collapse in the resistance of the B.M.A. against the introduction of the unamended National Health Service Act."

The response to this invitation, said Lord Horder, was unexpectedly prompt and large. At first letters came mainly from men and women who had not joined the service, but latterly they had come mainly from practitioners in the service. Altogether he had received over 1700 letters expressing concurrence that something should be done to ensure the freedom of medicine from outside control; and letters were still arriving at the rate of about 20 a day. He had also received several hundred additional letters, many of them offering constructive suggestions.

He had nominated six colleagues—three general practitioners and three specialists—to help in the analysis of these letters. As the work increased, these six added six others, again with equal distribution between general and specialist status, and with due regard to the provinces. This group of twelve had acted as an informal interim committee, under Lord Horder's chairmanship, with Dr. Reginald Hale-White as vice-chairman, Mr. Reginald Payne as hon. treasurer, and Dr. E. C. Warner and Dr. G. H. Rossdale as hon. secretaries. The meeting, said Lord Horder, was one of friends, friends of friends, and those who had written sympathetically; so far the profession as a whole had not been approached.

At the special representative meeting last May, the B.M.A. had its last chance of urging resistance against the dragooning of the profession by politicians; that chance was thrown away. "In January we marched unitedly and effectively: in May, more like a rabble, we surrendered." The trouble began, however, much earlier. "From the very start we have lacked dignity and a due apppreciation of our use and value in society. We let ourselves be used as pawns in the game instead of master pieces." The profession's own weakness was partly responsible for the National Health Service being born in dishonour; "for we allowed ourselves to be a party in the mad precipitancy of the Government, whereby the public was made to contract for health benefits which did not exist."

"What, today, is the result of all this? The living power of medicine, resident as this has always been, and

1. *Lancet*, 1948, i, 965.

always must be, in the personnel of the profession, has passed out of its hands to be lost—let us hope only for a time—in the dead machinery of the bureau. Medicine has indeed become . . . a branch of the Civil Service. We are no longer experts. We sit and sign forms. With no time to diagnose their diseases we pass our patients to other persons and to institutions, knowing full well that these cannot dispense the health benefits which may be needed.

"In the economic field doctors have been manœuvred into surprising positions. Some are faced with serious financial insecurity. Others are making bigger incomes than they formerly did, but are doing less doctoring in return. And the appalling thing is that it is Dr. Peter who is paying Dr. Paul."

The responsibility for a high standard in medicine lies with none but the doctor, for he alone can tell what is good doctoring and what is bad. "We must bestir ourselves and come to grips with the situation." The essence of good doctoring is diagnosis; and diagnosis calls for time and a close-up with the patient, both of which are at the moment denied to thousands of practitioners. Good doctoring calls also for two other things that concern the doctor personally and which seem now to be lacking—a feeling of satisfaction in the work he is doing, and a sense of economic security.

The purpose of the new organisation should be akin to that of the old city guilds, which stood for a high standard in the craft they pursued and took powers to preserve it in the public interest as well as in their own. The aim should be to keep the standard of British medicine and British doctoring at the high level which it has attained, and to assist the State in making the best that is in medicine available to the whole community.

Lord Horder concluded: "Our hand should be against no man. We are a breakaway from no other body; we exist for a primary purpose which I have tried to make clear. If, and when, we are confident that the B.M.A., whether by reconstitution or otherwise, and/or the Royal Colleges accept, and carry out, the obligation to the public for which we ourselves stand we can dissolve into thin air." As to the future of medicine, "I am still an optimist. We who are here are the custodians of medicine for our patients. Let us look to our charge. Today it needs all our vigilance and all our care."

FURTHER RESOLUTIONS

The meeting passed the following resolutions, the first proposed by Dr. L. W. BATTEN and the second by Dr. D. R. GOODFELLOW (Manchester):

> As this body is deeply disturbed by the way outside influences may affect the quality of medicine in this country, it is determined to do everything in its power to render the highest standards of practice possible in the future.
>
> That the executive committee be asked to consider ways in which freedom in medical matters can best be preserved by the profession.

OFFICE-BEARERS

The following office-bearers were appointed:

Chairman, Lord Horder; vice-chairman, Dr. Hale-White; hon. treasurer, Mr. Payne; hon. secretaries, Dr. Warner and Dr. Rossdale.

The executive committee is to consist of 20 members, of whom 10 were elected, as follows:

Dr. A. C. E. Breach (Orpington); Dr. S. F. L. Dahne (Reading); Dr. Frank Gray; Dr. A. V. Russell (Wolverhampton); Dr. G. M. Goodwille (Attleborough, Norfolk); Dr. D. R. Goodfellow (Manchester); Dr. Barbara Abercromby (Liverpool); Dr. Campbell Shaw (Bournemouth); Dr. J. G. Thwaites (Brighton); Prof. K. D. Wilkinson (Birmingham).

The minimum annual subscription was fixed at one guinea. A constitution is to be drafted by the executive committee and placed before the next general meeting.

THERAPEUTIC SUBSTANCES REGULATIONS

NEW regulations[1] made under the Therapeutic Substances Act, 1925, will come into force on Dec. 1.

Diphtheria Prophylactic.—The position with regard to this prophylactic is clarified. The Therapeutic Substances Regulations, 1931, have one schedule covering all types of this substance. This schedule is now amended setting out (1) the general provisions applicable to all types of the prophylactic, and (2) special provisions applicable to each type.

Antitoxins and Antisera.—The 1931 regulations contain ten schedules for the substances of this class which differ in a few words and phrases only. The regulations have now been recast to provide for (1) a general schedule stating the requirements common to all these substances, and (2) a series of short special schedules each relating to a particular antitoxin or antiserum. The provisions applicable to antidysenteric serum (Shiga), other antidysenteric sera, and antipneumococcal sera set out in the principal regulations have been omitted from the amending regulations. It is considered that sulphaguanidine has rendered the use of antidysenteric serum obsolete, and that sulphonamides and penicillin have done the same for antipneumococcal serum.

Additional Substances to be Controlled.—Preparations of human blood, and organic substances having the specific biological action of curare on neuromuscular transmission have been added to the schedule to the Act, as being substances or preparations the purity or potency of which cannot be adequately tested by chemical means. Preparations of human blood include any serum or plasma made from human blood and any dried product prepared from any serum, plasma, protein, or other substance. Organic substances having the specific biological action of curare on neuromuscular transmission include *d*-tubocurarine chloride and its preparations.

Penicillin.—A more precise definition of penicillin and preparations of penicillin to be controlled has been made.

Labelling of Therapeutic Substances.—Regulation 10 (1) of the 1931 regulations has been amended, requiring that the vial or other container in which a therapeutic substance is offered for sale shall bear a label affixed by the manufacturer. This amendment is designed to control the changing of labels by persons other than the manufacturers. A further amendment permits the required particulars to be indelibly marked on the vial in place of being printed on a label.

FACULTY OF OPHTHALMOLOGISTS

BETWEEN the two world wars several visits were made by groups of ophthalmic surgeons to European and American clinics. These were organised by the late Percival Hay, of Sheffield, on behalf of the North of England Ophthalmological Society, and were successful in the spread of knowledge and in international fellowship.

The idea has been taken up afresh by the Faculty of Ophthalmologists, and last spring three parties of twenty surgeons visited Holland, Switzerland, and Paris. The travellers are unanimous in praise of the unstinting cordiality and courtesy which they received at all the centres which they visited. Instruction and information on special techniques and research were freely given, evidently after careful preparation.

The party to Holland was organised and led by Mr. John Foster, of Leeds. Visits were made to the Hague, Scheveningen, Utrecht, Gröningen, Amsterdam, and Leiden, where Professor van der Hoeve, the doyen of Dutch ophthalmology, together with his assistants, read several discourses in English and demonstrated a corneal-graft operation. At Utrecht Professor Weve performed the operations of intracapsular extraction of cataract, diathermy for detached retina, and dacryocystorhinostomy.

The tour of Switzerland was organised by Mr. W. M. Muirhead and Mr. A. B. Nutt, of Sheffield. Zürich, Berne, and Geneva were visited.

The journey to Paris was organised by Mr. R. J. Buxton.

1. Therapeutic Substances Amendment Regulations, 1948. Statutory Instruments, 1948, no. 2418.

The Act in Action

2. THE GENERAL PRACTITIONER

As winter approaches, practitioners are taking stock. Some are finding things worse then they hoped, and others better than they expected; but nearly all agree that, whatever epidemics may befall the country, their section of the service will not break down. Acute illness has never gone untreated in Britain; so in this respect their burden will be no heavier than in other winters. If, however, in the busy winter months the doctor is to give due attention to the seriously ill, he will have to save time on surgeries swollen by the addition of those who for the first time are able to turn to him for the treatment of minor disorders.

Whatever the doctor's view, the public has welcomed the new service; and when the final count is made it may be found that between 90% and 95% of people have entered their names with practitioners. Both doctor and patient are pleased with their new and easier relationship. Before July 5 doctors were unhappily familiar with the words of the less well-to-do uninsured patient once on the road to convalescence: "I think I'll get along all right now, doctor"—meaning that the family wished to be spared further fees. That is ended. Patients are also gratified to observe that the new service is truly comprehensive, as is evidenced in the domiciliary consultant system—which, though surprisingly seldom used, seems to be working well. Complaints are few. The principal cause of complaint is the time spent in waiting to be seen at the surgery. A further cause—not strictly medical—is delay in payment of National Insurance benefits. Whereas formerly insured people who had become unfit for work were visited by the representative of a friendly society and received some immediate payment, the National Insurance certificate must now be taken to a local office and payment is delayed.

IN AND OUT

Those patients remaining outside the service are mostly the rich and the elderly. They include some who prefer to obtain the doctor's personal attention by personal contract, others who believe that in this way they will get better attention, and still others who, perhaps living at some distance from the surgery, are willing to pay for a visit not warranted by clinical need. In contrast with the experience of most others, a doctor outside the service who is practising in a residential area reports that the patients coming to her are of no particular financial, social, or age group. Unfortunately there are instances of ailing patients, ignorant of the allocation system, who have not benefited by the service because no doctor would accept them on his list.

In joining the service most people seem genuinely to believe that it really can provide for their needs. Sometimes, however, patients seem to have joined simply because they would otherwise be unable to obtain free medicines; and those doctors who have stayed out of the service, as well as some in it, argue emphatically that such patients should be allowed to obtain drugs without charge, even if the range were restricted to non-proprietary compounds. Patients sometimes have joined from a determination to get some return for their contributions under the National Insurance Act, believing mistakenly that what they contribute goes entirely towards the cost of the medical service. Others, again confusing the two Acts, think that they must enter their name with a doctor in the same way that they register for insurance.

In deciding whether to enter or to stand apart from the new service, many patients are undoubtedly influenced by the attitude of their doctors. Some of these underline the advantages to be gained by the private patient—more leisurely attention, visits on request, and consultations by appointment. Many of these doctors have always restricted themselves to a small number of patients, to whom they have given a very high order of medical care; and they point out that with a capitation fee sufficient to provide something approaching their former income they would not attempt to persuade their patients to stay out.

Other doctors do not discriminate between private and N.H.S. patients, except that they may visit the former on request, regardless of clinical urgency. One practitioner in the North Country says that quite a large number of his patients decided to stay out of the service until he pointed out that, except in respect of such visits, he proposed to give equal attention to everyone; all except three have now entered the service. Nevertheless, the understandable spirit of personal contract lingers on; and former private patients now commonly express their appreciation by presents.

GOING AND COMING

The war years and publicity in the press have impressed the lay mind with the idea that the doctor is a very busy man. The autumn is, of course, normally a slack season; but practitioners, whether in town or country, agree that they are making hardly any more—and sometimes fewer—visits than they usually do at this time of year. The public are responding well to the appeal to get in touch with the doctor early in the day when a visit is required; the occasional exceptions are mostly mothers reluctant to bring their children to the surgery, and patients who, knowing the doctor to be hard-pressed, hopefully decide in the morning not to send for him, only to find later in the day that their optimism is unjustified.

In some parts coöperation over attendance at surgery is not so good, patients tending to come en masse towards the end, in the hope of being seen at once. The numbers attending have risen, according to the area, by between a quarter and a half. Every account agrees that frivolous complaints are no commoner than before; in some parts, however, there is slightly increased readiness to attend with trivial disorders. As was to be expected, the start of the service has brought to light untreated illness in the old, in children, and in women. The amount of hitherto undisclosed illness is particularly large in women, many of whom have suffered for years from such chronic disorders as prolapse of the uterus without referring to a doctor.

SAVING TIME

Many practitioners are convinced that more will have to be done to reduce the time taken up by surgeries; and some, particularly in industrial areas, contend that the case for the immediate construction of health centres, from prefabricated units or by conversion of existing houses, is unanswerable. In some places waiting-rooms have always been too small, patients spilling over into street or alleyway. Such waiting-rooms—often not only small but dark and stuffy—are the best imaginable places for spreading infectious diseases and thus adding to the doctor's work. Even in the better-to-do districts some waiting-rooms are too small for the new demand; and in certain instances practitioners are having extensions built at their own expense, though well aware that the need will pass when centres are built. Moreover, centres, by affording more space and separate examination rooms, can save time in the interviewing of patients; and if a nurse or other qualified attendant worked there the doctor could be largely relieved of such time-consuming duties as the giving of injections and the application of dressings. It is even reasoned that if qualified nurses are too few the voluntary spirit should be given an opportunity for expression by the employment of V.A.D.s or similar auxiliaries. Health centres are pictured

not as a desirable supplement to be added when times are better but as an immediate necessity. Their construction would have two effects: first, it would benefit patients by enabling the doctor to give more time to his proper work; and secondly it would relieve hospitals of a host of trivialities which the practitioner now has to pass on to them. From a crowded surgery the patient with a scalp wound must perforce be sent to hospital. At a centre the nurse could cut the hair and clean the wound; and the doctor would find time to insert stitches.

Many maintain that in the long run better use of the doctor's time would be gained by improved health education, aimed at persuading patients to report serious illness in its earliest stages, and at helping people to recognise the minor disorders which do not need medical attention.

PAPER WORK

The record system under the Act differs little from that under National Health Insurance. All practitioners agree on the need for complete records, though some find it impossible at the end of a day to note each visit. Similarly, no serious objection has been voiced against the certificates issuable under the National Insurance Act, though it is sometimes held that their number should for convenience be fewer than the existing six—first, intermediate, final, convalescent, monthly, and voluntary. On the other hand, the additional certificates for clubs and employers—though a fee is chargeable—are a grave annoyance to many, who believe that all such further certificates should be abolished by using the insurance certificate for these purposes.

Since 1939 the practitioner has become conditioned to filling in certificates dealing with such varied topics as extra milk or coal, new houses, and brassières and corsets. These he writes ungrudgingly, though holding that some are a waste of his time and that others (notably form 2C for extra milk) should be renewable at longer intervals. One form, however, is most vehemently described as a pointless farce; this is O.S.C.1, which each patient has to obtain from his doctor before first having his vision tested. The object of this form is supposedly to ensure that patients with visual disturbance who have some other disorder shall receive medical attention. No practitioner interviewed believes that the present procedure has the slightest value to this end. "The local optician," said one, "knows a great deal more about eyes than I do. So any patient wanting his eyes tested is referred back to me by the optician if the visual disturbance is secondary to some other disease. In this way the patient has a double wait at my surgery." Some would welcome control on the patients seeking spectacles, but no-one appears to believe that even for this purpose the procedure is effective.

The time taken up by the patient wanting a certificate is not simply the time needed to reach a decision and sign the paper. A mother wanting extra coal often opens the interview by requesting examination of her baby's chest; only when the child has been stripped and examined is her true purpose disclosed. Others ask quickly enough for the form, and then say: "While I am here, doctor . . ." going on to explain some minor disorder which in itself would not warrant their coming to the surgery. There is thus good reason for reducing as far as possible the number of attendances for forms and certificates; and the doctor sometimes regrets that he is not empowered to instruct the pharmacist to repeat prescriptions.

OTHER EFFECTS

In some ways the doctor's work is now less complex. Some, for example, with fewer private accounts no longer need secretaries. Many more have gladly closed their dispensaries. Hitherto the practitioner dispensed medicines for any of several reasons: the patient's convenience; regard for a local tradition; a desire to keep down the patient's expenses; and profit to the practice. Doctors' dispensaries now survive only in country areas and occasionally as an additional service to private patients.

To the doctor's wife the new régime has made little difference. At first in some practices there was a steady flow of inquiries by patients uncertain how to obtain benefit under the Act. Now the commonest difference reported is a reduction in the stream of telephone calls throughout the day; this is attributed to greater heed for the doctor's convenience by those who no longer pay for each item of service. On the other hand, the burden is increased by overflowing waiting-rooms and prolonged surgery hours; and wives, it seems, await the establishment of health centres even more eagerly than their husbands.

TERMS OF SERVICE

It is still too early to judge the full effects of the new conditions on the practitioner's earnings; but certain trends are already clear. On the present showing, the income of some in residential and rich suburban areas has fallen by as much as 50–60%, whereas in compact industrial practices incomes have risen by a quarter or more. On the average practitioners seem to believe that their annual earnings will be reduced by about a third. At the same time the amount of work and responsibility has increased. Most contend that under the present system the capitation fee should be increased to at least £1; and it is thought that the appropriate Whitley council will be easily persuaded of the need. But opinion favours, as a preferable alternative, a sliding-scale of fees, to encourage small practices. The number of patients that each doctor can look after properly is set at between 2000 and 3000, according to temperament and the compactness of the practice. If patients were distributed equally between practices in each area, doctors would seldom find themselves with more than 2500 patients; yet some have very substantially more. The balance may partly right itself by patients wearying of waiting at overcrowded surgeries; nevertheless most practitioners wish that their income could be determined by some further criterion than numbers.

Perhaps the least contented of all doctors just now are those who, having achieved special experience and gained higher qualifications, entered general practice. They assert—not without reason—that they have done much to maintain and enhance standards of practice. Yet those who hold posts at hospitals in medium-sized towns believe that they may soon be supplanted by whole-time hospital officers; and in actual general practice they are financially on the same footing as all others. None of them seems confident that their case will receive attention. The younger are busily detaching themselves from general practice to devote all their time to a specialty; the older see themselves as the last of a dying race.

Other difficulties can perhaps be more easily overcome. For such equipment as cotton-wool, sutures, spirit, and needles, there is an allowance of 2*s.* 6*d.* per 100 patients per annum. Thus with 2000 patients the total allowance would go on 8 lb. of cotton-wool at 6*s.* per lb. All expendable equipment, it is argued, should be replaced free. There is particular discontent over the lack of any encouragement to purchase necessary apparatus; for here the purchaser cannot even claim income-tax relief. "The present arrangement," as one practitioner put it, "encourages us to try and get by without doing our job conscientiously."

Country doctors are outspokenly dissatisfied with the mileage allowance, in the determining of which, they say, regard should be had for the time lost to professional

work. Those with localised practices complain that, no allowance being made for distances under 2 miles, they have to bear most, if not all, of the expense of their car. As regards basic salary, this should come, it is maintained, not from the local pool but from the central, or a separate, fund. By a few, who compare the position of doctors with that of dentists and opticians, restriction of the global sum payable to practitioners is seen as an eventual handicap to professional initiative.

The young doctor wishing to enter general practice is still confronted by formidable difficulties. If he should try to start on his own, he discovers that houses are hard to find and expensive to convert; payment for his services under the Act comes three months in arrears; and local medical committees—even in apparently under-doctored areas—are very cautious in meeting his request for a basic salary.

CONCLUSION

Most practitioners regret that the price of more equal attention for all must be less attention for each. In the long view the only solution is to have more doctors, and in the short to conserve the doctor's time for his strictly professional work. At one pole the acutely ill patient, and at the other the patient with mild bronchitis, are likely to fare no differently than they have hitherto. Between these two extremes the difference threatens to be substantial. Many doctors have little time now to investigate home conditions, to give considered advice, or to attempt psychotherapy; and hardly any have the leisure to supply extra services—such as circumcision of infants, which many people prefer to have done by their own rather than by a hospital doctor. By some practitioners the start of the new service has been made the occasion for lightening the burden of contract; for example, sensing that patients no longer expect the strictly personal service hitherto demanded, a few have planned to zone their practices this winter. But most cling to the concept of personal service as the essence of general practice.

The majority of doctors, like the majority of patients, have faith in the service. Just now some are discouraged by an apparent lack of enthusiasm among those organising and administering the service at the top; the risk, it seems, is that all may forget that this service is the best yet provided. Others are disheartened that their professional colleagues on various bodies seem slow in integrating the service for the common weal, and some of the local medical committees are coming in for particularly severe strictures. Individualism, once counted a virtue, seems to spell disaster in the committee room. The present danger is that those who entered the service grudgingly may become confirmed in their resentment.

"Modern stress on the prevention of disease and the promotion of health has so far not affected the basic content or philosophy of the practice or teaching of clinical medicine to any appreciable degree. Clinicians still think almost exclusively in terms of diagnostic and curative service and look to the specialists in public health to provide the developments in preventive and promotive outlook and service which they freely admit to be desirable. The specialists in public health are able to influence administrative developments, but relatively unable to affect the basic philosophy of medical practice. . . . One of the most important factors in the implementation of a programme of Social Medicine will be a new scientific and philosophic approach to the science of ætiology in medicine which will give the clinician and the public health specialist a common approach to reform. . . . The essential point . . . is the concept that ætiology is usually multiple and that it should be approached from the point of view of three groups of contributory factors: (1) a constitutional trend or diathesis; (2) negative factors—i.e., deficiency of health-promotive factors; (3) positive factors—i.e., disease-producing agents. . . . It is already possible to give a rational although incomplete ætiology for all disease in terms of this triad."—Prof. J. F. BROCK, *S. Afr. med. J.* July 10, 1948.

Disabilities

17. ASTHMA

AFTER the serious disorders dealt with already in this series, asthma must seem but a minor disability; and indeed in a way it is. But not to the victim. The importance of a disorder within one's own personal universe is measured by a different rule from that one applies to the illness of others. Asthma is certainly a major factor in my life, as it must be with most sufferers. But the numerous physicians with whom I have discussed my case and those of my asthmatic patients have never seemed to appreciate the extent of the handicap. "You are all right between attacks?" they ask, and we usually reply inaccurately that we are. "Good" they say; "well this will lessen the frequency and intensity of the attacks. . . . And you know," they conclude happily, "no-one ever died of asthma."

I do not want to be unfair to my colleagues, and I know I must have treated patients much in this way. The reason is plain enough. Asthma is a condition in which successful therapy is extremely difficult as can be seen from the great variety of treatments.

For a long time I believed that one reason for the difficulty was that the name covered several diseases of widely varied ætiology. These included allergies to food, inhaled protein dust (dandruff, pollen, &c.), and bacteria; metabolic types probably associated with mineral imbalance; reflex irritation; autonomic irregularities; endocrine types; and purely psychological disorders—not to mention the cardiac and renal asthmas, which are separate entities. I now believe this to be a wrong approach. It seems better to regard the asthmatic attack as a constitutional response to an excitant. The immediate cause of the attack may be usually the same but not necessarily always so. A patient who is allergic to fish and various animal hair—as I am—may also start wheezing from purely reflex stimulation or psychological causes. A drop of saliva swallowed "the wrong way," touching some spot that seems to me to be around the pyriform fossa, starts an immediate spasm. Again, when breathing quite freely I once saw a child run into the road in front of an approaching car, and in thirty seconds I was hanging on to the railings—so bad was the dyspnœa.

Without the facilities of a Draper[1] it is impossible to analyse completely the constitutional type of the asthmatic; but a generalisation from personal observations may perhaps be allowed. Most asthmatics are temperamental, egocentric, introspective, and imaginative. They tend to be over-sexed rather than under-sexed. They are sensitive, in the lay sense of the word. More than most, they crave affection and attention, and many an attack can be traced to frustration in this direction. The physical type in my experience is generally asthenic, though I know a number of the athletic constitution. True pyknics seem to be seldom asthmatic; the condition is frequent enough in fat women over middle age, but here the basic type is obscured. My impression is that fewer asthmatics are blond than might be expected from the proportion of blonds in the population.

But enough of generalities. Let us turn to the disability. First I have phases of relative or almost complete freedom for weeks, and these are succeeded by weeks or months when every day or night is marked by some wheezing and dyspnœa. During the active phases attacks are more frequent at night and I wake breathless from once to five or six times. In the morning at these times there is nearly always wheezing and some cough, with expectoration of three or four plugs of extremely gelatinous mucus. A cup of tea as hot as

1. Draper, G. Human Constitution. Philadelphia and London, 1924.

possible aids this expectoration, and indeed generally affords a good measure of relief of the dyspnœa. By the time I set out on my rounds breathing is usually comfortable and may stay so most of the day. But a steep hill or several flights of stairs may suddenly produce a constricting feeling round the chest, and a sensation in the legs best described as a tingling and weakness. I halt and use my atomiser (of which more anon) and after a minute or so can go on at a slower pace and wary for the next attack.

The sensation in the legs is characteristic and I believe is due to anoxæmia. It can be duplicated easily in the arm by the sphygmomanometer cuff. The interesting points are that the onset of this vascular sensation may follow the respiratory spasm so quickly and that the weakness is so marked. Yet recovery from these symptoms can be equally rapid. Further they are not inevitable concomitants of the respiratory difficulty. The circulatory discomfort in the thighs and legs cannot be ascribed to cardiovascular disease, for in my free phases I can play vigorous tennis, squash, or golf without distress.

When the exigencies of practice prevent my having any exercise, attacks are more frequent and severe. I am convinced that every asthmatic should exercise regularly, and best under supervision so that activity can be properly graded. Loose arm-swinging exercises are admirable and should be done on rising and retiring. When I remember I practise them myself. Even when some degree of dyspnœa is present, loose arm-swinging in the widest arcs can be done, and will indeed help by improving thoracic circulation and "unlocking" the accessory muscles of respiration.

This again leads to another sign of the disorder, the characteristic posture and contraction of thoracic muscles during a bad attack; the shoulders are hunched, the dorsal curvature exaggerated. In a severe attack one grasps a bed-rail or the top of a high chair above one's head to pull up and support the chest. The "posture spasm" is extremely fatiguing and if not resolved adds greatly to the discomfort and distress of the attack. In my own case, and in many others I have observed, the correlation between rib and diaphragm movement seems to be out of step. It is very difficult—though not entirely impossible—to correct all this muscular irregularity oneself. Great relief is often experienced at once if the patient sits up and someone in the gentlest fashion supports his occiput and chin in either hand, directing the head upwards and slightly forwards, keeping the chin in. Then gentle manipulation of the levatores anguli scapulæ and supraspinati and muscles of the shoulders can considerably loosen the spasm. Properly synchronised pressure on the pit of the stomach helps to regularise the rhythm of breathing.

When dyspnœa is severe, emotional control is strained. I want to ask for something but am forced to gasp out only half the sentence. If this is not understood, or the request not complied with statim, I become disproportionately angry. This intensifies the difficulty of breathing, giving a good example of a vicious circle. I have observed this in others who equally with me recognise that the exasperation is irrational but still cannot control it. I regard this irritability in common with other distress symptoms, as resulting from anoxæmia. For this reason oxygen, with a little carbon dioxide, seems to be indicated early in any case of status asthmaticus.

Short of these severe attacks, which confine one to bed or to the house, there are long periods when asthma is, as it were, constantly round the corner. For hours one is conscious of one's breathing, though it is not unduly difficult; then a stimulus sets off a spasm. Recourse to the atomiser staves off the attack and in a few minutes one is reasonably normal again. This recurs again and again through the day, and bed-time brings the apprehension of a certainly disturbed night.

Bronchitis is a common concomitant. Probably a low-grade chronic bronchitis is present in nearly all asthmatic sufferers. A fresh superinfection may set up an acute attack, with a temperature, copious purulent sputum, cough, and a very cacophony of respiratory accompaniments. There is usually continual asthma but not quite to the extent of being a true status asthmaticus. The net result is an unhappy one for the patient.

Among my experiences with therapy I can list an operation on my turbinates, extensive trials with every remedy taken by mouth (including all the new antihistamine preparations), protein desensitisation, special diets, psychoanalysis, and treatment by an eclectic psychiatrist. All these were quite fruitless, and the three psychiatrists who interested themselves in me have destroyed my faith in the existence of any scientific approach in their branch of medicine. (Of course the sampling error is tremendous, but I can't help a conviction as strong as this one is.)

After I was gassed in 1917, when the trouble started, there was a good deal of pulmonary fibrosis. This was removed by a course of deep X rays. There was also a nasty chronic bronchitis, and this cleared up with an autogenous vaccine made from a bronchial swab. (If anyone wants a startling experience I can recommend a bronchoscopy.) But the asthma persisted. Injections of adrenaline, of course, gave relief; but they are uncomfortable, with unpleasant side-effects. Adrenaline in oil was no better. Asthma cigarettes helped, and produced pleasant lethargy; but I became convinced that they intensified the bronchitis by promoting excessive bronchial secretion. One trying bout of bronchitis was cured by inhalations of penicillin and oxygen. This was followed by a phase of almost complete freedom from asthma for over three months. I am going to try this again.

A few years ago I tried a proprietary inhalant based on a German product. This contains methyl atropine nitrate, papaverine hydrochloride, adrenaline, chlorbutol, and pituitary extract, and is administered by inhaling the atomised mist. If used promptly enough, this halts most of my attacks even though they may recur again soon. This particular preparation is the best palliative I know, and I have yet to find an asthmatic who is not helped by it. The response of course varies widely, but generally a good degree of relief is obtained, and many people can greatly extend their activities by its aid. For myself it makes life a deal more tolerable. Now I depend on it almost entirely, my only other aid being tea drunk as hot as possible.

No, there is one other thing; and here I admit failure though I keep on trying. It is at once to maintain an equable face to life, to take things easily, not to kick against the pricks, not to worry over what cannot be altered, to suffer fools gladly, to be calm. This, I confess, I cannot manage. But probably that is one reason why I am asthmatic.

". . . It would not . . . be an exaggeration to say that many patients today are seriously overinvestigated; that for lack of careful personal and social histories many unnecessary investigations are daily carried out; that insufficient thought is often given to the question of how far necessity and how far curiosity are the compelling motives in applying multiple and frequently uncomfortable tests; that surgery is often too lightly resorted to; that many patients are hopelessly confused by the numerous examinations and the visits paid to them by a variety of hospital officers and by the seeming lack of a warm, individual, personal interest in them; and that many are discharged at the end of their sojourn in hospital without any clear idea as to what is the matter with them, what their prospects are, or what their future treatment is to be . . . we can no longer justify what is often, in the first place, an unscientific, in the second (from the patient's point of view) a too exacting, and in the third a too costly system of diagnosis. . . ."—Prof. J. A. RYLE, *Brit. med. Students' J.* Autumn, 1948, p. 6.

In England Now

A Running Commentary by Peripatetic Correspondents

WHAT a grand institution tea in the laboratory can be! One of the most stimulating experiences for a young research-worker is to hear the big guns of his department booming at one another on a hotch-potch of subjects ranging from arteriosclerosis to atheism and from golf to gall-stones. Of even greater value to him is to have his current ideas and even ideals subjected to friendly informal scrutiny and criticism. It is on these occasions, too, that he becomes vaguely aware of the curious bush telegraph system existing between the laboratories of the world by which Dr. X is soon recognised as a "good man" and Dr. Y as an unreliable one. The stimulating atmosphere of a good departmental tea can only be fully appreciated in retrospect. One young worker left our department for a more lucrative position elsewhere. Within six months he was back again. We asked him what went wrong. He told us that the laboratory facilities were beyond reproach, but something was missing. That "something" he soon discovered was the informal departmental discussion. All the workers had lunch together but then they played bridge, read the newspapers, or played table-tennis. The big guns played with the big guns, and so on down the scale. Shop talk or talk on controversial topics was tacitly frowned on. Afternoon tea was worse, he said, for here the crossword puzzle held sway in each moody little group. Crossword puzzles and bridge! Shades of Koch, Pasteur, and Ehrlich! Our young friend is now recovering slowly from his terrible experience.

* * *

In spite of our meagre cheques, in spite of that green bugbear, form O.S.C.1, life for a G.P. might be worse. Not all patients want new teeth, new spectacles, and new corsets every time they come up. Some still come with interesting rashes, thought-provoking anæmias, undiagnosed diabetes, and the like. And if we care to make them so our surgeries need be little different, though admittedly larger, than those of the gay '30s. After all, most patients don't really want to be rushed off to an orthopædic surgeon if they have lumbago, or to a psychiatrist if they can't sleep. If we've been at the job long enough to get to know them, what they want is to see us. A bottle of lin. alb. to be rubbed in at night and a few moment's sympathetic listening to Mrs. Smith's housing problems is often the best treatment, and if we are worth our salt we'll enjoy giving it. Looked at in the right way, our morning surgery consists of sitting in a comfortable chair in a comfortable room while our friends tell us their problems. And can we pretend we don't enjoy telling our fellow creatures what they must and must not do?

* * *

Ours being a small hospital many miles from London patients with all kinds of conditions arrive for operation with a blind faith in one's capacity for performing a radical cure. To add to the variety I am sure that fate juggles with the normal incidence figures of disease. For instance, about twenty years ago, when partial gastrectomy was added to our hospital routine, I removed a large sarcoma from the stomach of one patient and a few months later an adenoma from another. In a large hospital, like the Mayo Clinic, these cases would be 15,000 gastrectomies apart, and I do not blame the eminent pathologist who subsequently wrote to me calling me a liar. Fortunately I had kept enough of the first specimen to save my good name, and it still exists as a museum piece in my teaching hospital. What's more, the patients survived the five-year period after operation. I believe the sarcoma case is still flourishing; he certainly was up till the end of the war when he was fighting somewhere or other.

Now along comes a case which appears to be unique in this country—a patient with intractable neuritis of his right arm and a skiagram showing, not the usual cervical rib, but an extra bony outgrowth underneath the clavicle articulating with the coracoid process of the scapula. This obviously required removal; but its site, deep to the bone in the root of the neck and nestling among the nerve-trunks and great vessels, called for a good deal of thought. I consulted two colleagues. The first very sensibly advised me to "sell the baby"—sound advice if the infant had proved coöperative. The other surgeon suggested division of the acromioclavicular joint and an attack on the osteophyte from underneath. As the patient was a talented organist and the centre of the social life of his community, the prospect of dividing most of his deltoid muscle and giving him an acromioclavicular dislocation as well filled me with horror. A long session with *Gray's Anatomy* suggested a practicable approach through the pectoralis major; so, after a rather hair-raising dissection under the middle third of the clavicle, with the subclavian artery and vein well in the foreground and all the brachial plexus in the middle distance, I found it was just possible to apply a sharp osteotome to the base of the outgrowth and after some contortions to hit it with a hammer. It was about then that we made the acquaintance of the pleura, which remained an unexpected and embarrassing companion for the rest of the proceedings. Eventually the operation was completed to our technical satisfaction, and it was with some relief that we found all movements and sensation intact when the patient regained consciousness. It was still more gratifying ten days later, when to celebrate the departure of his pain, he played brilliant coruscations on the ward piano.

Subsequent search in the archives seems to show that only two such cases have ever come to operation—one in Brazil and the other in the Argentine—though some 50, including one in England, have been noted by radiologists and anatomists. Why such a case should be presented to a poor general surgeon in the wilds when it would have been so much appreciated elsewhere I don't know. But Providence (a queer thing to call the Minister of Health) will no doubt see to it that in future only routine cases arrive at small hospitals.

* * *

I am the wife of one of those ex-Service doctors who did a refresher course on demobilisation, bought a partnership share pre-July 5, and made up his mind to join the scheme and make a go of it. Needless to say, like thousands of others I'm mother, wife, char, maid, receptionist-secretary, cook, and under-gardener. My sense of humour, though sore tried, still functions. The wells of sympathy have not yet run dry, though they came very near it when the regional medical officer called to see how we were getting on. He enjoyed my gingerbread, and, recognising my importance as a cog, sent for me to ask whether I had any complaints. I could only stutter that help would be much appreciated since the health centres were not forthcoming. Out they came, those slick well-tried clichés. He was sorry of course—weren't they all?—but *you* know how it is.

My dearest wish is that the Rt. Hon. the Min. himself should drop in at the rush hour, preferably when there are emergencies in both practice and kitchen. Perhaps *he* would be kind enough to open the front door, see to the tradesmen at the back door, exercise the dog and queue for the fish, give the child its supper, pacify an angry caller, soothe a worried one, comfort a sick one, and take in the bottles at the door and test their contents. Perhaps *he'd* go down on *his* knees and scrub the hall after 40–50 patients had walked over it.

I'm not against the N.H.S. or Mr. Bevan, but there are times when one forgets that we now get our medicine free.

* * *

RICHARD JEFFERIES

Nov. 8, 1848–Aug. 14, 1887

As a robin sings, his keen notes calling
clear beyond the rustling dreariness of rain
—gray November eve, the leaves a-falling—
like hope in pain,

So he sang at last, his spent hand bringing
to sunlit scene and shadow fragrancy and balm,
—hawthorn blooms again, the blackbird's singing—
Old England's charm.

Oft an exile's heart he's set a-throbbing,
—Wiltshire downs are distant, the alien city shrill—
in many a captive soul he's stemmed a sobbing,
and sings on still.

Letters to the Editor

BLOOD FOR TRANSFUSION

SIR,—The last sentence in your leading article on Oct. 30 states that "criticism comes best from those who help it most." Although I have only helped a little I beg space in your columns.

I have maintained a blood-transfusion service from this hospital for 15 years. I have met the needs of this area during that period and have never once, day or night, failed a doctor or hospital. During the 31 days of last month, for example, I called up 119 donors at short notice at all hours of the day and night. During the same month I was also responsible for supplying 1265 bottles of blood to the north-east London blood-supply depot team who toured Colchester and this district. During this period I took 5 bottles from the team for our own immediate needs, and these 5 are the only bottles I have ever taken from another source. In addition we have built up a Rh-negative panel of over 200 donors, most of whom are on the telephone or have made arrangements with a neighbour who is on the telephone. The above information, coupled with the fact that my name was mentioned in recent correspondence in your columns, is the excuse of a layman for writing to a professional journal.

I agree that very few donors would wear a badge. It is my invariable practice to tell donors that the donor who has just given blood is the best possible person to enrol new donors. It is, however, always difficult to persuade them to talk to their friends. In any case, I think the badge would be worn for a week and then replaced by the badge of the local football club.

I endorse every word in support of those hard-working people of the blood-supply depots. They are treated by the Ministry of Health as the Cinderella service. They are given old Army blankets, A.R.P. stretchers, and broken-down converted Army lorries with badly worn tyres. They travel about the country sitting in draughty lorries on crates of bottles, or something equally uncomfortable. Their personal comfort is not considered at all. They have an inadequate maintenance allowance when they are away; so they have to think carefully before they can book up at an hotel in any decent locality. It is most disturbing to see doctors and trained nurses acting as furniture removers and labourers. They must be given good, sound, reliable vans painted in distinctive colours, and they should have specially made white coats with a special device or badge on it. They must be given decent couches, clean white blankets, and plenty of clean pillows which can be changed 3–4 times a day if necessary. The Ministry of Food should be told that the refreshments should be "ad lib." If a donor wants 6 cups of tea and 12 biscuits, why should these not be provided? I hope that you will press this matter so that a very much overdue change may be made.

A lot more work needs to be done to instil into the doctors and hospitals that they must ask for the correct blood group and not always for group O. Homologous-group transfusions are nearly always given in this area; an occasional pint of A or B may be given to an AB recipient in grave emergency, but this has only happened once in 12 group-AB transfusions. For over three years now the pathologist here has typed and ascertained the rhesus status of all patients, male or female, who have transfusions, and automatically sera for cross-matching are taken and filed in a special container. Cross-matching is never omitted. Only in the direst emergency is the Rh status not ascertained, and on these occasions Rh-negative blood has always been given. Every pregnant woman in Colchester and district has the group and Rh status tested immediately she attends the antenatal clinic.

The only "blood bank" which we maintain is 2–4 bottles of group-O Rh-negative blood; and because of our quick call-up methods we have sufficient Rh-negative blood to meet all needs all the year round without any wastage; we also have one or two to spare for other hospitals in grave emergency. Many ex-Servicemen refuse to become blood donors because they have seen blood wasted in the Services, and it is becoming increasingly known by the lay public that time-expired blood cannot be made into plasma. Large towns and blood-supply depots are able to maintain blood banks without waste, but the small hospitals and the rural areas cannot; and a quick call-up is then the only solution. Furthermore, it is sound practice to call up a donor quickly; the average donor is a good sort and does not mind being inconvenienced to help save the life of a person gravely ill. I have never yet known a donor refuse a call, day or night, and I have never yet met an employer who refused to release a donor for an emergency call; and I speak from the experience of about 13,000 emergency calls.

All our donors receive a printed card giving the result of the transfusion, even when the patient dies. These cards are very valuable indeed. I am convinced that if all towns and centres took the same line and became self-supporting, with emergency donors to supply their daily needs, and if they organised their surplus donors who cannot respond to emergency calls, they could then supply blood depots with a considerable quantity of raw material for plasma. There would thus be enough blood and plasma for areas which cannot be organised, and there would be a corresponding reduction in the calls for plasma from the blood depots. It is the only satisfactory answer for remote districts, as the blood depots cannot serve these areas quickly.

We maintain our emergency panel by rigidly adhering to the following rules:

1. A special department is operated under a trained sister who is also responsible for seeing that the apparatus is properly cleaned, packed, and delivered to the wards and theatres. By this method donors do not get the impression that they are upsetting routine, as they do when suddenly deposited into another department of a hospital.
2. Comfortable couches and pillows are provided.
3. Adequate rest and plenty of tea are assured.
4. A house-officer, sister, or senior official always thanks the donors personally.
5. Donors are fetched and returned by car.
6. Donors are never kept waiting and are never left alone.
7. Only persons skilled in taking blood are asked to bleed donors; and unskilled ones are properly trained. A house-surgeon is never suddenly confronted with a donor if he has had no experience in doing this work. A donor returned to a factory with a bruised arm or with a hæmatoma is not just one donor lost; he talks about it and a dozen are lost.

By these methods we have only had one "faint" in three years.

I sincerely hope that you will press these matters in your columns so that a change may soon be made in this vital service.

Essex County Hospital, Colchester.

ALEC E. BLAXILL
Blood Transfusion Officer.

HOSPITAL MANNERS

SIR,—I have just returned home after four weeks in the antenatal ward of one of our finest teaching hospitals, and would like to add one or two points to your leader and the article to which it referred.

My outstanding impression is one of contrast between the superb quality of the surgery and anæsthetics and the failure to consider the human and personal problems of the patient. We were fortunate in having a friendly, cheerful, and efficient staff of nurses; but their powers, after all, are limited. We were all expecting babies; we all had anxious husbands; and our chief complaint was that visiting hours were inadequate.

There were three official visiting days, on two of which we were allowed visitors from 4 to 5 P.M. and again from 7.30 to 8 P.M. Most husbands were at work during the afternoon hour, which left them a half-hour visit on two evenings and one hour on Sunday afternoons. Saturday afternoons, when most husbands were free—and incidentally no teaching was done and the wards were deserted—we were allowed no visitors at all. Even a switch of evening visiting to two days on which we had no afternoon visitors would have made a great difference to our spirits, but this did not seem to have occurred to anyone.

By 7.30 every evening we were all washed, fed, tidied, and on five evenings were left with nothing to do but

read or listen to the Light Programme until lights out at 9 P.M. Why could we not have our husbands with us? What is the rationale of visiting altogether? Why do visiting hours vary so much from one hospital to another? I have just heard of two first-class hospitals where husbands can visit on seven evenings a week.

Then there seemed to us to be a conspiracy of silence over our condition, the proposed treatment, and the length of our stay. Patients were often in the dark as to why they were in hospital at all, and would lie with ears anxiously cocked during the professor's or specialist's bedside lecture. One young woman, who had been in the ward for five weeks, suddenly caught the ominous word "toxæmia," was treated to a lengthy discussion of possible complications, and left, presumably with soaring blood-pressure. Patients often surreptitiously scanned their case-notes or tried to question the students. Housemen were much too pressed for time to answer inquiries.

A similar disregard of the patients' point of view was shown in the experiments performed on them. These were in some instances accompanied by unpleasant after-effects. They were always resented; although no patient had the courage to object openly. The real grievance was that patients were not asked for their consent; I am sure this would rarely have been refused if the purpose of the experiment had been explained to them. Patients called the ward "guineapig ward" and were often worried in case the experiment might have "harmed the baby."

Food was sometimes adequate, but often insufficient or uneatable; during all the time I was in the ward no doctor, sister, or matron ever inquired about it. Being called at 5 A.M. meant that one never had quite enough sleep; I suppose this is unavoidable. But failure to provide such small comforts as a daily delivery of newspapers or the collection of patients' letters shows that it seems to be no-one's business, in an otherwise model hospital, to consider the patient other than from the obstetric point of view.

EX-PATIENT.

INDEPENDENCE IN RESEARCH

SIR,—Professor Twort in his letter on Oct. 16 has made a valuable reinforcement of the argument for individual research uncontrolled by Ministerial or other lay direction.

In my speech on the second reading of the National Health Service Bill (*Hansard*, May 2, 1946) I commented on the clause which describes provision for medical research.

I drew the attention of the House "to one of the gravest reproaches to be made against the Bill—namely, the ludicrously meagre reference to research. Nine lines of the Bill, in clause 16, deal with medical research. . . . Let us see what the Bill says on the subject of medical research. I will quote from the statement in the white-paper, and the white-paper everywhere seeks to give the most favourable interpretation of the clauses of the Bill. The first sentence strikes me as being rich in humour. It reads: 'The Minister is also expressly empowered by this Bill to conduct research'—that is, medical research. One might, I submit, as reasonably introduce a Bill expressly empowering the Minister of Health to navigate the *Queen Mary* from Southampton to New York. How diametrically opposed is this conception of medical research dictated from Whitehall to the procedure adopted at voluntary hospitals which have been the sources of medical advance. This procedure, which has produced results that have placed Britain in the very vanguard of advance in the science and practice of medicine, owes its success to the complete freedom which it gives to the staff. Our method is to pick a good man—and voluntary hospitals attract the best men and women—and when found to turn him loose in the wards or the laboratory as the case may be. The idea of directing research from a State department appears ridiculous to one who has been trained in the voluntary-hospital tradition." I then cited the achievement of Sir Almroth Wright and Sir Alexander Fleming, from my own hospital, St. Mary's, as illustrations of the value of complete liberty in the prosecution of research.

A very striking instance of the deplorable effects of political control on scientific research is cited in the narrative recently published in the *Times* of the deterioration already evident from the activities of Lysenko in Russia. His doctrines, universally rejected by authorities outside Russia, are foisted by Moscow on scientific workers under its control, with disastrous results to the whole economy of the country.

House of Commons. E. GRAHAM-LITTLE.

STANCE FOR FEEL

SIR,—In the lecture you published on Nov. 6 Lord Horder has done it again. "Eclipse is first, and the rest nowhere" when telling us how to conduct clinical medicine and to apply to it the evidence from "instruments of precision" and laboratories. But he uses one word in a way that needs amplifying. It is the word "touch." It includes the two sensations of "touch" and "feel." In writing this I make no criticism of Lord Horder. His generation had not distinguished them. It was left for ours—reckoning a generation in medicine as ten years.

Those physical signs of which the evidence goes to the central nervous system by the afferent nerve-fibres from the muscles and ligaments, are quite distinct from those in which it passes from the nerve-endings in the skin. Whether any of our sensations can function without muscular action may be doubted; it is certain that the proprioreceptive ones cannot do so. There is a conscious isotonic contraction of approach followed by a sustained isometric one.

If we examine ourselves when making observations of feel we find that:

(1) The physical signs resulting from them are best elicited when the muscular contractions of the upper limbs are made with the joints flexed—including pronation.
(2) They are less good when made with the joints extending—including supination.
(3) The proprioreceptive sensations are least efficient when the joints of one upper limb are extending and those of the other are flexed.
(4) The efficiency of their action is increased when the pectoral girdle is evenly balanced upon the chest.
(5) They become still better when the trunk is evenly balanced upon the lower limbs.
(6) The acme of their efficiency is reached when, the above being followed out, the joints of the lower limb are flexed—including internal rotation of the hip-joint with inversion of the foot.

It is noteworthy that, when the observer has reached this position, he has taken up that of the water-diviner.

Certain deductions for the guidance of clinicians may be made from these observations.

(*a*) In any examination involving the use of the hands a position should be taken up, whenever possible, in conformity with these rules, at least as far as the balance of the shoulder girdle upon the chest.
(*b*) If the examination is one of extreme delicacy, or of great importance, the position which gives the acme of efficiency should, if possible, be assumed.
(*c*) If, for some reason (as when decency forbids) the best position cannot be taken up, the examiner should assume the position that most nearly approaches it.
(*d*) Examination involving extensor positions of the upper limb should be avoided if possible, and one which employs extension on one side and flexion on the other should never be used, unless quite unavoidable.
(*e*) Any sloppy stance or general slackness of the muscles is bad medicine; just as it is bad to make observations of sight without efficient lighting when this is available, or to talk to a third person while auscultating a chest.
(*f*) The patient should always be put in a position in which the clinician can efficiently approach the part to be examined, unless pain, deformity, or other clinical condition forbids.
(*g*) While general rules for the position of patients may be laid down in accordance with these principles there will still be a variation, personal to the examiner, according to the way in which he uses his upper limbs.
(*h*) The nurse should therefore place the patient in the position asked for by the examiner. She should show no sign of unwillingness by word, facial expression, silence, or jerkiness of movement when asked to do this for the individual examiner rather than according to

the rule) for the unwillingness may be transmitted to her patients, to their detriment.

(*i*) Movement of a bed or other furniture must never be avoided, for fear of giving trouble, if it is necessary to allow the examiner to take up a proper position.

Great clinicians always put themselves in these postures by the light of nature; but we are not all great clinicians; and we need thought, and conscious attention to detail, in order to approach their standard of inefficiency.

London, W.1. T. B. LAYTON.

INFECTION THROUGH SOAKED DRESSINGS

SIR,—Sterile non-absorbent cotton-wool has many of the properties required by Dr. Colebrook and Mr. Hood (Oct. 30). A thick layer placed on the outside of the absorbent cotton-wool dressing will keep the exterior of the burn dressing dry for a long time. Sterile non-absorbent cotton-wool has been used as a bacterial air-filter for many years. I believe the U.S.A. shell-dressing used to consist of a pad of absorbent cotton-wool backed by non-absorbent cotton-wool. The two layers were surrounded by gauze.

Bradford. J. A. MYERS.

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SIR,—Mr. Cohen's letter last week in reply to my criticism (Oct. 2) of his paper accuses me of "flaunting certain physiological facts," and misconstrues what I said. I did not suggest that the effects of the injections he describes were due to vasodilatation in the tissues or to trophic nervous activity, as he states I did; nor did I make the ridiculous suggestion he attributes to me that thiopentone in the cases under consideration was injected solely into a nerve without entering the circulation. Obviously it did go into the circulation, but the very delay before the onset of unconsciousness, which Mr. Cohen pointed out is usual in these cases, indicates that the entry into the circulation is abnormal. All I suggested was that some of the injection irritated nerve-fibres.

Mr. Cohen does not believe vasodilator fibres supply the skin, but how does he explain the effect of stimulation of the peripheral ends of the posterior nerve-roots and the axon reflex of Lewis? Such stimulation causes the phenomenon of herpes zoster in the affected skin and œdema in the deep tissues. Unmyelinated vasodilator nerve-fibres of cholinergic type have been shown to be responsible for this and for the vasodilator effects, in a completely sympathectomised animal. If Mr. Cohen is not acquainted with severe œdema and ulceration as "trophic lesions" he can find references to this in any neurological textbook—e.g., Bumke and Foerster's *Handbuch der Neurologie*, vol. 5, or Wilson's *Neurology*, where the effects of irritation or section of the peripheral nerves are described. Œdema and trophic sores following irritation of the posterior nerve-roots are well seen in cases of herpes zoster, which may be followed by œdema and gangrene of the affected tissues and skin (see Bumke and Foerster). Ophthalmic zoster produces tremendous local œdema in the orbit and eye and often arterial and venous thromboses in the retina. If Mr. Cohen does not believe that 'Proctocaine' injection into peripheral nerves causes immediate vasodilatation and constriction both locally and at a distance, I suggest he should try such an injection for himself, as I have done on numerous occasions in the treatment of severe neuritis.

Mr. Cohen is somewhat naïve in suggesting that the intraneural injection would be required to be made into all the nerves of a limb in order to produce the symptoms he described. Concussion of a single nerve, as in causalgia resulting from bullet wounds, causes "trophic changes" and produces wasting and sensory loss in tissues supplied by nerves not directly damaged. Moreover, Mr. Cohen does not seem to be familiar with the phenomenon of ascending œdema of nerves, whereby the œdema due to damage to a single nerve branch ascends and descends the nerve to involve the nerve-roots of origin and other branches of these roots, and also roots entering neighbouring parts of the cord. If Mr. Cohen still does not believe that injections of drugs into peripheral nerves produce the effects he describes, I recommend him to read A. D. Speransky's *Basis for the Theory of Medicine* (1935), in which the effects of the application of drugs and chemicals to peripheral nerves in dogs and other animals are described at length. It produces changes both in the affected and opposite limb identical with those he records.

As regards the effects of acetylcholine on clotting I made this statement as a result of personal observations, which will be published later. In my letter I carefully did not mention liberation of acetylcholine into the circulation, but "in the blood-vessels"—meaning in the walls. Mr. Cohen's quotations on the effect of acetylcholine injection into the circulation are thus irrelevant. Acetylcholine liberated in the walls of blood-vessels leads to œdema of the vessel walls, as it does when it is liberated in other tissues, such as the skin or any tissue into which it is injected. It is this œdema of the blood-vessel wall which predisposes to clotting. The effect is not directly on the blood. Such phenomena are well seen in the retinal thromboses complicating ophthalmic zoster.

To conclude, I repeat that in spite of all Mr. Cohen's belligerency the criticism remains that he still has not shown that intra-arterial injection took place in the cases he described. Some of those who supplied him with cases stated that they believed the injections were intravenous, yet he assumes they must have been intra-arterial without adequate proof. Intra-arterial injection of thiopentone is usually harmless. I am not sure which hypothesis Mr. Cohen considers dies an honourable death, but I hope it is his own.

London, W.1. R. WYBURN-MASON.

APPLICATION FOR HOSPITAL POST

SIR,—Your correspondent "A.B." in the issue of Nov. 6 mentions a point over which many people appear to get confused.

The hospital with which I am associated sometimes advertises house-officer posts as "A or B2." This means that the hospital would prefer to appoint someone with not less than six months' previous experience, but that if the most suitable applicant is a newly qualified practitioner without previous experience he will not be entitled to B2 status and pay which allow for experience that he does not possess. It sometimes happens that all the applicants are without postgraduate experience.

Bishop's Stortford. RAYMOND HILL.

THE BALLISTOCARDIOGRAM

SIR,—I was greatly interested in the annotation on this subject in your issue of Oct. 30.

In 1917, when I was a member of the special board for the selection of pilots for the Royal Flying Corps, we utilised, for weighing the candidates, an adapted penny-in-the-slot weighing-machine. I noted that the needle pulsated synchronously with the pulse-rate. Anyone can satisfy himself of this fact by the expenditure of a copper on any similar apparatus. This observation led, later, to a small joint investigation with Major W. S. Tucker, D.SC., R.E., which culminated in the presentation of a paper to the Royal Society, entitled Recoil Curves as Shown by the Hot-Wire Microphone.[1]

In this communication the subject is portrayed standing; subsequently we found that far better results could be obtained by a suspended couch, the horizontal movements being controlled and standardised by piano wire tensed to the middle C. In the communication a variety of curves are illustrated showing the effect of exercise, breathing, &c., also the correlation of these curves in relation to the electrocardiograph curves and heart sounds. Unfortunately, this interesting piece of work had to be abandoned owing to staff changes and finance stringency in the civil-aviation department of the Air Ministry; and, as far as I know, nothing further has been done.

I have, however, always felt that there was a valuable place for this method if properly developed, since, as Major Tucker shows, these recoil curves lend themselves to ballistic analysis. Incidentally I consider "recoil curves" a better name.

London, W.1. C. B. HEALD.

1. Heald, C. B., Tucker, W. S. *Proc. roy. Soc.* B. 1922, **93**, 281.

THE PART-TIME SPECIALIST

SIR,—Mr. Deitch, in your issue of Nov. 6, draws some comparison between specialists doing limited part-time work in hospitals and "the full-time specialists, who have no time-limit to the hours worked." Without wishing to enter into his discussion of the relative entitlements of each group to undertake domiciliary visits, I should like nevertheless to say a word for the part-time specialist.

His remuneration is for an inpatient or outpatient session of $2^1/_2$–3 hours, although this session may in fact sometimes last twice as long and leave him no time for other work that half-day. If ever he makes any extra visit to his hospital for a special purpose, but for less than the statutory period, he is apparently entitled to no extra payment. His usual visits are all likely to be for dealing directly with patients and perhaps teaching about them. No remuneration is likely to be given for time spent in hospital for other purposes, such as attendance at joint clinical conferences, operations, or autopsies, performance of special investigations, and dealing with departmental correspondence. The full-time worker is at least in the enviable position of being better able to use his time profitably, in all senses.

The part-time worker must search his conscience as to whether or not he is justified in claiming as a "session" the extra odd hours in the week which he spends at hospital, either through overtime routine work or through the additional duties which he cannot and should not escape, if he is to add to his knowledge and improve his work. Payment on the basis of attendance at a limited inpatient or outpatient session takes no account of much more that is—or at any rate has been—willingly contributed.

EX-SERVICE SPECIALIST.

GROUP PRACTICE

SIR,—"Consultant" is probably right in condemning group practice, but he misses the point entirely. A man with his fellowship doesn't go into general practice as a vocation; he does so for a livelihood, hoping one day to be a whole-time consultant. Meanwhile he operates.

It is probably easier for a camel to go through the eye of a needle than for a G.P. to be appointed to the staff of a general hospital and be allowed to devote all his energies to a surgical specialty.

Longtown, Cumberland R. RUTHERFORD.

THE MEDICAL CIVIL SERVICE

SIR,—Recently commenting on the greatly increased prescription-rate under the National Health Insurance scheme, Mr. Bevan is reported to have said: "Because things are free is no reason why people should abuse their opportunity," and "People must not rush to doctors when they do not require the doctor. We do not want to build up a nation of hypochondriacs."

The truth is that things are not free, and Mr. Bevan should not abuse his position and intelligence by pretending that they are. The average individual, who finds that he is paying some £10 a year in National Health Insurance, not being a Government department, and thus used to the idea of operating at a loss, will naturally wish to make the system pay, and will be tempted to rush to the doctor on the least excuse, when formerly he might have thought twice about doing so. Our own native good sense can eventually be relied upon to prevent our becoming a nation of hypochondriacs under a system whose natural tendency is to make us such.

Another example of Mr. Bevan's tortuosity is his reported statement in the House of Commons that the number of doctors joining the National service is a sign of the faith they have in the Minister's word. The fact, of course, is that, shrewdly not relying on so inadequate a motive, the Minister's economic threat of no compensation to those joining after July 5 furnishes a much more obvious explanation of their actions.

Equally humorous are Mr. Morrison's recent remarks about "our determination that Britons never shall be slaves."

Well, after the recent struggle for the liberty of the medical profession, there is peace among medical civil servants, but it is the peace of slavery. With the Minister of Health as the sole ultimate employer, and with no possible appeal to the courts against wrongful dismissal—a tyrannical right which he has insisted on acquiring—the writer's request for anonymity (repellent in a free society, but forced on him in self-protection) is a measure of the social change since July 5.

London, W.1. CHIRURGICUS.

*** If in nothing else, our correspondent is mistaken in supposing that the average person is paying some £10 a year in National Health Insurance. The portion of his weekly National Insurance payment which is devoted to the National Health Service is 8½*d.*, or 10*d.* if he is self-employed.—ED. L.

Parliament

Shortage of Nurses

IN the House of Lords on Nov. 9 Lord CROOK, in calling attention to the grave shortage of nurses, said the matter was one which we ought to look at in relation not only to the nurses themselves but also to our own efficiency as a nation. He was convinced that the success of the new health service would be determined by the number of our nurses. The shortage was no sudden event; it had existed since the end of the first world war. Today we had more nurses and trainees in the hospitals than ever before, yet we also had a graver shortage. Although there were 7000 more nurses employed than a year ago, and 31,000 more than in 1938, and although there were 51,000 student nurses training in hospitals today as against 43,000 in 1938, the shortage persisted. At the appointments office of the Ministry of Labour 33,000 vacancies were now registered, and hospital committees estimated that to meet present-day needs 50,000 were needed. But even that fell short of the number needed to carry out essential reforms and to provide for the potential growth of the health service. The lowest estimate of those needs was a further 25,000, to which must be added the nurses needed to make good the ordinary annual wastage, perhaps 10,000 a year, from the loss of student nurses and ordinary resignations.

The public failed to realise that over the last half century our nursing service had grown right out of its former relation with the growth of the population. A nursing service of 68,000 at the beginning of the century had been increased to 191,000, partly because of the expanding population but largely because of our new conception of social care and welfare. We began the century with a hospital or nursing service based mainly on the treatment of the sick poor. We had now developed an all-in nursing service covering many things other than institutional treatment. Indeed only some 60% of our nurses were engaged nowadays in institutions; the other 40% were employed in new health services related to prevention and care. School nurses, for instance, who were not known until 1908, now numbered 2500, or 1 nurse for every 2000 children, and we hoped to achieve a proportion of not more than 1000 children to each nurse. There were also the demands of the health-visitors scheme, the infant-welfare centres, nursery classes, tuberculosis dispensaries, blood-transfusion services, and rehabilitation centres. Lord Crook also emphasised the needs of the industrial health service and pointed out that the 7000 nurses deployed in that work at the end of the war had now dropped to 4000.

The Working Party, he continued, had made it clear that it was not true that pay was the fundamental difficulty in the nursing profession. What was wrong was that the ancient idea of the cloistered life of the sister, on which the nursing service was based, was continuing far too long. No doubt the nursing profession would remain on a loftier plane than many others, but it must be moulded to the new conceptions of personal freedom that had swept over this country in the past 25 years. The nursing profession had no more right to encroach on the personal life of its members than any other profession. He did not deny that a good many rules were necessary in running an institution which has the responsibility for young girls sent by their parents for training. But there ought to be some sense of balance between two extremes. To achieve it would be one of the tasks of the new management committees. The

girls might well, he suggested, be given more privacy inside the nurses' homes, better food, and shorter working hours. Domestic work should be taken away from nurses. To do this he recognised it would be necessary to tackle the shortage in domestic staffs by organising a system of grading with attractive terms and a uniform.

One of the tasks which he thought local consultative committees should assume was to get over to nursing staffs some new ideas. For instance the number of part-timers must be increased, whatever the staffs thought at the moment. We must make them understand that only by that means could the reforms be carried out and the present shortage reduced. He shuddered to think where they would be, particularly in the chronic hospital service, without the services of the 21,000 part-timers who had entered this employment during the past year or two. Another of the new ideas to which we must become accustomed was the extended employment of married women and male nurses, who must be eligible for promotion to some senior posts.

We must, Lord Crook ended, realise that we can no longer run the nursing services only on a Florence Nightingale tradition. They could still keep the tradition but nursing must be organised as a profession with proper terms and conditions which either sex could accept.

Lord RUSHCLIFFE held that the major cause of the shortage of nurses was wastage during training, which amounted to something like 50 or 60%. No doubt many were from the start unfitted to be nurses, but he was satisfied that many left nursing because they felt frustrated. In his view the wastage would not be checked unless the responsibility for the training of nurses was separated from that of providing hospital nursing services. A nurse, like a medical student, should have opportunities of learning her job at the bedside, but at present she found that much of her time was taken up in doing work which ought to be done by a housemaid.

Lord AMULREE pointed out that one of the things that had never been made very clear was what was the job of a nurse. Many patients did not need full nursing attention, some for instance went into hospital merely for investigation. He suggested that if some wards were turned into admission or investigation wards, many nurses could be freed to look after people who were more ill. Again, many surgical patients, 10 or 12 days after their operation, though not yet fit to return home, could do without full nursing care so long as there were no difficulties or complications. A third type of patient who could also free a good many nurses were the chronic sick in institutions all over the country. By encouraging the doctors to reable these patients it was possible to speed circulation in these wards and lessen the boredom of work among these patients for the nurse.

Lord SHEPHERD, Lord in Waiting, in reply, pointed out that there had been no diminution of the rate of recruitment in the profession. Thus we were not, he declared, confronted with the task of shoring up a decrepit institution, but to arrange for more rapid progress. Nursing staffs now totalled 180,000, or 28,000 more than ten years ago, and numbers were steadily increasing. Hospitals employed 52,000 trained nurses, and 44,000 other nursing staff. The number of students in training was 48,000. A further 16,000 nurses were employed by local authorities and about 20,000 in miscellaneous services and private practice. Nevertheless, of the 582,000 beds in hospitals, 64,000 were not provided with nursing services.

Shortages had arisen because more hospital beds were occupied than before the war. Many thousands of patients were waiting admission. The number of births had risen since 1940 and many more midwives were needed. Demands for nurses in other fields, such as industry and schools, had increased, and greater demands were being made by the Armed Forces. To meet existing needs and introduce a 96-hour fortnight 48,000 nurses must be recruited. The Government had lately circulated to management committees a red-book dealing with the recruitment and conditions of service of nurses, midwives, and domestic staff. The shift system was one of the ideas mentioned. The book was issued not only for guidance but represented the policy of the Government. The separation of responsibility for training from the hospitals was also being considered, and the Government's decision would be made known before long. They believed, Lord Shepherd added, that for training there should be some other authority than those who had merely the management of hospitals.

Male nurses, he continued, had increased from 16,000 in December, 1943, to 24,000 in June this year. The Ministry of Labour were active in the enrolment of men and women for the nursing service. They had so far placed 135,000 nurses and midwives in employment and training and were now placing them at the rate of 14,000 a year.

The recommendations of the Working Party had been carefully considered, and measures which could be taken immediately without legislation were being tried. These matters covered the selection of student nurses, the training of sister students, and the training of senior staff. The Nuffield Provincial Hospitals Trust were engaged on an inquiry into the duties of each member of the hospital team, the results of which should be of great assistance in the solution of staff problems. Presumably the point raised by Lord Amulree would be dealt with by that body. Some long-term measures would entail new legislation, and, as announced in the King's Speech, a Bill would be introduced this session. In the recruitment of staff part-time service was not being neglected. Between 7000 and 8000 trained nurses, and about the same number who were not State-registered but had nursing experience, had recently returned to nursing work on a part-time basis.

QUESTION TIME

Basic Salary

Mr. SOMERVILLE HASTINGS asked the Minister of Health whether, in view of the fact that the granting of basic salaries under the National Health Service Act, 1946, was determined to a large extent by doctors who would themselves suffer financially if those were granted, he would take action to relieve these doctors of their invidious position.—Mr. ANEURIN BEVAN replied: It was the doctors themselves who asked for this modification of my original proposal. Mr. HASTINGS: Does not the Minister regard it as contrary to public policy to allow people to help make decisions in which they are financially interested?—Mr. BEVAN: The doctors are always able to make an appeal to me against the decision of the executive council if they feel aggrieved.

Dr. S. SEGAL: Is the Minister aware that the local executive councils are doing their utmost to dissuade doctors from opting for the basic salary; and will he see whether it is possible to create a separate pool out of which these salaries could be paid so that any doctor who wished to have a salary could do so as a right, and without any means test?—Mr. BEVAN: I doubt whether the local executive councils are the people who are trying to dissuade doctors from taking the basic salary. It may be that members of the medical profession locally attempt to dissuade the doctors. But if a doctor feels aggrieved he may appeal to me. If the profession wants an alteration in the procedure for which it asked itself it can appeal to me.

Cost of the National Health Service

Sir ERNEST GRAHAM-LITTLE asked the Minister if he would give an approximate estimate of the cost of the National Health Service during the first three months of its operation.—Mr. BEVAN replied: The total sums issued from the Exchequer in respect of England and Wales during the three months ended Sept. 30, to meet the cost of the service, amounted to £54,500,000 after taking into account receipts. These sums include working balances held by the statutory bodies operating the service and include provision for certain non-recurring items of expenditure arising from the taking over of hospitals.

Legal Report on Partnerships

Mr. HUGH LINSTEAD asked the Minister whether he had yet considered the report of the Legal Committee on Medical Partnerships; what action he proposed to take on that report; and if legislation was needed, when it was likely to be introduced.—Mr. BEVAN replied: I received this report on Nov. 8 and I am considering it.

Free Medicine for Private Patients

Sir WAVELL WAKEFIELD asked the Minister if in view of his refusal to permit private patients to obtain pharmaceutical services free of charge he would withdraw the pamphlet, *The New National Health Service*, in which it was stated that any person could use the whole or any part of the service; and, in view of this misleading statement, if he would issue a new pamphlet giving a factual statement of what people were entitled to receive.—Mr. BEVAN replied: People are perfectly free to use any part of the service; but there must be a limit to the extent to which parts can be subdivided. I should not feel justified in supplying medicines or appliances ordered by doctors who were not taking part in the service and are under no obligation to observe its rules.

Sir WAVELL WAKEFIELD: Is the Minister aware that many people feel that they are being grossly misled by this circular; and is he further aware that people feel that, having paid for this service, either directly or indirectly by taxation, they are entitled to receive a part of the service, as stated in the circular, free of charge?—Mr. BEVAN: I am under an obligation—and I should have thought that I should have been supported in this by all members of the House—to defend expenditure. It ought not to be possible for a doctor who is not in the service, and therefore not subject to the discipline of the service, to prescribe for his private patients. Sir WAVELL WAKEFIELD: Is the Minister aware that it is not the doctors but the patients about whom we are concerned?—Mr. BEVAN: A patient has the remedy in his or her own hands—to join the service.

Plastic Spectacle Lenses

Mr. CHARLES SMITH asked the Minister whether he proposed to provide spectacles with plastic or other unsplinterable lenses under the National Health Service either for all who preferred them or for any special categories of users.—Mr. BEVAN replied: I am considering whether it is possible to supply unsplinterable lenses under the National Health Service and, if so, what conditions should apply.

Earnings of Dentists

Sir THOMAS MOORE asked the Minister what were the average monthly earnings of dentists under the National Health Service.—Mr. BEVAN replied: I am afraid I am not yet in a position to supply this information. I have always made it clear to the dental organisations that while there is no question of going back on the Spens report, I intend to check the timings of the various operations (on which fees are based) when the scheme has settled down.

He added that over 85% of the dentists in the country were already in the service, which was evidence, he thought, that the dentists were satisfied.

Resignations from School Dental Service

Mr. BARNETT JANNER asked the Minister of Education what had been the effect on the school dental service of the introduction of the National Health scheme; and what steps he was taking to ensure the retention of sufficient dentists for the school dental services under the new arrangements.—Mr. GEORGE TOMLINSON replied: A good many school dentists are resigning to set up practice under the National Health Service and recruits are not coming forward to fill their places. In consultation with the Minister of Health I am giving close attention to the means of securing a settlement of the salaries of full-time dentists in the employment of local authorities.

Mr. HASTINGS: Is it not a fact that those dentists who leave the school service can make at least double the income outside, and is not the right course to raise the salaries of the school dentists?—Mr. TOMLINSON: I think I intimated that that is the point to which we are giving attention.

Family Allowances

Mr. ARTHUR LEWIS asked the Minister of National Insurance if he would state the total number of family allowances that were paid and cash received by recipients.—Mr. TOM STEELE replied: At Oct. 25, 1948, approximately 2,850,000 families were receiving family allowances in respect of 4,530,000 children in Great Britain. This represents a weekly payment of rather over £1,100,000.

Obituary

JOSEPH BLOMFIELD

O.B.E., M.D. CAMB., F.F.A. R.C.S.

Dr. Blomfield, consulting anæsthetist to St. George's Hospital and for many years editor of the *British Journal of Anæsthesia*, died in London on Nov. 9.

Born in 1870 in London, the son of Louis Blumfeld, he was educated at University College School and at Caius College, Cambridge, where he took the natural sciences tripos in 1891. Three years later, after completing his clinical studies at St. George's Hospital, he graduated as M.B. Camb., proceeding to his M.D. in 1897. In the same year he was appointed anæsthetist to several London hospitals, including the National Dental Hospital and St. Mary's where he was also a teacher of his specialty. Later he also joined the staff of the Grosvenor Hospital for Women and Children, the Metropolitan Hospital, and the King Edward VII Hospital for Officers. At his own hospital he became senior anæsthetist and lecturer in anæsthetics, and he was the author of the history of the hospital which commemorated its bicentenary in 1933.

[*Elliott & Fry*

With this background of wide and varied experience Blomfield's counsel and judgment commanded respect at the committee table. As early as 1910 he was a member of the anæsthetics committee of the British Association, and he long held office as chairman of the anæsthetics committee of the Medical Research Council and the Royal Society of Medicine. He also served as president of the anæsthetics section of the society and as president of the Association of Anæsthetists. When the Royal College of Surgeons instituted its new faculty of anæsthetists he was one of the first fellows to be elected. Practising through years of revolutionary change in anæsthesia, he played a considerable part in developing and stabilising new methods, towards which his attitude was welcoming but cautious. He was, for example, one of the first in this country to explore the uses of 'Avertin' (bromethol), on which he reported with Sir Francis Shipway in 1929.

Not the least of his contributions to his specialty was his editorship of its journal, to which he gave discriminating service till the war interrupted its publication. Beside writing chapters on anæsthetics for *Pye's Surgical Handicraft*, *Latham and English's System of Treatment*, and *Choyce's System of Surgery*, he published a textbook on *Anæsthetics* which reached a 4th edition in 1917 and was followed in 1922 by his *Anæsthetics in Practice and Theory*.

As an editorial contributor to our own columns, he was for many years a valued and entertaining colleague. In those relatively spacious times it was his habit to drop into the office after lunch, wearing a button-hole, smoking a cigar, and bearing a manuscript which could be deciphered only by the expert. (When he bought a typewriter the results were so remarkable that our printer begged him to return to the pen.) His notes on anæsthesia showed wit and judgment; and he was always prepared to write on other subjects, having a distinct journalistic talent as well as associations with Fleet Street. His vigour and zest for life were long almost untouched by the years, and it is said that until the beginning of the late war he ran round the Inner Circle of Regent's Park daily before breakfast. One Christmas after his retirement he answered an appeal from the Post Office and spent some strenuous days in loading vans with parcels. Later he had a serious operation, but he was able to return to a quiet life at his home in Isleworth, whence he reappeared once or twice a week to lunch with old friends at the United University Club and enjoy a game of bridge. He was, and remained, a companionable man, with a charm all his own.

Dr. Blomfield was twice married. He is survived by a son of his first marriage and by his widow, Dorothy Kathleen Bell, secretary of the Society of Genealogists.

FREDERICK HENRY HEALEY

M.D., B.SC. BIRM., D.P.M.

Dr. F. H. Healey, who died at his home at Hellesdon, on Nov. 4 at the age of 48, had been superintendent of the Norwich Mental Hospital since 1938.

A Birmingham man, he obtained a first-class degree in medicine at Birmingham University in 1924, and the following year he began his mental-hospital career when he was appointed an assistant medical officer at Chester Mental Hospital. In 1927 he took his D.P.M., and in 1931 he became deputy superintendent of the Derby Borough Mental Hospital. The same year he was awarded with commendation his M.D. in psychological medicine for a thesis on syphilis in relation to psychosis. From 1933 to 1937 he had further experience in mental-defective and mental-hospital work in Essex, Birmingham, and Somerset, till he took up his Norwich appointment in 1938.

C. D. R., a member of his staff, writes: "Dr. Healey inspired us by his own untiring energy and unfailing response to those in need of help. He kept the hospital abreast of all modern advances in inpatient therapy, but it was in his efforts to extend the boundaries of psychiatric treatment beyond the gates of the mental hospital that he spent himself most devotedly. He extended the existing outpatient clinics, he founded new ones in the areas which the hospital serves, and he did much to establish the Norwich child-guidance clinic. He visited patients in their own homes, not only as a consultant but to continue with their treatment, and he saw many outpatients at the hospital and at his own home. He made it easy for patients to seek early and without apprehension the psychiatric help which they needed."

C. N. adds: "Dr. Healey was a man of tremendous energy. To keep in touch with his staff he would visit the hospital wards, often at seven in the morning, so that he might know the work done by the night as well as the day staff. In his office he worked at tremendous speed. He never wasted either time or words. A visit to his office was short, and, business over, the visitor would be launched from the room. But in spite of the speed at which he worked, his work was never hurried and was always thorough. He disliked what he considered to be unnecessary form-filling, but his certification forms were a model of what they should be. Though a good administrator his heart and soul was in clinical medicine. He believed in the treatment of the individual by the individual. Honest, truthful, and sincere, in dealing with matters which required tact and diplomacy honesty of purpose was his first principle. His early death will cause much sorrow. But on looking back at his life, though the 'acts of the drama' seem all too short, I cannot help but feel, that 'the drama was complete.'"

Dr. Healey married in 1926, and he leaves his widow with a daughter and two sons.

Appointments

Hospital for Sick Children, Great Ormond Street, London:

ARNOTT, D. C., M.B. Lond., D.C.H.: supernumerary registrar, department of physical medicine.
BRIMBLECOMBE, F. S. W., M.B. Lond., M.R.C.P.: house-physician.
JOLLY, H. R., M.A., M.B. Camb., M.R.C.P.: house-surgeon.
LAWSON, D. N., B.A., M.B. Camb., M.R.C.P.: resident asst. physician.
NASH, F. W., M.B. Lond., M.R.C.P.: supernumerary medical registrar.

City of Liverpool Maternity and Child-Welfare Department:

Asst. M.O.:
FRAZER, JEAN, M.B. Lpool.
MORGAN, LUCILLE, M.B. Lpool, D.C.H.

Lancashire County Health Service:

Divisional M.O.:
CARROLL, J. D., M.B. N.U.I., D.P.H., D.C.H.
CRIBB, G. T., M.B. Brist.
CURTIN, MARY, M.B. N.U.I., D.P.H., D.C.H.
ELWOOD, W. J., M.B. Belf., D.P.H.
FETTES, W. Y., M.B. Aberd, D.P.H.
RUTHERFORD, H. W., M.B. Aberd., D.P.H.

Notes and News

LONDON'S VOLUNTARY HOSPITALS

THE King's Fund has now published its last Annual Statistical Summary,[1] completing an unbroken series since 1904. These form the only official record of the work performed by the voluntary hospitals of London, and their finances.

At the end of last year the total bed complement (including 2278 pay-beds) was 21,799, against 21,616 for 1946 (increase 183) and 19,510 for 1938 (increase 2289); the number of beds open for patients was 17,893, against 17,371 for 1946 (increase 522) and 18,651 for 1938 (decrease 758); while the average number of beds occupied daily was 14,667, against 13,768 in 1946 (increase 899) and 16,104 for 1938 (decrease 1437). Outpatient attendances totalled 9,351,518, against 8,922,015 in 1946 (increase 429,503) and 10,343,408 in 1938 (decrease 991,890). Total maintenance expenditure amounted to £12,121,000, against £8,669,000 in 1946 (increase £3,452,000) and £4,946,000 in 1938 (increase £7,175,000), and the excess of total expenditure over total income was £2,113,000, compared with £1,336,000 in 1946 and £274,000 in 1938. The average cost per occupied bed for all hospitals was £639 compared with £490 in 1946 and £233 in 1938, and the respective costs per outpatient attendance were 5*s.* 3*d.*, 3*s.* 11*d.*, and 2*s.*

NEWS OF THE R.A.M.C.

IN the *Army Medical Services Magazine* the R.A.M.C. at last has a journal written "by all ranks and for all ranks." The first issue contains news of the Corps the world over, articles of general interest, some lively editorial articles, and a supplement describing the recent jubilee. Amply illustrated and cheerfully written, this magazine should help to bring together past and present members of the Corps. It is to be published quarterly at first, and is obtainable, price 4*s.* 6*d.* per annum, from Messrs. Gale & Polden Ltd., Wellington Press, Aldershot, Hants. The editor should be addressed at the R.A.M.C. Depot and Training Establishment, Crookham, Hants.

M.O.H.

M'Gonigle, of Stockton-on-Tees, who died in 1939, is most widely remembered for his study of the vital statistics of the residents of a slum area before and after their transfer to a model council estate. Their death and morbidity rates, instead of going down in the new quarters, went up, because they were spending too much on rent and too little on food. The disturbance this caused at the time might well have formed the nucleus of a film of action; but the Central Office of Information have missed their chance in *One Man's Story*. Here the routine duties of an M.O.H.'s office are suggested by laboured scenes of "human understanding" through which a beatified and unlikely M'Gonigle moves like the Passing of the Third Floor Back: the live wire has been successfully insulated in layers of glorified red-tape. This is a pity, for the subject had great possibilities, the photography is very good indeed, and there are some pleasant side touches, among them the slight wry grimace of the farmer whose cow's milk is to be tested for streptococci. The film has been made for the Foreign Office, presumably to show the world how an English M.O.H. thinks about his work. Foreigners, however, will know better than to believe that anyone thinks quite like that.

A MODIFIED PUNCH

Dr. L. Rendell Baker, senior assistant in the department of anæsthetics of the Welsh National School of Medicine, has designed a time-saving punch for Copeland-Chatterton

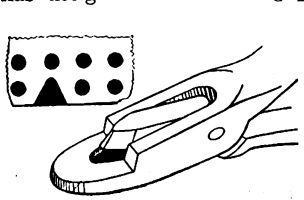

Fig. 1.

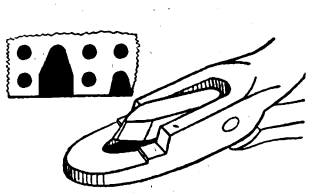

Fig. 2.

1. King Edward's Hospital Fund for London: Statistical Summary of the Income, Expenditure, Work, and Costs of 159 London Hospitals for 1947. From the Fund's offices, 10, Old Jewry, E.C.2. Pp. 79. 1*s.*

record cards. The punch supplied for use with these cards cuts only single-depth slots (fig. 1); double-depth slots must be cut with scissors. In the department's workshop the punch has therefore been modified by filing back the shoulders (fig. 2) leaving a step. Thus altered, the punch will cut slots of single or double depth with equal facility and accuracy.

University of Cambridge

The Raymond Horton-Smith prize has been awarded to Dr. David Vérel for his M.D. thesis on postural hypotension.

University of Glasgow

On Nov. 6 the degree of M.D. was conferred on Tom McEwan, and the degree of PH.D on I. C. Michaelson.

Royal College of Physicians of London

Dr. W. H. Wynn will deliver the FitzPatrick lectures at the college on Tuesday and Thursday, Dec. 7 and 9, at 5 P.M. He is to speak on the Pestilences of War.

Royal College of Surgeons of England

At a meeting of the council of the college held on Nov. 11, with Lord Webb-Johnson, the president, in the chair, Mr. R. H. O. B. Robinson was elected a member of the court of examiners. Prof. Henry Cohen was appointed Moynihan lecturer. Mr. L. Crossfill (Epsom College and Barts) was nominated as the 56th Jenks scholar.

Diplomas of membership, and in ophthalmic medicine and surgery, in child health, and in physical medicine were conferred on those named in the report of the comitia of the Royal College of Physicians in our issue of Nov. 6 (p. 753). The following diplomas were also conferred :

D.M.R.-D.—C. J. Alexander, C. W. P. Bradfield, R. G. Britt, J. H. L. Conway-Hughes, A. M. Fraser, P. H. K. Gray, C. H. Kitchen, R. E. Lawrence, Ronald Levy, R. H. C. Manifold, Stephen Moor, N. D. W. Morrison, Richard Paul, J. McK. Reid, H. L. Ross, Martin Spiro, J. L. Steven, B. A. Stoll, D. R. Syred, E. J. S. Townsend, R. F. Williams.

D.M.R.—I. G. Brown, H. G. Frank, W. D. Fraser, Robert Gibb, Prabhat Kumar Haldar, Eileen H. Harrison, G. M. Holme, A. E. Jones, A. H. McCallum, J. R. MacLeod, R. D. Nash, Uma Shankar Prasad, T. M. Prossor, W. M. Ross, Nirode Bijali Roy.

On Thursday, Dec. 9, at 5 P.M., Sir Reginald Watson-Jones will deliver the Robert Jones lecture at the college, Lincoln's Inn Fields, London, W.C.2. He is to speak on the Reactions of Bone to Metal.

Royal College of Physicians of Ireland

On Nov. 5 the following were admitted to the membership :

P. B. B. Gatenby, Manik Ghosh, R. J. Kernohan, R. M. Peet, R. W. Temple.

Registrar-General for Scotland

Mr. E. A. Hogan, an assistant secretary in the department of Health for Scotland, has been appointed registrar-general of births, deaths, and marriages in Scotland, from Dec. 1, in succession to Mr. J. G. Kyd, who is retiring.

International Congress of Comparative Pathology

This congress will hold its fifth meeting in Istanbul from May 17 to 20, 1949. The congress covers all aspects of human, plant, and veterinary pathology, and considerable latitude is permitted in the choice of subjects for discussion. Further information can be had from Mr. R. E. Glover (secretary of the British national committee), Royal Veterinary College, London, N.W.1, or from Prof. N. R. Belger, Taksim, Siraserviler 75/3 Istanbul.

International Congress of Otolaryngology

This congress will be held in London from July 18 to 23, 1949, under the presidency of Mr. V. E. Negus. Subjects selected for discussion include Antibiotics and Chemotherapy in the Treatment of Nasal Sinusitis and its Complications, when the opening speakers will be Sir Alexander Fleming, F.R.S., Sir Lionel Whitby, and Dr. A. C. Furstenberg (Ann Arbor); Treatment of Aural Vertigo, openers Prof. F. Nager (Zurich), Prof. C. Nylen (Uppsala), and Dr. W. J. McNally (Montreal); and Non-malignant Strictures of the Thoracic Œsophagus, openers Dr. Gabriel Tucker (Philadelphia), Prof. J. Terracol (Montpellier), and Dr. P. G. Gerlings (Amsterdam). On July 25 and 26 meetings will also be held at Oxford, Cambridge, and Edinburgh. Further information may be had from the secretaries of the congress at 45, Lincoln's Inn Fields, London, W.C.2.

International Congress on Rheumatic Diseases

The seventh International Congress on Rheumatic Diseases, at the invitation of the American Rheumatism Association and the New York Rheumatism Association, is to be held at the Waldorf Astoria in New York from May 30 to June 3, 1949. The congress is sponsored by the International League against Rheumatism.

Health Scheme in Northern Ireland

The Northern Ireland minister of health and local government states that 730 doctors have joined the new service, which means that there must be very few general practitioners who are not taking part. Over 90% of the total population of Northern Ireland have registered. Few dentists have remained outside the scheme, 258 being in contract with the board for the provision of general dental services. The calls made by the public upon the dental service have been greater than were expected, and up to the end of October, 55,516 persons have had treatment completed.

Royal Society

A Royal medal has been awarded to Prof. James Gray, F.R.S., for his researches in cytology, ciliary movement, and particularly his anatomical and experimental studies of animal posture and locomotion. Prof. A. V. Hill, F.R.S., receives the Copley medal for his researches on myothermal problems and on biophysical phenomena in nerve and other tissues, and Prof. R. A. Fisher, F.R.S., the Darwin medal for his distinguished contributions to the theory of natural selection, the concept of its gene complex, and the evolution of dominance.

New N.H.S. Formulary

In announcing the forthcoming publication of a new formulary for doctors and chemists to use in the National Health Service, Mr. Hugh Linstead, M.P., secretary of the Pharmaceutical Society of Great Britain, said : "It is not a formulary prepared by the Ministry of Health under the cheeseparing eye of the Treasury. It has been prepared by a joint committee of the Society and the British Medical Association and will be submitted by it to the Ministry for official adoption. It does not provide for cheap medicine but for good medicine."

Welfare of Handicapped People

The Secretary of State for Scotland has appointed a council under the chairmanship of Lord Stevenson to advise him "on matters pertaining to the welfare of handicapped persons with particular reference to the provisions of the National Assistance Act." The other 18 members include Mr. W. Veitch Anderson, F.R.C.S.E., Prof. T. Ferguson, M.D., and Dr. J. G. M. Hamilton. The secretary is Mr. R. I. Hulley, Department of Health for Scotland, St. Andrew's House, Edinburgh, 1.

Conference Grants

The British Council has a small fund to enable overseas delegates to attend conferences held in the United Kingdom on scientific subjects, including medicine. Conveners of conferences to be held between April 1, 1949, and March 31, 1950, should apply to the director, visitors department, British Council, 3, Hanover Street, W.1, giving particulars of their conference and the number of delegates (and their nationalities) who they think will need help. Application should if possible be made before Jan. 15 next.

Patronage of Hospitals

In the management of hospitals under the National Health Service Act, offices such as president and vice-president, which imply executive responsibilities, will not be continued. But the Ministry of Health points out that there is no reason why committees and boards should not invite those who have held these offices, or others, to accept appointment as patron, vice-patron, or honorary president. It is understood that the King and the Queen, and other members of the Royal Family who have hitherto been patrons or vice-patrons of hospitals, will continue to act in that capacity without any steps being taken by the committee or board concerned. It is understood that where they have been president or vice-president they will be prepared to consider an invitation to become a patron or vice-patron in future; or where they have had, or wish to have, a particularly close tie with an individual hospital, an invitation to become honorary president.

Kent Pædiatric Society

A meeting of the society will be held at Lingfield Epileptic Colony, Lingfield, Surrey, on Friday, Nov. 26, at 2.30 P.M. The meeting will include a visit to the special school attached to the colony.

An Old-fashioned Christmas

The Minister of Health has expressed the wish that the tradition of Christmas festivities for the patients and staff of hospitals should be continued in the new service, and hospital management committees and boards of governors have been authorised to spend up to 5*s*. per head of patients and resident staff from the Exchequer moneys at their disposal. This sum may be supplemented as the committee or board think fit from any endowment or free money available to them, and by any gifts made for the occasion.

Employment of Foreign and Colonial Doctors

Certain doctors with foreign qualifications wishing to work in Britain under the Medical Practitioners and Pharmacists Act, 1947, must be selected for a hospital post before being provisionally admitted to the Medical Register. A Ministry of Health circular requests regional h spital boards and hospital management committees "to give sympathetic consideration to the difficult position of these practitioners." The circular points out that there is considerable unemployment among Polish doctors, already on the register, who have been engaged in the Polish Resettlement Corps. "It is important that there should be no prejudice against the employment of such practitioners." The hope is also expressed that no discrimination will be exercised against coloured doctors seeking hospital appointments.

Retirement of Dr. Garfield Williams

The Very Reverend Garfield Williams, M.B., is next week retiring from the deanery of Manchester, on medical advice.

While at St. Bartholomew's Hospital he became interested in the Student Christian Movement, and later as its London secretary he visited Japan, China, and America. In 1910 he was appointed vice-principal, and superintendent of the science department, of St. John's College at Agra. Four years later he was ordained and became principal of St. Andrew's College, Gorakhpur. For work in the United Provinces during the 1914-18 war he was appointed O.B.E. In 1920 he returned to this country, and after teaching for a year at Rugby he was appointed foreign secretary of the Church Missionary Society in charge of education. Between 1924 and 1929, while secretary of the missionary council of the National Church Assembly, he was responsible for the five volumes of *World Call* reports describing the activities of the Anglican community overseas. In 1929 he became dean of Llandaff and two years later dean of Manchester.

Births, Marriages, and Deaths

BIRTHS

DANSIE.—On Nov. 1, the wife of Dr. E. R. Dansie—a son.
HADLEY.—On Nov. 16, in London, the wife of Dr. G. D. Hadley—a daughter.
JACKSON.—On Nov. 7, in London, the wife of Mr. Ian Jackson, F.R.C.S.—a son.
KENNARD.—On Nov. 8, in London, the wife of Dr. H. W. Harbrow Kennard—a son.
MANN.—On Nov. 10, in London, the wife of Dr. W. N. Mann—a son.
MARKOWE.—On Nov. 12, in London, the wife of Dr. Morris Markowe—a daughter.

MARRIAGES

ANDERSON—LEDGERWOOD.—On Nov. 13, in London, D. A. P. Anderson, M.B., to Myrtle Ledgerwood.
KAYE—WIGRAM.—On Nov. 6, at Shalbourne, Christopher Henry Kaye, B.M., to Kathleen Maude Wigram.
KER-GIBSON—BENHAM.—On Nov. 11, at Guildford, Arthur William Ker-Gibson, lieut.-colonel, R.A.M.C. retd, to Iris Benham.
NIEMYSKI-DONALD.—On Nov. 1, at Worthing, Anatol Niemyski, M.D., to Barbara Gertrude Rosemary Donald.

DEATHS

BLOMFIELD.—On Nov. 9, in London, Joseph Blomfield, O.B.E., M.D. Camb., F.F.A., aged 78.
DALYELL.—On Nov. 1, at Greenwich, Sydney, Elsie Jean Dalyell, O.B.E., M.B. Sydney.
FERRAR.—On Nov. 8, in Dublin, Benjamin Banks Ferrar, B.A., M.D. Dublin.
GILLESPIE.—On Nov. 9, at Barrowmore, Milnathort, David Gillespie, M.C., M.D. St. And.
GRIFFITHS.—On Nov. 3, at Cross Hands, Carmarthenshire, David Henry Griffiths, M.R.C.S.
HINDE.—On Nov. 8, Francis Richard Berthon Hinde, M.D. Edin., aged 84.
HUTCHINSON.—On Nov. 12, at Littlehampton, Robert Hilton Hutchinson, B.A. Camb., M.R.C.S.

West Kent Medico-Chirurgical Society

On Friday, Dec. 10, at 8 30 P.M., at the Miller Hospital, Greenwich, S.E.10, Sir Howard Florey, F.R.S., will deliver the Purvis oration. His subject is to be New Chemotherapeutic Substances of Microbial Origin.

World Health Organisation

The executive board has approved the admittance of the following international non-governmental organisations into relationship with W.H.O.: International Union against Venereal Diseases, International Union against Tuberculosis, International Union against Cancer, World Federation for Mental Health, International Committee of the Red Cross, International Hospital Federation, International Academy of Forensic and Social Medicine, International Leprosy Association, and International Association for the Prevention of Blindness.

CORRIGENDUM: *Period of Transmission in Epidemic Disease.*—In Dr. R. E. Hope Simpson's article of Nov. 13 the formula on page 759, column 2, line 10 should read: $Y' \pm {}^1/_2(y + x)$.

Diary of the Week

NOV. 21 TO 27

Monday, 22nd

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. D. H. Brinton: Intracranial Aneurysm. (Part II.)
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. F. K. Sanders: Results of Nerve Section.
5 P.M. Prof. J. H. Dible: Inflammation and Repair.
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Dr. F. Avery Jones, Mr. Hermon Taylor: Gastroscopy.

Tuesday, 23rd

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. J. A. Charles: Victorian Medical Administrators and their Significance for Today. (Bradshaw lecture.)
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. Cuthbert Dukes: Significance of the Unusual in the Pathology of Intestinal Tumours. (Imperial Cancer Research Fund lecture.)
5 P.M. Prof. J. D. Boyd: Development of Urogenital System.
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Mr. A. K. Monro: Abnormalities of the Cutaneous Circulation in the Lower Limb.
EDINBURGH POST-GRADUATE BOARD FOR MEDICINE
5 P.M. (Royal Infirmary.) Prof. Robert Platt: Renal Failure.

Wednesday, 24th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. W. D. W. Brooks: Pulmonary Tuberculosis. (Part II.)
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Professor Boyd: Development of Cardiovascular System.
5 P.M. Prof. E. C. Dodds, F.R.S.: Sterol Metabolism.
MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Dr. F. E. Camps: Colchester Taxi-cab Murder (1943).
HONYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Dr. Thomas Anderson: Pneumonia.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow
5 P.M. Mr. A. Dickson Wright: Vascular Surgery. (John Burns lecture.)

Thursday, 25th

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Professor Dodds: Sterol Metabolism.
5 P.M. Professor Dible: Inflammation and Repair.
INSTITUTE OF NEUROLOGY, Queen Square, W.C.1
5 P.M. Dr. W. Feldberg, F.R.S.: Acetylcholine and the Central Nervous System.

Friday, 26th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. T. L. Hardy: Regional Ileitis.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. N. H. Martin: Applied Physiology of the Parathyroid.
WESTMINSTER MEDICAL SCHOOL, Horseferry Road, S.W.1
5.30 P.M. Prof. Dugald Baird: Social Factors in Obstetrics.
LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. Franklin Wood: X-ray Kymography of Heart and Lungs.
EMPIRE RHEUMATISM COUNCIL
4.30 P.M. (Apothecaries' Hall, Black Friars' Lane, E.C.4.) Dr. W. S. C. Copeman: The Rheumatic Diseases. (Opening of weekend course.)

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THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6535 LONDON: SATURDAY, NOVEMBER 27, 1948 CCLV

CONTENTS

CARCINOGENIC AND ANTICARCINOGENIC SUBSTANCES *

E. C. DODDS
M.V.O., M.D., D.Sc. Lond., F.R.C.P., F.R.I.C., F.R.S.
COURTAULD PROFESSOR OF BIOCHEMISTRY IN THE UNIVERSITY OF LONDON, AT THE MIDDLESEX HOSPITAL

THE production of cancer in man was long supposed to be a very slow process. Almost a lifetime of irritation of the scrotum by soot was thought necessary to produce the chimney-sweep's squamous epithelioma; mule-spinners' carcinoma was held to be due to long-continued exposure of skin to clothing soaked in a carcinogenic oil; cancers of the mouth were ascribed to the chronic irritation of jagged teeth, pipe-stems, &c., and many other forms of carcinoma were attributed to general non-specific chronic irritation over a long period.

Subsequent work, however, proved that there was something extremely specific about the action of soot in producing chimney-sweep's carcinoma. Yamagiwa and Ichikawa (1915) showed that cancer could be produced in rabbits with tar, applied to their ears; Passey (1922) produced an epithelioma in a mouse by the application of soot; and Cook et al. (1932) produced cancer in mice by the application of certain pure chemical substances.

In 1921 Kennaway began to try to isolate the active carcinogen from tars. This work can be summarised in three stages. First there was the demonstration that carcinogenic substances could be formed from materials containing only carbon and hydrogen. Next a study of the emission spectrum of such tars showed that the spectrum was of the same type as that of the polycyclic hydrocarbons. This led to the classical synthesis by Cook et al. (1932) of several polycyclic hydrocarbons and the demonstration of their carcinogenic activity. Finally came the isolation by Hieger (1933), in Kennaway's team of a pure carcinogenic polycyclic hydrocarbon from tar.

The first synthetic compound shown to be carcinogenic was 1 : 2 : 5 : 6-dibenzanthracene (fig. 1). Many polycyclic hydrocarbons were synthesised, chiefly derivatives of anthracene, benzanthracene, benzpyrene, and cholanthrene (figs. 2–5). Biological investigation revealed big differences in the quantitative activities of these compounds.

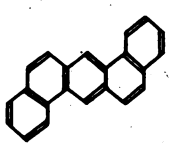

Fig. 1—1 : 2 : 5 : 6-dibenzanthracene.

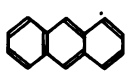

Fig. 2—Anthracene.

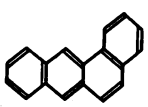

Fig. 3—1 : 2-benzanthracene.

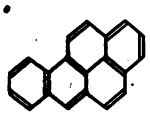

Fig. 4—3 : 4-benzpyrene.

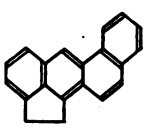

Fig. 5—Cholanthrene.

The very highly active compounds produced tumours in almost 100% of treated animals, whereas the less active compounds produced a lower percentage of tumours. Again, the length of time necessary for the production of a tumour varied with the molecular configuration, some compounds requiring only half the time of others.

The experiments at the Cancer Hospital emphasised the necessity of continuous painting of mice for a long time, and the conclusion drawn from these experiments and from clinical observations of industrial cancer was that after several months in small animals, corresponding to decades in human beings, the agent or chemical causes a characteristic alteration in the cell which finally makes it malignant. Peyton Rous (1947) looks on the human body as being subjected to carcinogenic influences of various types, a summation of which over years produces cancer. I wish to call attention to objections to this theory of long-term action.

SHORT-ACTING CARCINOGENS ?

Cancer of the penis, like soot cancer and the cancer induced by painting the skin of mice, has been attributed to irritation over a long period. The source of this irritation is removed by circumcision, and it is well known that the condition never develops in circumcised Jews, who have almost all been circumcised in the second week of life. Kennaway (1947), however, has now shown that in Moslems, who are circumcised in early boyhood and never as babies, the incidence of carcinoma of the penis is the same as in the uncircumcised non-Jews. This suggests that the carcinogenic potentiality is conferred on the epithelium of the penis during the first few years, and that the carcinoma which develops forty or fifty years later had its foundation when the child was uncircumcised. The findings cannot be explained by removal of the cancer-bearing area, since the cancer often appears on the body of the penis rather than the foreskin itself.

These observations call for a new outlook on carcinogenesis. Is this phenomenon confined solely to carcinoma of the penis, or can we find evidence of it in other parts of the body? We can learn a valuable lesson from industrial cancer. While the cancers appearing after a lifetime in the tar industry, or in cotton-spinning, seem to correspond to the effects of painting mice for a long time there are forms of industrial cancer which present a certain parallel to carcinoma of the penis.

In the manufacture of copper sulphate and in the refining of nickel the carbonyl process is used extensively in the British Empire and in this country. (The results obtained in Great Britain are considered here, because in this country the question is not complicated by radioactivity of the ores as in some of the Continental mines.) The workers in these industries have a high incidence of *cancer of the respiratory passages*, especially a particularly destructive form of carcinoma of the turbinate and ethmoid bones. Statistical analysis proves the causal relationship between exposure to the dust in these processes and the development of the cancer. The point that is significant to our argument, however, is that a man may be discharged from the works after two or three years' exposure and be pronounced physically fit after a most rigorous medical and otolaryngological examination; and yet in later years he may develop a carcinoma of the ethmoid terrifying in its destructive qualities (Amor 1938). Here then we have another example of a carcinogen acting over a limited period, causing some alteration in the cells which eventually, years afterwards, produces a malignant growth. Of the nature of the carcinogen in these cases little is known. Some workers have suggested that it is a combination of the carbonyl with certain metallic compounds; and others that arsenic in the dust is responsible.

Carcinoma of the bladder is a frequent accompaniment to work in the chemical section of the dye industry (Goldblatt 1947). The fact that workers handling the machinery of a dye-works are subject to constant attacks of hæmaturia has been known since the industry began. A proportion of these patients develop papilloma of the bladder, and some of these papillomas become malignant. The number of substances capable of causing these changes is very great, and they have often been reviewed. The most important and the most serious offenders are

* From a lecture delivered at the 8th International Biochemical Congress held in Paris, October, 1948.

β-naphthylamine and benzidine (figs. 6 and 7). Aniline, from which the cancer was originally called aniline workers' cancer, probably does not act as a carcinogen to the bladder: the actual carcinogen is probably one

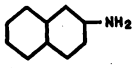

Fig. 6—β-naphthylamine.

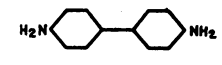

Fig. 7—Benzidine.

of the by-products associated with the manufacture and working up of aniline. Careful statistics, compiled not only in British works but also in America and in Germany, show that it is unnecessary to have a continuous exposure over many years, but that exposure for two or three years may be sufficient to lay the foundation of this malignant propensity which may manifest itself fifteen or twenty years later. There are definite and exact records of persons who have been taken out of the industry absolutely symptomless, and on cystoscopy have shown no abnormality, yet in later years have developed malignant papillomata.

An entirely new and unexpected hazard has come to light in the use of *beryllium*, used in making electric-light bulbs and wireless valves. Until recently beryllium was regarded as entirely harmless, but several reports have now proved that the dust can give rise to a specific form of pneumonitis which is sometimes fatal. At necropsy the lungs show a neoplastic change precisely similar to that of sarcoidosis. Metastasis has not yet been described, but an osteogenic sarcoma has been produced in the rabbit with beryllium. Several workers have reported changes in the radiological and microscopical appearances of the lungs of persons exposed to the dust from beryllium compounds (Pascucci 1948, Van Ordstrand et al. 1945, Agate 1948). A report of a symposium at the Saranac Laboratory for the Study of Chest Diseases (*Journal of American Medical Association*, 1948) states that:

> "the unit lesion is a chronic granuloma composed of proliferative cells with widely scattered giant cells. . . . Spontaneous remissions and disappearance of roentgenologic shadows have not been noted. . . . Another characteristic is delayed onset, sometimes five years after the termination of exposure."

Research-workers have possibly been too obsessed with the production of carcinoma by polycyclic hydrocarbons, and it may well be that a study of some of these new compounds may shed fresh light on carcinogenesis.

ŒSTROGENS

So far we have only considered the production of cancer by agents external to the body. A vast number of experiments have also been made to see whether the body itself can produce them. For example, the possible carcinogenic effect of the female sex hormone has been studied.

The early stages of the œstrus cycle induced by œstrogens are characterised by proliferation and later keratinisation of epithelium, both processes closely resembling the early stages of cancer. If the naturally occurring œstrogenic hormones are painted for a long time on the skin of susceptible mice, no local tumour appears; so we are justified in concluding that œstrogens are not surface-acting carcinogens like the polycyclic hydrocarbons. Lacassagne (1932, 1936, 1938) has shown, however, that œstrogens can act as powerful carcinogens under certain conditions. He found that administration of œstrone to young mice increased the incidence of spontaneous mammary carcinoma in later life. This striking observation was rapidly confirmed, and there is now evidence that, if the strain of mice is one in which spontaneous mammary tumours do not occur, the treatment is without effect; but that in a strain with a definite incidence of mammary tumours œstrogen treatment causes a significant increase in that incidence. The same results are obtained with the synthetic œstrogens, which indicates that the causal factor is œstrogenic action, apart from molecular configuration. It must be pointed out in passing that, important as these results are from a theoretical point of view, they do not constitute a contra-indication to the clinical use of œstrogens, since the doses given to human beings are fractional compared with those administered by Lacassagne to mice.

ANTICARCINOGENIC SUBSTANCES

We are faced, therefore, with the fact that in man it is possible to change tissues to such an extent that they will later develop into carcinomas. Admittedly we do not know whether the change established during the first exposure is a continuous one that goes on until a malignant change takes place, or whether this assumption of malignancy is due to another factor or series of factors acting on the prepared ground.

The question arises whether it is possible by chemical treatment to make an organism insensitive to carcinogens. Extensive experiments have revealed only one method of protecting sensitive animals from the carcinogenic action of polycyclic hydrocarbons on the skin, and this immunity is only temporary. It is naturally impossible to cite experiments on man, but one can give a very definite example in the case of the mouse. Berenblum (1929), studying the effects of chronic irritation of the skin in experiments on animals, was particularly interested in the effect of combining a chronic irritant with a carcinogenic hydrocarbon. He chose dilute mustard gas (dichloro-diethyl-sulphide) as the chronic irritant, and was amazed to find that, if the skin was treated with a dilute solution of this substance in acetone, no amount of subsequent painting with carcinogenic hydrocarbons appeared to have any effect. Later, however, he found this immunity to be only temporary (Berenblum 1931), and we can only conclude that in this treatment the skin was temporarily immunised by some chemical change. Though the vesicant action of mustard gas is not understood, that it has some profound influence on the cells is shown by the fact that it can cause mutation of the genes in drosophila (see below).

The study of supposedly anticarcinogenic substances does not help us very much, since the list includes such a heterogeneous collection as cantharidine, carbon-dioxide snow, and heptaldehyde. Haddow (1935, 1938) and Haddow and Robinson (1937) suggested that certain carcinogenic hydrocarbons can reduce the rate of growth of animal tumours that they have induced. Briefly, Haddow (1935) showed that the intraperitoneal injection of certain carcinogenic hydrocarbons was followed by reduction of the rate of growth of transplanted Jensen rat sarcomas, and that two non-carcinogenic polycyclic hydrocarbons — anthracene and phenanthrene — were inactive. Pybus and Miller (1937) showed that the administration of 1 : 2 : 5 : 6-dibenzanthracene to mice bearing spontaneous tumours had an inhibitory effect. Haddow and Robinson (1937) extended their observations to tumours induced by carcinogenic hydrocarbons and showed that growth was inhibited.

The mechanism of this inhibitory effect has been much studied, and the problem really reduces itself to whether the inhibition is the result of a specific action on the growth originally produced by it or the result of a non-specific action on the general health of the animal. Stamer (1943) has shown that at least in the case of 9 : 10-dimethyl-1 : 2-benzanthracene the effect is not specific but is probably exerted on the general health of the animal. Thus animals treated with this substance do not eat well and lose weight. In an elaborate series of investigations Stamer showed that, if the diet of a control

series of tumour-bearing animals was reduced to keep the weight of the controls equal to that of the treated animals, the same amount of inhibition of growth took place. This crucial experiment was extended to other hydrocarbons, and it seems from Stamer's work that Haddow's effect is due to a dietary factor.

DISORDERED METABOLISM

Running all through the great numbers of studies on carcinogenic and anticarcinogenic substances we continually come across the suggestion that malignancy may be due to disordered metabolism, caused either by interference with the nutrition of the cell or by the poisoning of some enzyme system. Haddow concluded from his work that malignancy may arise in the first place from inhibition of the activity of the cell, which in its turn produced some irreversible change. As we have seen, Stamer's experiments appear to show that this action can be explained by the restriction in food intake of the animals treated with the hydrocarbons. The same inhibitory effect on the incidence of tumours in mice was produced by Tannenbaum (1940a and b) simply by restricting the animals' diet. This worker, from a careful scrutiny of certain insurance-company statistics, concluded that overweight persons have an increased liability to cancer. It has also been shown that the hepatomas and cholangiomas produced by the azo-compounds can be hampered or prevented by various dietary supplements, such as riboflavine (Miller et al. 1941, Miner et al. 1943). On the other hand, pyridoxine seems to encourage the development of these tumours. Biotin supplements also appear to stimulate tumour production (Du Vigneaud et al. 1942), and this effect can be annulled with avidin. White (1944) has found that the limitation of cystine and lysine in the diet of mice renders them less liable to mammary tumours. All these findings suggest that diet may play some part in malignancy.

FOLIC ACID AND ITS ANTAGONISTS

Great interest has developed in America during the last few years in the folic-acid group of substances, and it seems that in this series are several having a definite influence on the malignant process. In a recent visit to America I was able to discuss the problem with workers in this field. Those mainly concerned are at the Lederle Laboratories and at the Sloan-Kettering Institute and the Memorial Hospital, New York. The following is a very brief account of a vast amount of work, and I am indebted particularly to Dr. C. P. Rhoads, director of the Sloan-Kettering Institute, for permission to give the latest and in some cases unpublished results.

Folic acid was recognised as an essential growth factor some time ago, and its constitution has been established and its synthesis accomplished. It was early recognised that folic acid played an important part in the diet of man, and it was rapidly shown to have a profound influence on the bone-marrow. Folic acid causes a remission in pernicious anæmia but, unlike the liver factor, will neither prevent nor cure the subacute combined degenerative lesions in the spinal cord.

The molecule of folic acid enables several variants to be synthesised, and these have been examined for their folic-acid activity and for their effect on new growths in animals and in tissue culture. In some cases clinical trials have been made with them.

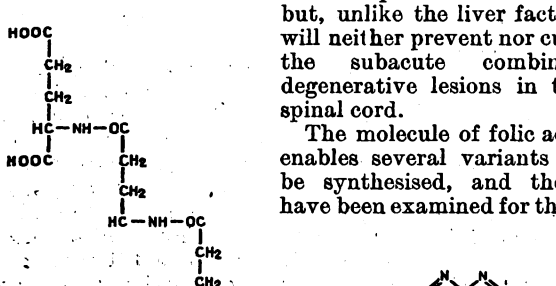

Fig. 8—Teropterin (Pteroyl-γ-glutamyl-γ-glutamyl glutamic acid).

Two substances producing an effect like that of folic acid on the tumours of animals were tried clinically. These were teropterin and diopterin (figs. 8 and 9). The

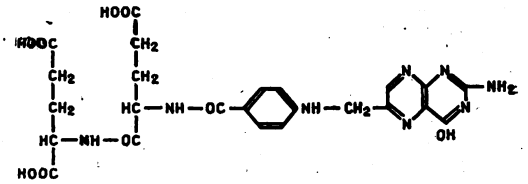

Fig. 9—Diopterin (Pteroyl-α-glutamyl glutamic acid).

more promising results have been obtained with teropterin. It has been claimed that this substance administered to patients with malignant disease stimulates their metabolism so that they appear to recover considerably in health. Gains in weight have been reported, and it has been claimed that in some cases there has been a noticeable effect on the tumour, as seen at biopsy. Opinions are divided in America about the effect of these substances. Several experienced workers claim that it is largely psychological and that, when a carefully controlled experiment is performed with controls, no difference can be detected between the controls and the treated cases. I definitely gained the impression when in the United States that the interest in teropterin had largely evaporated.

Interest has now swung over to a group of compounds known as anti-folic-acid substances. The administration of some of the synthetic modifications of folic acid to animals had an inhibitory effect on the bone-marrow, with the result that profound anæmia was established. This effect could usually be reversed in most cases by the administration of folic acid, and the justifiable conclusion was that these new substances acted as inhibitors of folic acid. Precisely the same results were obtained with

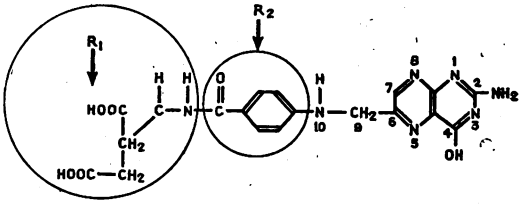

Fig. 10—Folic acid.

bacteria, and the stimulating effect of folic acid on their growth could be reversed by the addition of these anti-folic-acid substances. With some of these substances the effect was so profound that the animal died before the effect could be reversed by folic acid.

The American workers consider that the presence of folic acid is essential for the growth of cells. This can be shown by tissue-culture experiments; and, if anti-folic-acid compounds are added, the cell will die very rapidly. It is thought that only a few hours' deprivation of folic acid is needed to produce irreparable damage to the cell. The American workers suggest that by suitable anti-folic-acid treatment it may be possible to damage the malignant cells, which they feel are more sensitive to the action of anti-folic-acid compounds than are the normal cells.

The folic-acid formula is now numbered as in fig. 10. The following substances have been thoroughly investigated.

Aminopterin.—In this substance amino groups are introduced in the 2- and 4-positions. It is very toxic, but completely reverses the folic-acid effect both in bacteria and in animals.

It also inhibits œstrogens. Hertz (1948) has shown that aminopterin will inhibit the action of stilbœstrol on the chick oviduct. It must be admitted, however, that the dosage which produces inhibition is close to the toxic dose, and it seems that the specificity of this action is not yet proved. If a specific anti-œstrogenic action can be demonstrated for these compounds, a very important discovery will have been made. Aminopterin also has a slight but definite inhibitory action on the growth of spontaneous and transplanted tumours in animals. Farber et al. (1948) report that it caused definite remissions in 5 children with acute leukæmia, but there were also severe toxic reactions.

A-Methopterin.—In this compound there are amino groups in the 2- and 4-positions and a methyl group on the N_{10}. This substance is one-tenth as toxic as aminopterin and is said to possess all the properties of aminopterin—i.e., it is anti-folic-acid and anti-œstrogenic and it inhibits growth of tumours in laboratory animals and of malignant cells in tissue culture.

In view of the extremely promising results obtained in the laboratory with A-methopterin it has been subjected to clinical trial. Up to now nothing has been published about this, but Dr. Rhoads (private communication) informed me that promising results had been obtained.

'*Amino-AN-Fol*' has amino groups on the 2- and 4-positions and R_1 is aspartic acid.

'*AN-Fol-A*' has an amino group at the 2-position, a hydroxyl group at the 4-position, and R_1 is aspartic acid.

A sulphanilamide analogue of aminopterin has been made in which amino groups are at the 2- and 4-positions, R_2 is benzene sulphonic acid, and R_1 is glutamic acid.

This very brief summary of the American work can give no idea of the tremendous amount of energy expended. There can be no doubt of the great theoretical importance of this new group of substances, and the clinical results are awaited with interest. A complete bibliography of the recent American papers is included in the references.

COLEY'S FLUID

Until the last ten years no substance administered by any route to a patient with carcinoma affected the development of the tumour, except possibly Coley's fluid (see Nauts et al. 1946). Coley observed that patients with inoperable malignant disease were often better after an acute infection, such as erysipelas. He prepared cultures of various bacterial types, such as *Strep. viridans*, and claimed that by injecting the toxins of these organisms he could induce a regression of primary and secondary tumours, and that tumours susceptible to these toxins became hæmorrhagic and necrotic. Extensive clinical trial has shown that no uniform results can be obtained, and this treatment is probably not used anywhere today. There is sufficient testimony that results were obtained; but again we are faced with the fact that by making the patient thoroughly ill and cutting down his diet it is possible to limit the disease.

STILBŒSTROL

Since the time of John Hunter it has been known that castration sometimes reduces the size of the prostate, but only towards the end of last century was it realised that the only form of prostatic enlargement benefited by castration was that due to carcinoma. From then until 1940 castration as a treatment of carcinoma of the prostate varied in popularity, though there was no doubt of its efficacy in most cases. Huggins and Clark (1940) and Huggins and Hodges (1941), using acid serum-phosphatase to assess prostatic activity, showed that in the dog the activity of the prostate depended entirely on androgen secretion. In carcinoma of the prostate, particularly when associated with secondary deposits in bone, the amount of acid serum-phosphatase was greatly increased. Huggins et al. (1941) knew from his experiments on the dog that administration of androgens increased the acid serum-phosphatase, whereas removal of the testes or the administration of œstrogens diminished the amount of acid serum-phosphatase. Huggins and his co-workers also knew that the administration of large doses of œstrogen inhibited the anterior lobe of the pituitary gland and abolished the secretion of the gonadotrophic hormone. By combining these observations they postulated that the administration of a powerful œstrogen to patients with carcinoma of the prostate would lead to an improvement in their symptoms. The naturally occurring œstrogens are only active by the parenteral route, and it was therefore impossible to use these for the experiments. It is obvious that, if Huggins's assumption was correct, it was essential to have a powerful orally active œstrogen.

Experiments were begun in the Courtauld Institute in 1930 to investigate the specificity of the œstrus response. A very simple substance, 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene (Cook et al. 1933) was found to have definite œstrogenic activity, though of a much lower degree than that of the naturally occurring œstrogens. By extending these observations it was possible in 1938 to produce the stilbœstrol series of synthetic œstrogens (figs. 11–13),

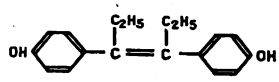

Fig. 11—Stilbœstrol.

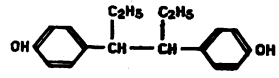

Fig. 12—Hexœstrol.

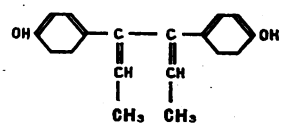

Fig. 13—Dienœstrol.

of which the most active is stilbœstrol (Dodds et al. 1938). These substances have the great advantage of being active when given by mouth, and they were therefore the ideal substances for use by Huggins to test his hypothesis.

Huggins found that the administration of stilbœstrol controlled the local and secondary growths of carcinoma of the prostate, and this form of treatment has made it possible for many patients to live for years without symptoms. There appears to be little doubt that this form of treatment is a kind of biochemical castration through the action of stilbœstrol on the anterior lobe of the pituitary gland. We can therefore say that the first attempt at the chemotherapy of cancer which has been highly successful from the practical point of view is really not a fundamental contribution to the cancer problem at all, since its action is indirect and non-specific.

ANDROGENS

Androgens have been used in the treatment of carcinoma of various sites in women on a purely empirical basis, the argument being that a male hormone might possibly inhibit the growth of cells in the female body. Such an assumption is unwarrantable, and the idea that androgens are entirely foreign to the female body is no longer held. Examination of the urinary ketosteroids in normal women has shown a constant level of excretion of androgens. The androgen used is usually testosterone propionate, administered by either subcutaneous or intramuscular injection. Recently its administration in sublingual pellets has been advocated. It is impossible to assess its value, since the conditions under which it has been administered have been largely uncontrolled and unsuitable for statistical analysis. There exists, for example, a series of papers on the use of testosterone-propionate injections in women who have had a radical operation for carcinoma of the breast, and it is claimed that the incidence of secondary deposits is lessened (Loeser 1948). It is obvious that to substantiate such a

claim a very large series of cases would have to be investigated. It is also claimed that in carcinoma of the female genital tract dosage with testosterone propionate reduces the incidence of secondary deposits; but the same criticism applies. Again, claims have been made that primary growths of the breast have diminished under treatment. Some workers have used very large doses and believe that they can arrest the development of inoperable carcinoma of the breast.

Androgens have very serious drawbacks if large doses are given for a long time, since masculinisation always appears—growth of hair on the face, deepening of the voice, and enlargement of the clitoris. It is difficult to see how testosterone acts on the development of cancer. Perhaps it acts by inhibiting the anterior lobe of the pituitary gland, an action of testosterone which is well recognised, but it is very much less active in this respect than œstrogens.

NITROGEN MUSTARDS

The use of nitrogen mustards (fig. 14) in the treatment of malignant disease originated in the discovery by

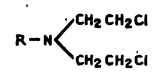

Fig. 14—Nitrogen mustards (β-chloro-ethyl amines).

Auerbach et al. (1942, 1943) that mustard gas and substances allied to it produced mutation of the genes in drosophila. Clinical trials have been made with the β-chloro-ethyl-amines in the treatment of those forms of malignant disease associated with very rapid cell proliferation. These trials have been reviewed by Rhoads (1946). The most extensive trials were made in Hodgkin's disease. Relief of symptoms and regression of lymph-nodes lasting 4–8 months may usually be expected, if the patient responds to the first course of treatment. A subsequent relapse will respond to a further course of treatment, but after this the remissions are progressively shorter. Nitrogen mustards have also been used in lymphosarcoma, giant-follicle lymphoma, lymphatic leukæmia, myeloblastic leukæmia, and a few miscellaneous cases. Rhoads (1946) sums up thus:

> "Their use is limited by their toxic effect on the blood-forming organs, but on the other hand is probably justified in the treatment of any active extensive neoplastic process if other methods of control have proved to be without benefit."

URETHANE

Urethane, like the nitrogen mustards, appears to act chiefly on the blood-forming organs, and this is the reason for its use in leukæmia. Paterson et al. (1947) have reported on the use of urethane in 38 cases of myeloid leukæmia and 26 cases of lymphatic leukæmia. As with the nitrogen mustards, remission is in most cases only temporary, followed by relapses which may or may not respond to further treatment. Again, it is a matter for the clinician to weigh the undoubted risk of toxic effects against the substantial palliative effect which can be obtained in otherwise hopeless cases.

NUCLEOTIDES

Investigation of the effects of nucleotides on tumour growth has been in the hands of Gulland and Parsons (see Parsons and Barakan 1947). This work is only in its infancy, but appears to be well worth continuation.

CONCLUSION

The summary I have given must have a depressing effect. When one considers the vast amount of labour expended during the last fifty years to gain this meagre knowledge, one wonders how much more will have to be done before the cancer problem is solved. It is perhaps unwise to take this rather depressing view, since it does not necessarily follow that, if it has taken us fifty years to reach the present stage, in another fifty years we shall merely have doubled the amount of knowledge we have now. One has only to think of the centuries of observations made on the question of suppuration, with no progress whatsoever, and the rapid progress against that age-old enemy under the genius of Pasteur.

One very significant fact emerges from this study—that there are a great many ways of producing cancer, with no fundamental connexion between them, but that, having once started the process, we have no means of stopping or checking it by direct action. All the anti-carcinogenic substances and agents act indirectly. Perhaps we shall not discover a directly anticarcinogenic substance until another Pasteur arises.

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SURGERY IN HÆMOPHILIA

A CASE OF SPINAL SUBDURAL HÆMATOMA PRODUCING PARAPLEGIA

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THE following case is reported for three reasons—first, as an example showing that major surgery may be undertaken in hæmophilia without undue risk provided transfusions of fresh blood are given until all wounds are healed; secondly, as a case of spinal compression of unusual causation; and thirdly, as a rare complication of hæmophilia.

A boy, aged 16 months, was transferred to the Nuffield Department of Surgery on Nov. 15, 1947, on account of a flaccid paraplegia of six days' duration. He came of an undoubtedly hæmophilic family (fig. 1).

Previous History.—The patient was the youngest of three children; born a month prematurely, he weighed 5 lb. 3 oz. at birth, and was breast-fed for a month only. He gained weight satisfactorily. The first teeth erupted at 4 months. He sat up at 6–7 months, but did not begin to walk until 14 months—i.e., 2 months before his illness began. He apparently did not walk so well as his brother and sister; he had a peculiar way of throwing his head back and of walking on his toes, rather hurriedly, as though to offset by speed his uncertain balance. In his frequent falls he would bruise easily. He was lively, cheerful, and somewhat excitable, but could not talk except for making a few inarticulate baby noises. He had none of the infections of infancy.

Present History.—On Oct. 31, 1947, apparently without any preceding injury except for his usual falls, he awoke unusually late, at 10.15 A.M., seemed to remain drowsy and fell about more than usual. His legs, especially the right one, appeared to be weak. After his evening feed he vomited three times, and after the third vomit he fell unconscious and remained limp and pale, with eyes rolling from side to side, for about half an hour. His own doctor had him admitted to the Northampton General Hospital that night. On admission the child's temperature was 102°F, his neck was retracted, and he showed photophobia and redness of the tonsils and ear-drums. A throat swab yielded a scanty growth of hæmolytic streptococci. The cerebrospinal fluid (C.S.F.) contained 21 red cells per c.mm. A blood-count showed 4,100,000 red cells per c.mm. and Hb 80%. The bleeding-time was 2 min. and the clotting-time, as estimated by the capillary method of Dale and Laidlaw over 12 min. He was treated with sulphadiazine and made a satisfactory recovery within a week.

Arrangements for his discharge had been made when, on Nov. 8, neck-rigidity and pyrexia recurred. Next day he had complete paralysis of both legs and retention of urine. These signs persisted, though on the 10th slight movement could be elicited in the right vastus medialis muscle and in the right toes. Lumbar puncture was attempted on Nov. 9, 10, and 12, but failed. A cisternal puncture was performed on the 12th, and the C.S.F. contained protein 55 mg. per 100 ml. and 1813 cells per c.mm., mostly erythrocytes. Of the white cells 76% were neutrophils and 24% lymphocytes. Culture of the fluid was negative. On Nov. 13, the patient was given a blood-transfusion of 350 ml. of group-O blood (his own group). Two days later he was transferred to the Radcliffe Infirmary.

On admission his temperature was 98°F, pulse-rate 132, and respiration-rate 28 per min. He looked fairly healthy but was fretful, with a little thrush in his mouth. There was head-retraction with stiffness of the neck and he had a flaccid paraplegia with absent abdominal reflexes, knee-jerks, and ankle-jerks. The right plantar reflex was extensor; the left could not be elicited. On pinching there were a little dorsiflexion of the right toes and ankle and a flicker in the adductor muscles of the right thigh but no spontaneous movements; there were no responses on the left side. No definite sensory level could be made out, but pricks even to the feet seemed to distress the child. The upper limbs moved normally, and their tendon-jerks were present and equal. The bladder was distended to 1 in. below the umbilicus; it was catheterised and slowly decompressed. The urine contained no albumin, sugar, or acetone.

Two attempts at lumbar puncture failed, only clot in the needle and a drop of dark brown blood being obtained. A cisternal puncture yielded moderately bloodstained C.S.F. containing 1800 red cells and 8 white cells (3 polymorphs, 5 lymphocytes) per c.mm., protein 90 mg. per 100 ml., and chlorides 730 mg. per 100 ml. 'Pantopaque' 2 ml. was injected into the cisterna magna, and the subsequent myelogram showed a complete arrest, the pantopaque forming an inverted U opposite the 8th and 9th thoracic vertebræ (fig. 2*a*).

Diagnosis.—We were thus faced with the unusual emergency of acute spinal-cord compression of uncertain origin in a hæmophilic infant. The legs had been paralysed for a week without any sign of recovery. Hæmatorrhachis was a possible diagnosis, but an inflammatory condition could not be excluded. In our decision to explore the lesion by laminectomy we were guided by the general consideration that decompression was the only possible treatment if the child were ever to walk again, and it had to be risked in spite of the tendency to bleed.

Operation (Nov. 15, 1947).—*Laminectomy of the 7th to the 12th thoracic and the 2nd lumbar laminæ. Removal of large solid subdural clot.*

The child was first given open 'Trilene' and then gas and oxygen through a mask. He was given 1/3 pint of fresh blood and remained in a favourable condition during the operation, which lasted 2 1/2 hours.

The final skin incision reached from the 7th thoracic to the 3rd lumbar spines. The lowest five thoracic and the second lumbar laminæ were removed. The first lumbar lamina was left intact. Wherever it was exposed the dura was blue and tight. When the dura was opened, clot bulged through the incision, but it nowhere extruded spontaneously, being too solid. The clot was difficult to remove with the sucker, especially over the conus, and forceps and pituitary rongeurs were necessary; it seemed that the clot was almost on the point of organising. In places it was up to 15 mm. thick. It was a solid mass, mostly at the back of the cord but also surrounding it to some extent asymmetrically. Some was sucked away from the sides of the cord. The arachnoid was intact throughout, and pantopaque globules were visible underneath. The cord was orange-yellow and severely flattened below the lumbar enlargement but it assumed its normal shape after the clot had been removed. Then the cord was pulsating and jugular compression made the fat-globules of pantopaque move. A glimpse through a small incision opposite the 2nd lumbar vertebra showed the roots of the cauda equina embedded in clot, which was too difficult to remove without damaging the roots.

The dura was left open over the cauda equina but was closed over the cord with interrupted silk sutures about 15 mm. apart. The muscles and lumbar dorsal fascia were sutured with interrupted double silk and linen-thread stitches, and a rubber drain was left at the bottom of the wound. The skin was sutured in the usual way. There was no abnormal bleeding during the operation.

Immediate Postoperative Condition.—Apart from a rise in temperature to 102°F, in pulse-rate to 140–160 per min, and in respiration-rate up to 50 per min. for 2 days, the patient's immediate postoperative condition was promising. The

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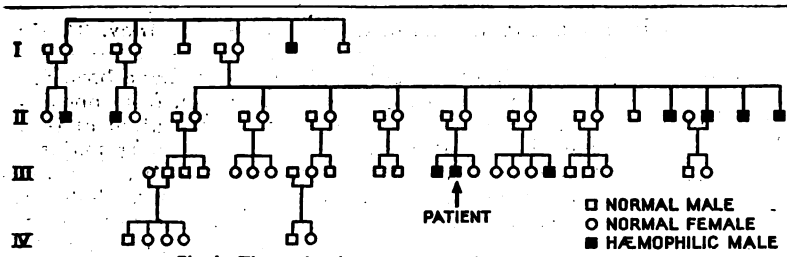


Fig. 1—The patient's pedigree, showing hæmophiliacs.

drain was removed on the 4th postoperative day, and his general condition returned to the preoperative level. He was given bladder washouts and daily blood-transfusions of 50 ml. (see below).

Healing of Wound.—A deep subcutaneous hæmatoma developed under the wound, and on Nov. 25, 10 days after the operation, a frank secondary hæmorrhage took place. When the skin sutures were removed, the upper third of the wound gaped. The bleeding came from the depths and was arterial, and the patient lost 100 ml. or more of blood before the bleeding was stopped with fibrin foam and packing. A large transfusion (350 ml.) was at once given, and next day the hæmoglobin was 70%. The wound was closed over 'Oxygel' (oxydised absorptive cellulose), but 2 days later the sutures began to cut out, and on Dec. 1—i.e., 16 days after operation—there was another hæmorrhage from the wound. This was easily stopped with fibrin foam and packing. During the next 5 days C.S.F. leaked from the wound. The leak stopped on Dec. 7, and from then onwards the wound gradually healed within 10 weeks. *Staph. aureus* and on a few occasions *Strep. fæcalis* and *Proteus* were cultivated from the wound from Nov. 28 onwards. The staphylococcus was relatively insensitive to penicillin, 6–50 units per ml. being required to prevent its growth. Dressings were done with penicillin-'Sulphamezathine' powder, and during the last fortnight silver nitrate was applied to the redundant granulations.

Chemotherapy.—Systemic penicillin, 15,000 units 3-hourly, was given from Nov. 16 to Nov. 28, a total of 1·56 mega units. Sulphamezathine, mainly for the bladder infection, was given in doses of 0·5 g. 8-hourly from Nov. 24 to Nov. 28, 1947, and from Jan. 1 to Jan. 26, 1948, and sulphadiazine 0·5 g. 4-hourly from Nov. 28 to Dec. 17.

Bladder Function.—The patient was fitted with an indwelling catheter from the outset, and daily bladder washouts were given with boracic or potassium permanganate solutions for 2 weeks. By Nov. 24 the bladder was grossly infected and *Bact. coli* and *Proteus* were found in the urine for the next few weeks. After tidal drainage had been started on Nov. 30 the urine became clearer; there were recurrences of up to 4000 pus cells per c.mm. (Dec. 10), but on Jan. 26, 1948, only a few cells were seen. On Dec. 9, 1947, reflex evacuation of the bladder was established and tidal drainage discontinued. A transient superficial sacral bedsore was present during the 5th and 6th weeks, but healed satisfactorily.

General Condition and Paraplegia.—About a week after the operation, withdrawal reflexes to painful stimuli were seen in both legs, more so on the right side. These became gradually more vigorous. Slow voluntary movements began in the right leg, at the end of the 3rd postoperative week, and in the left leg about 2 weeks later. The power in both legs improved further, except for the muscles distal to the left knee. From the 9th week the patient began to sit up, and by the 10th week he could crawl but tended to fall to the right side. The right leg seemed to have recovered completely by the 10th week. Knee-jerks and ankle-jerks, however, remained absent on both sides; the right plantar reflex was extensor, and the left could not be elicited.

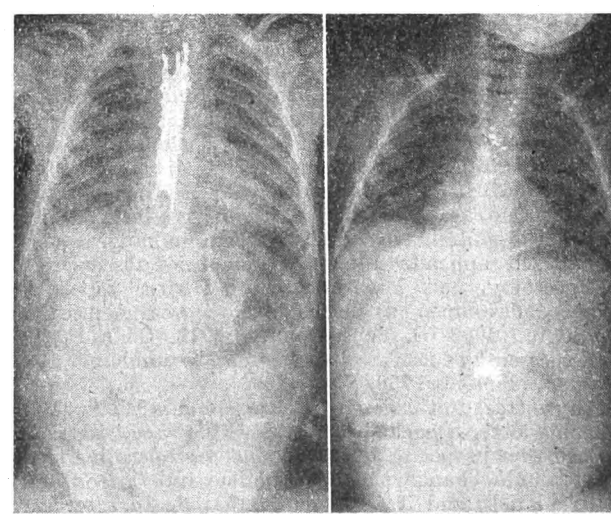
Progress.—After the secondary hæmorrhages and smaller hæmorrhages from transfusion wounds the patient had several acute rises of temperature, but after the 7th week he remained apyrexial. From the 5th week he gradually became more cheerful and began to play with his toys and to make contented noises. He was discharged on Jan. 30, 1948, in the 11th postoperative week. Myelography, with the contrast medium still present in the spinal canal, showed globules of pantopaque scattered over the whole spine, with an arrest at 3rd lumbar vertebra (fig. 2*b*).

Follow-up Examination (March 10, 1948).—Two and a half months after discharge the patient had begun to stand and walk with support. He still had a complete foot-drop and the calf muscles were wasted by $^3/_4$ in. on the left side, but movements of knee and hip were quite strong, and the right leg was normal. The right knee-jerk was now present, but the left knee-jerk and both ankle-jerks were absent. The plantar reflexes were flexor. He still had no proper control of his bladder, and the urine tended to dribble. Radiography of the spine showed the same arrest of the contrast medium at the 3rd lumbar vertebra. The scar on his back was sound and not more than 3 mm. wide.

TRANSFUSIONS

Two days before admission the patient had received a transfusion of 350 ml. of whole blood. During the 66 days from Nov. 15, 1947, to Jan. 19, 1948, he was given 62 transfusions of fresh blood to keep his condition as near normal as possible and to promote healing of the laminectomy wound. The transfusions were continued until the wound had completely healed. The usual quantity given was 50 ml. On four occasions he received larger quantities to compensate for blood-loss: during and immediately after the operation a pint was given by cannula into the left internal saphenous vein at the ankle; after the secondary hæmorrhage from the wound on Nov. 25 he received 3 5 ml., and next day 300 ml. by needle into the right external jugular vein; on Dec. 1 200 ml. was given by the same route after a further hæmorrhage.

The technique of transfusion was modified after the first postoperative week, during which the patient had been given five transfusions into the veins of the legs. It seemed clear that he was going to need a long series of daily transfusions, and it was decided to use venepuncture rather than to cut down on the veins. The right external jugular vein was selected as the most suitable. Up to 7 or 8 daily consecutive transfusions could be given by this route before the vein thrombosed, and it took 7–10 days for the vein to regain its patency. This vein was used on 21 occasions. When it was not usable, the transfusions were given by cutting down on the veins of the wrist or the dorsum of the hand and inserting a cannula. Unfortunately there was no vein adequate for venepuncture on the left side of the neck. It was found possible to use the same incision repeatedly (up to 6 times) by opening it up each day and inserting the cannula into the same vein. Initially the vein was tied off, but with increasing experience it was left patent and the same hole in the vein was used each time. A mild infection developed in these small wounds, but each healed cleanly within 4–7 days, except two from which there was a mild secondary hæmorrhage which delayed healing for a further week. A special drip apparatus with a capacity of 50 ml. was used for the



(*a*) (*b*)

Fig. 2—Cisternal myelogram: (*a*) before operation, showing contrast medium arrested at T9; (*b*) after operation, showing contrast medium arrested at L3.

small transfusions. Seven donors were used, some of them on 7 consecutive days.

What was probably a transfusion reaction developed on Dec. 5, when the patient's temperature rose to 103°F and he developed a macular rash an hour after a transfusion of 50 ml. The patient was well again within a few hours, and the same donor's blood was given next day without untoward effect.

Sedation for the transfusions into the jugular vein had to be heavy. Normally, chloral hydrate gr. 22 was given by mouth and paraldehyde 3 ml. intramuscularly, with the addition of paraldehyde directly into the drip during the three prolonged transfusions. For the transfusions by cannula only sufficient sedative was used to produce drowsiness and amnesia.

HÆMATOLOGICAL FINDINGS

On admission, 2 days after the transfusion of 350 ml. of blood the coagulation-time (Lee and White's method) was 9 min., the bleeding-time was 11 min., and the platelets numbered 270,000 per c.mm. (Lempert's method).

Two weeks after the operation the coagulation-time was 5 min.

Seven days after the last transfusion the coagulation-time was 23 min.; in Quick's test for hæmophilia citrated plasma recalcified after being spun for 5 min at 1000 r.p.m., clotted in 214 sec. (normal 90–125 sec.), and at 3000 r.p.m. clotted in 364 sec. (normal 105–145 sec.). Clot retraction was normal (42% serum expressed).

DISCUSSION

The fear of surgery in hæmophilia has been expressed, with few exceptions, in all published accounts of hæmophilia up to the present day. In the Babylonian version of the Talmud, originating in the second century A.D., it is ordained that a woman who has lost two sons from hæmorrhage after circumcision shall be exempt from the obligation of having a third son circumcised. Legg (1872) stated in his treatise: "In every case on record, where amputation has been done, or large artery tied, or any of the great operations of surgery performed, as, for example, lithotomy, the patient has died either from the bleeding caused by the operation itself, or of the bleeding for the relief of which the operation was undertaken." More than sixty years later Friedrich (1935) estimated the surgical risk in hæmophilia at 35%, and would not advise operation even with such strong indications as acute appendicitis, intestinal obstruction, cancer, or orthopædic deformities. In America Birch (1937) found that death in 22% of her cases of hæmophilia was due to surgery, and in Holland Kooreman and Hecht (1943) estimated this figure at 10%.

An analysis of the operations performed on hæmophiliacs is illuminating. In Birch's (1937) series of 25 deaths after surgery in hæmophilia the operations were circumcision in 15, tooth extraction in 6, tonsillectomy in 1, lancing of throat to relieve pressure symptoms in 1, lancing of hæmatoma of scalp in 1, and vaccination in 1. It is reasonable to believe that most of these lives might have been saved if blood-transfusion had been available. Seven other cases of fatal operations have been reported in some detail. Four of these were for gangrenous or perforated appendices, 1 a perinephric abscess, 1 a gastrectomy, and 1 a nephrectomy after which the patient developed a severe streptococcal septicæmia (Dahlgren 1908–09, Schloessmann 1912, Conrad 1925, Wossnessensky 1930, Custer and Krumbhaar 1935, Mertz and Meiks 1938, Vance 1939).

In contrast to this gloomy background is Weil's (1931) optimistic view, backed by a vast experience. He maintained that proper preoperative and postoperative treatment could change the hæmophiliac into an ordinary surgical risk, and it seems clear that death after such minor procedures as vaccination is unnecessary, since fresh blood can be run in through a vein faster than it can escape from a superficial scratch. The greatest danger in hæmophilia is pressure on some vital organ, as in our case.

Reports of 15 successful operations have been found. These are of all degrees of magnitude, from opening of hæmatoma, correction of squint, amputation of thumb, and plastic operation on the knee, to more major procedures like amputation of whole limbs, removal of gangrenous appendix, gastro-enterostomy, cholecystectomy, splenectomy, prostatectomy, and even mastectomy for carcinoma of the male breast (Lane 1840–41, Feissly 1924, Weil 1931, Blalock 1932, Hinman 1933, Jones and Tocantins 1934, Firor and Woodhall 1936, Tavernier 1938, Sköld 1944). To this list may be added from our personal knowledge appendicectomy, splenectomy, amputation of leg, mastoidectomy, and dozens of tooth extractions.

Without discussing the prevalent views of the nature of hæmophilia it may be said that the rational treatment at present is blood-transfusion. Local applications have not proved effective, and the plasma fractions that may replace whole blood are not at everybody's disposal.

It is of historic interest that what was perhaps the first successful operation on a hæmophiliac was followed by blood-transfusion. This was the correction for squint carried out by Lane (1840–41). The patient bled for days and was in extremis; a transfusion was given, and he sat up and drank a glass of wine.

The effect of blood-transfusion in hæmophilia lasts only one or two days. To keep the patient as near the normal state as possible before, during, and after the operation, while the wound is healing (often an unduly protracted affair in these cases), the transfusions should be repeated at regular intervals. To be guided by the clotting-time of the blood is unsafe, because it is not invariably a true indication of the tendency to bleed. Very occasionally after many transfusions the patient may develop an anticoagulant (antibody), and subsequent transfusions are then ineffective (Lawrence and Johnson 1942, Munro and Jones 1943, Craddock and Lawrence 1947). An essential too often sadly neglected in the proper handling of every hæmophiliac is the preservation of injectable veins.

Of the many forms of hæmorrhage that complicate hæmophilia, bleeding into the central nervous system is one of the rarest and most fatal. Aggeler and Lucia (1944), in their comprehensive review, collected 32 published cases, to which they added 1 of their own. A few more have been traced. Lane (1840–41) mentioned two members of a well-known hæmophilic family who died of cerebral hæmorrhage. Fonio (1936) described a case of left-sided hemiparesis with epilepsy following intracranial bleeding some years previously. Andreassen (1943), in his survey of hæmophilia in Denmark, found some cases of intracranial hæmorrhage, but the available information was too scanty to determine their exact character. He observed a case of hæmatomyelia following a fall from a chair, with paralysis and sensory loss of the legs, incontinence of urine, and complete recovery in $3^1/_2$ months. Sköld (1944), in a similar survey in Sweden, reported 5 hæmophiliacs with intracranial hæmorrhage, of whom 3 died and 2 recovered in about a fortnight.

From a study of the published reports it is difficult to assess definitely the prognosis of spinal-cord compression by blood-clot. Either the reports do not give satisfactory evidence about the exact situation of the clot within the spinal canal (extramedullary or intramedullary, cord or cauda equina), or the degree of recovery is not unequivocally stated. It seems, however, that full spontaneous recovery has been observed only in cases of compression of the cauda equina (Bulloch and Fildes 1912, Feissly and Curchod 1925). Death has been the most common sequel. The total of relevant cases reported does not exceed a dozen, and no attempts at treatment by laminectomy have been reported.

Though it was impossible in our case to remove that part of the clot which surrounded the roots of the cauda equina, the finding and removal of a solid hæmatoma constricting the spinal cord, followed by partial recovery, justified our decision to operate.

SUMMARY

Paraplegia due to a subdural spinal hæmatoma in a hæmophiliac was partly cured by laminectomy.

Hæmatorrhachis is one of the rarest complications of hæmophilia and is usually fatal if not dealt with surgically.

The surgical risk in hæmophilia can be greatly diminished by giving small daily blood-transfusions, continued irrespective of the hæmatological findings until the wound has healed.

Pressure on a vital organ presents the greater danger to the hæmophiliac.

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AIR INFECTION WITH DUST LIBERATED FROM CLOTHING

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RESPIRATORY infections may be spread by air carriage of the causal organisms, by contact, by fomites, or by direct spraying with secretion droplets. That they are mainly transmitted by air carriage is suggested by their very high incidence, clinical and subclinical, and the rapidity of their epidemic spread (Wells and Wells 1936, Wells et al. 1939), by their seasonal periodicity, which is apparently due to domestic ventilation varying with outdoor temperature (Wells 1944), and by the success of air disinfection in reducing their incidence in schools and convalescent homes (Wells et al. 1942, Harris and Stokes 1945).

Pathogenic micro-organisms can enter the air in two ways: in droplet spray produced by speaking, coughing, or sneezing, and in dust liberated as a result of friction and movement from the skin and clothing of infected persons, from their bedding, or from the floor and furniture of their rooms.

As regards droplet spray, Wells (1934) has shown that the larger droplets fall out of the air within one or two seconds, while the smaller droplets (under 0·1 mm. in diameter) evaporate immediately to form minute solid residues, "droplet nuclei," which may remain air-borne for several minutes or hours. It is well established that sneezing, coughing, and speaking contaminate the air with very large numbers of droplet nuclei containing salivary commensal organisms—e.g., 10,000–1,000,000 per sneeze, 10–1000 per cough, and 10–100 per hundred spoken words (Wells and Wells 1936, Bourdillon et al. 1942, Duguid 1945). However, the importance of droplet spray as a cause of air infection should not be overestimated, since it appears that pathogenic organisms are contained in only a small proportion of the droplets and in only a very small proportion, if any, of the droplet nuclei (Hare 1940, Hare and Mackenzie 1946, Duguid 1946a and b).

There is much convincing evidence to show that air is readily infected with dust-borne pathogenic organisms. Tubercle bacilli, pneumococci, hæmolytic streptococci, diphtheria bacilli, and pyogenic staphylococci have been found in the floor dust of rooms occupied by infected persons; and contamination of the air with hæmolytic streptococci and diphtheria bacilli has been demonstrated in relation to sweeping and other dust-raising activities (Cornet 1889, Avery et al. 1917, Stillman 1917, White 1936, Brown and Allison 1937, Thomas 1941, Cruickshank 1941, Crosbie and Wright 1941, Edward 1944, Hamburger et al. 1944, Green et al. 1945, Allison and Hobbs 1947). Dust-borne infection of air has been shown to result from disturbance of bedding (Thomas and van den Ende 1941), and from shaking of handkerchiefs (Dumbell et al. 1948). The skin and clothing of infected persons are a further important source of infected dust; hæmolytic streptococci have been demonstrated on the skin of the hands and face, on the handkerchiefs and on the inner and outer clothing of persons with upper respiratory-tract infection (Hare 1941, Hamburger and Green 1946, Colebrook and Ross 1947). Throat carriers contaminated the air with large numbers of hæmolytic streptococci derived from their clothing in an experiment designed to preclude air infection by droplet spray or by raising of dust from the floor and furniture (Green et al. 1945). Air has been contaminated with *Staph. aureus* by the shaking of pyjama jackets (Bourdillon and Colebrook 1946).

Wells et al. (1946) draw a sharp distinction between dust-borne air infection and droplet-nucleus air infection according to particle size and duration of air carriage; droplet nuclei are small, remain air-borne for long periods, are dispersed widely indoors, can penetrate to the lungs, and cause epidemic infections; infected dust particles are large, settle rapidly giving only localised and short-lived air contamination, and cause endemic infections of nose and throat. The validity of this distinction is not altogether certain. Air carriage for between half an hour and two hours has been demonstrated for a small proportion, 2–10%, of sneeze-produced droplet nuclei containing salivary commensal organisms (Bourdillon et al. 1942, Duguid 1946b). There is little comparable evidence about the duration of dust-borne bacterial contamination of the air, but this seems to be not very much shorter. In one experiment heavy air contamination with hæmolytic streptococci persisted for over 15 min. subsequent to its production by shaking clothes (Green et al. 1945).

In the present study measurements were made of the bacterial contamination of air produced by liberation of dust from the skin and personal clothing during bodily movement, of the duration of air carriage of the bacteria-carrying dust particles, and of the effectiveness of gowning as a means of preventing such contamination of air.

METHODS

The tests were made in a specially constructed test chamber of 100 c. ft. capacity (8 ft. high × 3½ ft. × 3½ ft.), which had a close-fitting door and was not

ventilated. The interior surfaces, walls and floor, were soaked with spindle oil to prevent liberation of dust from them. For bacteriological examination air was withdrawn by a short tube through the wall of the chamber to a slit sampler outside (Bourdillon et al. 1941); the entrance to the air intake was 3 ft. from the floor and was screened from above to prevent dust from falling directly into it. With a slit-plate distance of 2 mm. air was sampled at the rate of 1 c. ft. per min. on to plates of either ordinary blood-agar or heated blood-agar ("chocolate-agar") for easier recognition of greening by *Strep. viridans*. The plates were incubated aerobically at 37°C for 18–24 hours (longer incubation led to frequent spoiling of plates by "spreaders"). After the surface of the agar had been scored by parallel cuts with a scalpel, the colonies were counted with a binocular plate microscope (×20); the microscope was required for sure recognition of the smaller colonies. In special tests with carriers a selective medium for *Staph. aureus* was used: an alkaline nutrient agar containing mannitol, lithium chloride, and 0·005% of tellurite (Ludlam 1948).

The principal experiments were made with four healthy men who were not carrying pathogenic bacteria. Bacterial contamination of the air was produced by one man entering the chamber quietly, closing the door, undertaking some standard form of activity while occupying the chamber for 10 min. (keeping his mouth closed to prevent the production of droplet spray), leaving the chamber, and closing the door. The standard activities tested were as follows:

(1) *Standing motionless*, avoiding so far as possible the slightest movement.

(2) *Slight activity*, standing fairly still for most of the ten minutes, but on four occasions making movements in a pretence at changing culture-plates in an imaginary slit sampler, bending the body, and reaching out the arms.

(3) *Vigorous activity*, "marking time" at walking pace continuously throughout the 10 min., raising the feet, and swinging the arms.

(4) *Undressing and dressing*, taking off all clothes and replacing them once during the 10 min.

(5) *Brushing clothes*, applying 40 strokes with a sterilised brush to the front of the jacket and trousers.

Each experiment was carried out as follows: In the *control period*, before occupation of the chamber, two 10 c. ft. air samples were taken. During the 10 min. *activity period*, while the chamber was occupied, four 2 c. ft. samples were taken. Further samples were taken at intervals during the *die-away period*, the four hours after termination of activity and occupation of the chamber. During the occupation of the chamber, the temperature inside was usually 50–60°F, and the relative humidity 50–70%.

In these experiments nearly all the observed amount of bacterial contamination of the air must have been due to liberation of dust from the subject's skin and clothing, since raising of dust from walls and floor was prevented by the oil treatment, and droplet spray was avoided by the subject keeping his mouth closed.

RESULTS

The accompanying table shows in detail the results obtained in 17 experiments with one of the non-carriers. An exactly similar series of 17 experiments was made with each of the other three non-carriers; the results, being similar to those in the table, are not given in detail, but figs. 1 and 2 show average air-contamination values for all four series of experiments taken together. These averages were calculated from all the activity-period observations made in equivalent experiments with the four subjects.

While the chamber was unoccupied there was little infection of the air; the average of the control-period observations was 2 bacteria-carrying particles per c. ft. of air. Bacterial contamination of the air was always increased on occupation of the chamber, the amount depending on the kind of activity undertaken by the

NUMBER OF BACTERIA-CARRYING PARTICLES PER C. FT. OF AIR IN A 100 C. FT. CHAMBER DURING VARIOUS ACTIVITIES

Period (min.)	Standing motionless			Slight activity						Vigorous activity						Undressing and dressing	Brushing clothes
	No gown	Surgical gowning	Dust-proof gowning	No gown		Surgical gowning		Dust-proof gowning		No gown		Surgical gowning		Dust-proof gowning		No gown	No gown
	BA	BA	BA	BA	CA	BA	CA	BA	CA	BA	CA	BA	CA	BA	CA	BA	BA
Control:																	
0–10	6	4	3	1	1	2	1	1	1	1	3	2	2	2	2	1	3
11–21	5	4	4	1	2	2	1	2	1	1	4	1	2	2	1	2	2
Activity:																	
22–24	13	13	15	74	167	74	60	18	12	528	1332	527	366	17	35	858	815
24½–26½	11	18	7	142	307	114	95	22	16	1215	1953	986	865	29	37	2814	845
27½–29½	9	10	5	223	368	207	118	24	25	1233	2002	1201	864	45	53	3340	765
30–32	12	9	5	240	387	201	139	25	26	1321	1683	1108	914	42	49	2485	1125
Die-away:																	
33–35	9	11	6	181	250	86	100	21	21	928	1139	850	675	33	43	1545	839
37–39	16	7	9	126	203	64	72	23	19	819	808	556	457	23	34	1623	468
42–44	13	10	11	112	135	53	38	22	17	450	686	354	516	17	28	1237	259
52–54	14	14	8	71	31	44	22	11	10	268	321	204	213	14	21	645	115
72–74	11	12	24	30	9	19	8	8	5	140	122	82	84	9	12	212	21
92–102	7	4	..	21	7	13	2	7	4	96	59	35	45	5	7	96	11
152–162	4	4	..	12	4	8	1	5	1	43	30	13	14	2	3	30	6
212–222	2	3	..	11	3	5	1	3	1	22	10	8	3	2	1	11	6
272–282	..	..	..	..	1	..	1	..	1	9	8	4	3	3	1	5	4
Experiment no.	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*

BA, blood-agar; CA, chocolate-agar; .., no sample taken.

occupant (fig. 1), and on whether or not a sterile gown was worn over the ordinary clothes (fig. 2).

Contamination of Air when Clothing was not Covered.—When a person with ordinary clothing entered the chamber quietly, stood motionless for 10 min., and then left quietly, the air contamination was increased only a little, an average of 9 bacteria-carrying particles per c. ft. of air being present during this occupation. With slight activity of the occupant greater air contamination was produced—an average of 129 bacteria-carrying particles per c. ft. Even greater air contamination was produced by vigorous activity—an average of 837 bacteria-carrying particles per c. ft.; by undressing and dressing an average of 1672 bacteria-carrying particles per c. ft.; and by brushing clothes an average of 501 bacteria-carrying particles per c. ft.

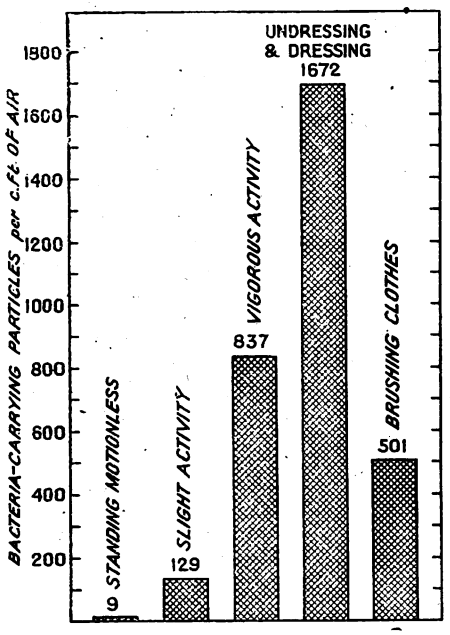

Fig. 1—Average air infection in occupied chamber.

Because dust particles settle at different rates, it is impossible to calculate from the numbers found per c. ft. the exact total number put into the air during the 10 min. activity period. However, a minimum may be calculated from the first observation made in the die-away period. This sample was not started until a minute after the occupant had left the chamber. It is assumed that by this time the dust particles had become uniformly dispersed throughout the entire 100 c. ft. of the chamber; dispersion was aided by the air disturbance caused when the occupant opened and shut the door on leaving the chamber. The number of infected dust particles per c. ft. found in the first sample of the die-away period was multiplied by 100 to give the total number in the chamber at that time. This calculation showed that, on average, at least 12,000 bacteria-carrying particles capable of remaining air-borne for more than a minute were liberated into the air during 10 min. of slight activity, and at least 67,000 such particles during 10 min. of vigorous activity. If the standard slight activity of these experiments is about equivalent to the average activity of daily life, the air must normally become contaminated from personal clothing at the rate of about 1,000,000 bacteria-carrying dust particles per person per day.

Contamination of Air when Clothing was Covered with a Sterile Gown.—Two methods of gowning were tested for their effectiveness in preventing contamination of the air with bacteria from the skin and clothing. The first is designated "surgical gowning." A sterile surgical gown was worn over the ordinary clothing. This gown was of the usual type, made of light cotton cloth, long and loose, reaching to below the knees, tied at the back with tapes, loose and open beneath, and having sleeves reaching to the wrists. Sterile rubber gloves were worn with the gown cuffs tucked inside them. Disinfected long rubber boots were worn which covered the lower parts of the trouser legs. The usual surgical cap and mask were worn. With this surgical gowning the average bacterial contamination of air by slight activity was 57%, and by vigorous activity 59%, of that found in the comparable experiments without gowning. Such a reduction, by less than half, may be considered practically valueless. This mode of gowning was insufficiently effective probably because the dust particles from the skin and clothing were freely expelled through the gaps at the back of the gown where it was tied with tapes, and through the wide opening at the foot.

An attempt was made to design a complete dust-proof covering without any gaps through which dust-laden air could escape from the clothing and friction-exposed areas of skin. As a dust-proof gown we used a modified boiler suit. This was a one-piece costume of heavy close-woven cotton twill which covered the body, arms, and legs. The pocket slits were sewn up. A 'Zip' fastener was fitted instead of buttons to close the front. Elastic bands were put over the sleeve cuffs so that these gripped the wrists closely. A heavy canvas sock was sewn to the bottom of each trouser leg to form a complete covering for the foot and shoe. The collar was enlarged and made to tuck over and inside the collars of the jacket and shirt beneath. The ordinary clothing was thus completely covered without gaps at the feet, wrists, neck, or elsewhere for escape of dust-laden air. The suit was sterilised by autoclaving. In preliminary experiments the head was completely covered with a hood, and the hands were greased or gloved, but these additional precautions did not give increased protection and were not continued; not being exposed to friction the head and hands were not an important source of air infection. Bacterial contamination of the air was very much less in tests with dust-proof gowning than in tests without gowning or with surgical gowning. With dust-proof gowning the average bacterial contamination of air by slight activity was 12%, and by vigorous activity 4%, of that found in the comparable experiments without gowning.

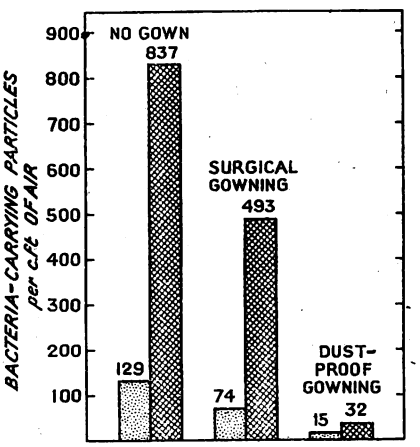

Fig. 2—Influence of gowning on air infection: stippled columns, after slight activity; hatched columns, after vigorous activity.

Duration of Air Carriage of Bacteria-carrying Dust Particles.—Bacterial contamination of the air remained appreciably above the control level usually for over 20 min., and sometimes for as much as 2 hours, after the termination of dust-raising activity. Fig. 3 shows the persistence of air infection following slight activity observed in a single experiment. For the experiments with a maximal recorded air infection of over 1000 bacteria-carrying particles per c. ft. the average time until disappearance of all but 10% of these particles was 35 min. Since much importance was attached to this considerable persistence of dust-borne bacterial contamination of the air, a possible but unlikely cause of error was carefully considered. Infected dust particles drawn into the air-sampler intake tube during the activity period might adhere to the walls of the tube and

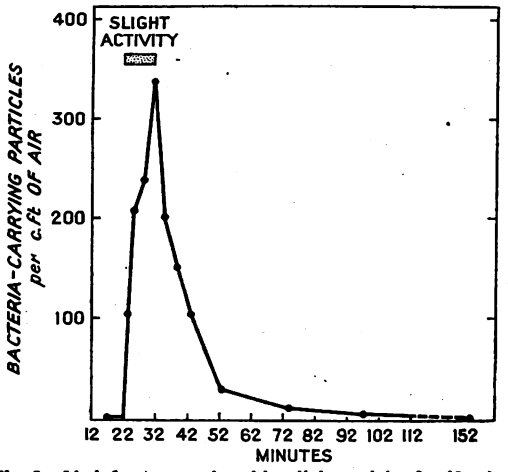

Fig. 3—Air infection produced by slight activity for 10 min.

then, during the taking of later samples, become freed, and pass into the sampler. To exclude this possibility experiments were made in which the air was heavily infected by vigorous activity and, to avoid contamination of the intake tube, no samples were taken during the activity period or during the die-away period until 30 min. after the person had left the chamber. The samples taken after this time showed amounts of air infection much above the control level (37, 38, 71, 33, and 86 bacteria-carrying particles per c. ft. in five experiments); this confirmed the long duration of air carriage of infected dust.

RESPIRATORY-TRACT BACTERIA

Since the subjects of the experiments described above were not carriers of pathogenic organisms, the bacteria recovered from the air were exclusively non-pathogenic—mainly saprophytes normally resident on the skin and clothing. Proof was desired that persons with respiratory infection would disseminate pathogenic organisms on a proportion of the dust particles from their clothing. The presence in air of *Strep. viridans* has been suggested as a reliable indicator of contamination from the upper respiratory tract (Gordon 1903, Wells and Wells 1936). Therefore, in experiments made with chocolate-agar plates, those described above, and also a few made with a fifth subject (carrier Y), the number of colonies resembling *Strep. viridans* was noted.

A few such colonies were found in almost every experiment with each of the five test subjects. On plates exposed in 35 experiments, which bore a total of 141,694 colonies, there were 424 colonies (0·30%) which resembled *Strep. viridans* and were surrounded by zones of greening. However, on microscopical examination of smears from blood-agar and nutrient-broth subcultures of 168 of these colonies, only 10 showed streptococcal morphology and chain formation. The remaining 158 (94%) were gram-positive cocci grouped in pairs, tetrads, and clusters, but not in chains. These apparently corresponded to the "putative streptococci" which Buchbinder et al. (1938) found comprising 60% of the green-producing streptococcus-like colonies obtained in sampling air, and which he regarded as probably streptococci derived from the respiratory tract but altered in morphology and other characteristics as a result of their aerial environment. However, the possibility must be considered that the "putative streptococci" are not true streptococci but micrococci which normally reside as saprophytes on the clothing. Thus, in the present experiments the extent of bacterial contamination of the air from the respiratory tract via clothing is indicated not by the 0·30% of air-borne bacteria which gave streptococcus-like colonies with greening but by the 0·018% which were proved microscopically to be chain-forming organisms.

Experiments with two nasal carriers of *Staph. aureus* gave a more convincing illustration of the extent to which pathogenic organisms may be disseminated from the respiratory tract via clothing dust to the air. Both carriers regularly yielded heavy growths of *Staph. aureus* from the anterior nares, and scanty growths of *Staph. aureus* from the jacket front, the jacket sleeves, and the trouser legs; often a few *Staph. aureus* were obtained from the chin and the hands, but usually none from the skin of the arms, legs, and chest. In carrier X the secretions of the anterior part of the mouth usually contained *Staph. aureus* (in four of the tests counts were made showing 30, 40, 5000, and 200,000 *Staph. aureus* per ml. of secretion); whereas carrier Y did not yield *Staph. aureus* on culture of the secretions of the anterior part of the mouth. Only organisms found to be coagulase-positive were recorded as *Staph. aureus*.

Experiments were made with the carrier dressed in his ordinary clothes undertaking vigorous activity for 10 min. in the chamber; to prevent air infection by droplet spray the carrier refrained from speaking and wore a surgical mask over his mouth and nose. In every one of fifteen experiments a few *Staph. aureus* were recovered from 10 c. ft. of the chamber air in samples taken during the activity period and the next 10 min. In nine experiments with carrier X a total of 76 *Staph. aureus* particles were found in 90 c. ft. of air; *Staph. aureus* comprised about 0·12% of the total bacterial content of the air thus infected with dust from clothing (the total bacterial content was estimated from counts on chocolate-agar plates exposed alternately with the plates of selective medium used for counting the *Staph. aureus*). In six tests with carrier Y a total of 48 particles carrying *Staph. aureus* were found in 60 c. ft. of air; the staphylococcus comprised about 0·06% of the bacterial content of the air.

For comparison with this observed amount of dissemination of *Staph. aureus* from the respiratory tract via clothing to the air, further experiments were performed with the same carriers to measure the dissemination of *Staph. aureus* directly into the air in droplet nuclei produced by sneezing. To prevent air infection with dust from his clothing the carrier was dressed in the sterile dust-proof gown and was instructed to avoid unnecessary movement while in the test chamber. In each experiment carrier X gave two sneezes induced by tickling the nasal mucosa with a small cotton-wool swab; carrier Y gave four vigorous simulated sneezes. The sneezes were given in quick succession, delivered from a standing position and directed towards a wall of the chamber 3 ft. away. To allow sedimentation of the large droplets, sampling was not begun until a minute after the last sneeze; then two air samplers were put into operation simultaneously, the slit sampler to take 10 c. ft. in 10 min. and a sieve plate sampler (modified from Du Buy and Crisp 1944) to take 46 c. ft. in 2 min. The air intake of the latter sampler was 1 ft. above the floor and was screened to prevent droplets falling directly into it. Thus, in each experiment 56 c. ft. of air (over half the air content of the chamber) was sampled within a few minutes after the sneezing. Nine such sneezing experiments were made with carrier X; in eight of these the air did not contain any particles (droplet nuclei) carrying *Staph. aureus*; in one experiment 11 *Staph. aureus* particles were found in the 56 c. ft. of air. Six tests of sneezing were made with carrier Y; in four of these the air did not contain any particles carrying *Staph. aureus*, in one test a single *Staph. aureus* particle was found in the 56 c. ft., and in one test four *Staph. aureus* particles were found in the 56 c. ft. Air infection with sneeze droplet nuclei was thus considerably less than the air infection with clothing dust produced by the same carriers.

The frequent presence of viable *Staph. aureus* on the clothing of carriers is related to the considerable resistance

of this organism to drying. One experiment was made to demonstrate survival in the dried state. Large numbers of *Staph. aureus* remained alive for over a month when dried in nasal secretion on a handkerchief. A sterile handkerchief was infected by a single nose-blow from carrier X, was placed at once in a sterile jar with loose cap, and was kept in the dark at room temperature; elution in sterile broth and making of plate counts showed that after a month the handkerchief still contained about 4,000,000 viable *Staph. aureus*.

DISCUSSION

Transmission of Respiratory Infections.—The present observations make it clear that very large numbers of bacteria-carrying dust particles are liberated into the air from the skin and clothing as a result of normal bodily activities, and that many of these particles may remain air-borne for over half an hour. It is suggested that dust particles from clothing are not inferior to sneeze-produced droplet nuclei in supplying the physical means for air-borne transmission of infection. In particular, bacteria-carrying dust particles do not appear to be much coarser and more rapidly sedimenting than bacteria-carrying droplet nuclei, as suggested by Wells et al. (1946). Our finding that 10% of the bacteria-carrying dust particles remained air-borne on average for about 35 min. is to be compared with the finding by Bourdillon et al. (1942) and Duguid (1946b) that sneeze-produced bacteria-carrying droplet nuclei remained air-borne to the extent of 2–10% for 30–120 min.

The relative importance of dust and droplet nuclei as vehicles of aerial infection can be decided finally only by comparative quantitative observations of the dissemination of pathogenic organisms on these different vehicles. Our present observations with two carriers of *Staph. aureus* showed that the air was infected more regularly and to a greater degree by the raising of dust from clothing than by sneezing; 124 dust particles carrying *Staph. aureus* were recovered from 150 c. ft. of air contaminated by vigorous bodily activity for 150 min., whereas only 16 droplet nuclei carrying *Staph. aureus* were recovered from 840 c. ft. of air contaminated by 42 sneezes.

Surgical Asepsis.—The pyogenic organisms most often infecting wounds—*Staph. aureus* and *Strep. pyogenes*—commonly originate from the respiratory tract of carriers. Dissemination of infection from the respiratory tract via clothing dust to the air constitutes a means whereby surgical aseptic technique may be breached; infected dust particles may settle from the air on the operation wound, the surgeon's hands, instruments, and dressings. *Staph. aureus* and *Strep. pyogenes* have been demonstrated in the air of operating-rooms by Hart (1938), Hart and Schiebel (1939), and MacDonald (1940). Hart attributed frequent unexplained infections in clean operation wounds to this aerial infection. Colebrook and Ross (1947) demonstrated infection of the air of a burn dressing-room with *Strep. pyogenes*, which was proved by typing to be derived from a small sore on the surgeon's elbow; apparently the gown worn was not effective in preventing the dissemination of infected dust from this site.

Our present findings show that a large amount of dust-borne bacterial contamination of the air may be caused by ordinary body movement, and that some of the infected dust particles may remain air-borne for a time more than sufficient to allow their drifting to the operating-table from all parts of the theatre and from rooms and corridors adjoining. The loose cotton gown usually worn by surgeons was unable to prevent bacterial contamination of the air from the skin and clothing. Air infection is likely to be produced if surgeons, nurses, anæsthetists, students, or other attendants enter the operating-theatre or its gallery while clad in their ordinary clothes covered only by a loose gown.

Precautions Necessary in Bacteriological Examination of Air.—When examining air for its total bacterial content, an observer should take precautions against himself infecting the air, lest the counts obtained should reflect mainly his own activities in manipulating the air sampler and not the natural air contamination of the place examined. The movements involved in operating an air sampler have been proved sufficient to produce heavy bacterial contamination of air, by the present observations for slight activity, a mimicry of operating the slit sampler. Hitherto, when taking air samples, we have tried to minimise such contamination by wearing a sterile surgical gown, cap, and mask; in view of our present findings we intend in future to use a sterile dust-proof gown.

SUMMARY

The number of bacteria-carrying dust particles liberated from a person's skin and clothing into the air of a small chamber as a result of various bodily activities has been measured by examining the air with a slit sampler.

Large numbers of bacteria-carrying dust particles were liberated by even slight activity—e.g., about 1000 per min. by a person making movements equivalent to changing culture plates in a slit sampler. Very large numbers were liberated by more vigorous activities—e.g., about 10,000 per min. by a person "marching." Some 10% of these bacteria-carrying dust particles remained air-borne for half an hour.

Experiments with nasal carriers of *Staph. aureus* showed that the air was infected with this pathogenic organism more regularly and to a greater degree by the liberation of dust from clothing than by sneezing. *Staph. aureus* was present in about 0·1% of the bacteria-carrying dust particles which entered the air from the clothing of carriers.

Air contamination with dust-borne bacteria from clothing was reduced only a little—e.g., to about half—when a sterile loose cotton gown of the usual surgical pattern was worn over the ordinary clothing, but it was reduced very greatly—e.g. to a tenth or a twentieth—when a sterile dust-proof gown was worn.

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RESISTANCE TO PROGUANIL (PALUDRINE) IN A MAMMALIAN MALARIA PARASITE

(PLASMODIUM CYNOMOLGI)

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DRUG resistance is a recurring problem in chemotherapy. It had been of great importance in dealing with the sulphonamides, tryparsamide, &c., but has been conspicuous by its absence in the case of most antimalarials. Quinine-resistant strains of malaria have never been reported; resistance to mepacrine ('Atebrin') is almost unknown. The widespread introduction of proguanil ('Paludrine') in the treatment of malaria raised the question of the possible development of resistance by malaria parasites to this drug. Bishop and Birkett[1] and Williamson et al.,[2] working independently, showed that malaria parasites in chicks (*P. gallinaceum*) could be made highly resistant to paludrine but not to other antimalarials (with the possible exception of pamaquin). The resistance was not diminished by passage through mosquitoes. This provisional report records an attempt to induce resistance to paludrine in *P. cynomolgi*, a malaria parasite of monkeys closely similar to *P. vivax* of man.

EXPERIMENTS

The experiment was started in June, 1947, with a baboon (98) heavily infected by means of sporozoites. When the infection developed, small doses of paludrine were injected intramuscularly. The doses were designed to reduce the number of parasites in the blood without abolishing them altogether, but there were often long negative periods owing to overdosage, to immunity reactions by the host, and to the spontaneous remissions in the course of the parasitæmia which are common in infections of *P. cynomolgi*. The action of paludrine is exerted slowly and it is usually necessary to wait two days to discover the effect of any given dose. The original baboon (98) is still under experiment, though it relapses only at six-weekly intervals. Two other baboons and one rhesus monkey have been subinoculated from it and treated in the same way.

No precise determination of the initial sensitivity of the strain was made, owing to scarcity of monkeys at the time; but two daily doses of 0·03 mg. per kg. made the blood free from parasites, and three doses of 0·01 mg. per kg. on alternate days slowly suppressed an attack of malaria. L. H. Schmidt (personal communication), in a detailed investigation of the sensitivity to paludrine of the same strain of *P. cynomolgi* in over 100 infections, has found that daily doses of 0·075 mg. per kg. for seven days will always abolish the blood parasitæmia; and that daily doses of 1·25 mg. per kg. for seven days will permanently cure 100% of trophozoite-induced infections.

After fourteen months of treatment with subeffective doses of paludrine, doses of 25–30 mg. per kg. have failed to abolish the blood parasitæmia in all 4 treated monkeys. This dosage is approaching the maximum tolerated level, which is about 40 mg. per kg. daily. Thus the resistance seems to have increased about 1000 times (in round figures from 0·03 mg. to 30 mg. per kg.). This investigation is being continued. Schmidt (loc. cit.), working on similar lines, has succeeded in obtaining a strain of *P. cynomolgi* completely resistant to the maximum tolerated dose of paludrine.

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SUMMARY

A strain of monkey malaria (*P. cynomolgi*) has been subjected to repeated subeffective treatment with paludrine. After fourteen months its resistance to paludrine has increased about 1000 times, so that doses approaching the maximum tolerated one are only partially effective.

In view of the close similarity between *P. cynomolgi* and *P. vivax*, it seems probable that benign tertian malaria in man might become resistant to paludrine, though this process would probably take a long time to complete even under favourable conditions.

We are indebted to Mr. E. C. England and Mr. D. Garlick for technical assistance.

SIMPLIFIED FLOCCULATION TESTS FOR DIFFERENTIAL DIAGNOSIS OF JAUNDICE

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IT has been suggested by Dreyfuss (1948) that the turbidity obtained on mixing certain pathological sera with a solution of thymol in barbitone buffer (Maclagan 1944a) may partly be due to the dilution of the serum in a hypotonic solution. He has described a test, using simple dilution of serum with water, which gives results closely correlated with those of the thymol-turbidity test. Wiseman (1934) described a test for malaria in which serum was flocculated by addition to water, and about two years ago Dr. A. A. Miller drew our attention to a dilution test, using 15% alcohol as diluent, which was introduced by Naidu et al. (1942) as a diagnostic test for malaria. We have since used a modification of this test in parallel with some other "liver-function" tests (Mawson 1948) for the differentiation of obstructive jaundice from infective hepatitis, and have also applied it to sera from patients with cirrhosis of the liver. We have at the same time compared results obtained with the colloidal-red test (Ducci 1947) with those obtained with the colloidal-gold reaction (Maclagan 1944b).

Alcohol-turbidity Test.—To 7·5 ml. of 15% ethyl alcohol in distilled water add 0·3 ml. of serum. Invert gently twice and leave for 30 min. at room temperature. The turbidity is read in a King (1942) photo-electric colorimeter with an Ilford spectrum orange filter, with 15% alcohol in the control tube. One unit of turbidity is defined as the turbidity produced by a dilution of normal serum in 0·85% sodium chloride, containing 10 mg. of protein per 100 ml., when 2 ml. of the serum dilution is mixed with 6 ml. of 3% sulphosalicylic acid (Mawson 1942). This is equal to the unit used by Maclagan (1944a) for the thymol-turbidity test.

Colloidal-red Test.—This was carried out as described by Ducci (1947) except that the solution of colloidal Sudan IV was made to 80 ml. instead of 800 ml.

RESULTS

Alcohol-turbidity Test.—With the sera of 165 apparently normal blood donors the mean alcohol turbidity was 1·2 units. The standard deviation was 0·72, giving a normal range (mean $\pm 2 \times$ S.D.) of 0–2·6 units. In 13 cases of obstructive jaundice there was a mean alcohol turbidity of 1·9 units (S.D. 1·2), and 8 cases of infective hepatitis gave a mean of 7·8 units (S.D. 3·6). The difference between the means is significant, being 4·4 times the standard error. All cases of infective hepatitis gave alcohol turbidities above normal (range 3·8–15·5 units). The range in obstructive jaundice was 0·2–4·4 units. Of the 13 sera 4 gave results which were above normal (2·8, 2·8, 3·6, and 4·4 units). From patients with hepatic cirrhosis 5 sera have been tested, giving results of 5·8, 6·2, 6·5, 8·0, and 11·0 units.

Colloidal-red Test.—This was compared with Maclagan's colloidal-gold reaction in 60 pathological sera. The results were identical except in 2 cases, where the disagreement was so slight as to be without significance.

DISCUSSION

The sera studied have been too few for conclusions to be drawn about the relative discriminant value of the alcohol-turbidity and thymol-turbidity tests or to decide the extent to which the results of the two tests are correlated. Our purpose is to draw attention to the simplicity of the alcohol-turbidity and colloidal-red tests and to suggest that they may repay further investigation. The alcohol-turbidity test has the limitation that overnight flocculation nearly always occurs, whereas Maclagan (1947) has pointed out that additional information can be derived from the thymol-turbidity test by observing the flocculation which takes place only with certain sera when the tubes have been allowed to stand. In the case of the colloidal-red test, the results are somewhat more difficult to read than those obtained with the colloidal-gold test, owing to the slightly turbid or opalescent appearance of the reagent.

SUMMARY

A test in which serum is diluted with 15% alcohol has been compared with Maclagan's thymol-turbidity reaction, and the results have been found to be very similar.

Ducci's colloidal-red test gave results identical with those obtained with Maclagan's colloidal-gold reagent.

The reagents required for the alcohol-dilution and colloidal-red tests are simpler to prepare than those required for Maclagan's liver-function tests.

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MULTIPLE ABDOMINAL CATASTROPHES

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THE main interest in this case lies in the remarkable number of abdominal catastrophes from which the patient recovered. It also illustrates one or two principles and some methods of treating difficult lesions.

CASE-RECORD

A man, aged 56, was admitted on Feb. 21, 1946, with three days' history of abdominal pain, associated with constipation, and increasing distension. He had had no previous abdominal trouble, but was an epileptic.

He was not very ill. The abdomen was much distended and tympanitic. There was no local tenderness, and no masses were felt. The rectum was empty. Intestinal obstruction due to carcinoma of colon was diagnosed, and the patient was taken to the operating-theatre, where the anæsthetist suggested the diagnosis of volvulus.

First Operation.—Under general anæsthesia, the abdomen was opened through a right lower paramedian incision, and an enormous volvulus of the sigmoid colon was delivered, untwisted, and deflated by a rectal tube. Deflation was materially aided by attaching a sucker to the end of the rectal tube. The tube was left in the rectum, and the abdomen was closed.

His postoperative course was extremely satisfactory, and the patient did very well until Feb. 27, when his bowels were not open. Next day his abdomen began to distend again, and on March 1 it was obvious that the volvulus had recurred.

Second Operation.—Under general anæsthesia a large oblique muscle-cutting incision was made in the left iliac fossa. The distended twisted loop was delivered through this, untwisted, and emptied. A double-barrelled colostomy was made, and the redundant loop was excised.

The patient did well for about five days, when he began to vomit. He was put on intravenous salines and gastric suction, and improved after a day. On March 12 he began to vomit and to be distended. He was again put on suction and salines but did not improve, and after 36 hours it was fairly obvious that he had a small-bowel obstruction.

Third Operation.—On March 14, under general anæsthesia, the abdomen was opened through a left lower paramedian incision. Two loops of ileum were found adherent and obstructed near the colostomy. Separation of these relieved the obstruction, and the abdomen was closed. The patient was kept on gastric suction and intravenous saline.

On March 16 the patient was gravely ill with a gross paralytic ileus and an extremely distended abdomen. Treatment by suction, saline, and morphine was maintained, and he slowly recovered from this, with a period of diarrhœa from the colostomy. On the 28th he was much better, and the colostomy was functioning normally. On the 30th his colostomy did not act. He began to vomit once more, and his abdomen rapidly became distended. He was again put on intravenous saline and gastric suction. Later that day he had not improved, and he had all the physical signs of a small-bowel obstruction.

Fourth Operation.—Under general anæsthesia, the right paramedian incision was reopened. A large mass of grossly adherent gut was found near the previous incision, which appeared to have ruptured subcutaneously. It was too adherent to allow separation of the gut, and an anastomosis was made of a distended to a collapsed loop above and below this area.

After this he progressed uneventfully until April 5, when left abdominal wound ruptured and gut was found in the dressing.

Fifth Operation.—Under general anæsthesia, the gut was returned to the peritoneal cavity. The rupture into the peritoneal cavity had taken place in the upper part of the wound. In the lower part, the skin had separated, but the skin edges were firmly adherent to loops of bowel, which formed the base of the wound. The opening in the peritoneal cavity was closed with through-and-through sutures. It was impossible to close the skin; so a large 'Vaseline' pack was placed in the wound and retained with stout silk sutures. Patient continued to do extremely well. He was given several blood-transfusions, put on a high-protein diet, and began to regain weight.

Sixth Operation.—At the end of April, the colostomy spur was crushed; and on May 3, after a preliminary course of succinyl sulphathiazole, the colostomy was closed.

At this time the patient's abdomen presented a healed right lower paramedian scar; a large elliptical wound on the left side, the floor of which was formed by adherent coils of gut; and the closed colostomy incision (fig. 1). Two days after the operation his bowels opened normally, and plans were made to skin-graft the uncovered coils of gut; but on May 8 a fistula developed in one of the exposed coils. The opening was about $^1/_8$ in. in diameter, and through it poured out small-gut contents copiously. It was dressed for two days with aluminium hydroxide and closed with a thread mattress suture. This appeared satisfactory for two days, when another fistula appeared 1 in. above the first. It was then decided to use a dressing which would both absorb the succus entericus and provide material for the ferments to digest thus using them up and preventing digestion of the skin and abdominal wall. The wound was dressed with a generous mound of dried milk, and this was changed as soon as it had become partially digested, usually in about $1^1/_2$–2 hours. Under this régime, the wound began to epithelialise

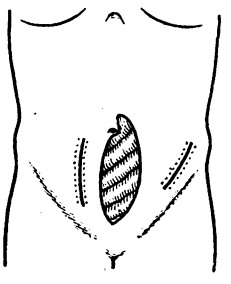

Fig. 1—Anterior of abdomen showing operation scars and wound through which coils of small gut are visible.

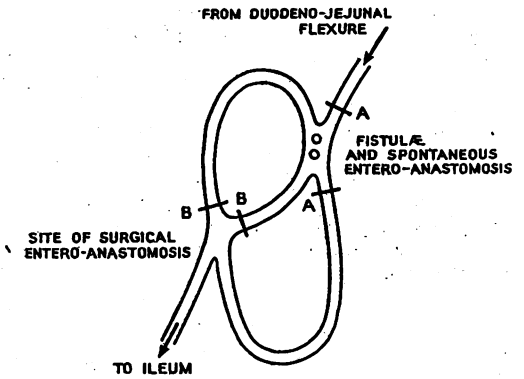

Fig. 2—Appearance of small gut found at seventh operation: A, site of future anastomosis; B, site of future resection (see fig. 3).

steadily, though both fistulæ were open and discharging freely.

On May 31 the patient's general condition was very good; the skin wound was much smaller, and both fistulæ were active. During the next fortnight there was very little progress, and the dried-milk dressing was changed for a mixture of soya flour and dried milk. With this dressing, the rest of the wound healed except in the immediate vicinity of the fistulæ, which appeared to be growing larger and discharging more. On July 5 an attempt was made to close the fistulæ with a rubber button inside the gut and another outside the gut, both held in position with thread ties. This reduced the amount of external discharge, but even after four weeks there was no change in the size of the fistulæ and there was no evidence of healing. Since each fistula was a fairly large opening with no track but simply mucosa pouting through thin skin, it was apparent that it would not heal spontaneously. The patient's general condition was much better than it had been, and the skin was in good condition; so it was decided to operate on the fistulæ.

Seventh Operation.—On Aug. 9, under general anæsthesia, an elliptical incision was made to include the fistulæ and scar. Normal tissue was found above and below, and the peritoneal cavity was opened. No adhesions were found, in spite of the six previous recent abdominal operations. The ellipse of skin with the attached loops of gut was easily freed and delivered. The gut was traced from the duodenojejunal flexure. There were two sites of anastomosis, a spontaneous one in the region of the fistula and another lower down which had been made to relieve the last attack of intestinal obstruction. The whole had a figure-of-eight appearance (fig. 2). The fistulous area was resected and an end-to-end anastomosis was done; the redundant loop was cut away next to the entero-anastomosis and the blind ends were closed (fig. 3). The abdomen was closed with through-and-through 'Nylon' sutures and deep thread through peritoneum and linea alba. The patient was put on intravenous saline and gastric suction.

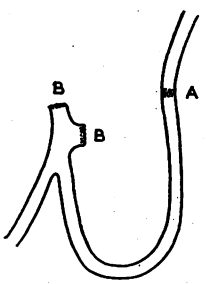

Fig. 3—Resection of fistulous gut and anastomosis done at seventh operation: A, anastomosis; B, closed gut.

His general progress after operation was extremely satisfactory, and within a few weeks he was up and about. The wound suppurated for some time, and the thread sutures were discharged at intervals. When the patient was discharged, there were still some small stitch sinuses and a ventral hernia, for which a belt was ordered.

DISCUSSION

This patient had in turn:

(1) Volvulus of the sigmoid colon reduced.
(2) Recurrence of the volvulus, excision of loop, and colostomy.
(3) Small-bowel obstruction.
(4) Severe paralytic ileus.
(5) Second small-bowel obstruction.
(6) Ruptured abdomen.
(7) Closure of colostomy.
(8) Small-gut fistulæ.
(9) Resection of fistulæ.

The main interest of the case lies in: (1) the surprising number of complications that developed and the fact that the patient successfully recovered from seven major abdominal operations within fewer months; (2) the fact that his volvulus recurred so quickly in spite of derotation and drainage of the loop with a rectal tube; and (3) a useful method of dealing with intestinal fistulæ, the principle being to provide adequate protein, carbohydrate, and fat in the dressing so as to use up the enzymes in the succus entericus and prevent them from acting on the adjacent tissues. Such a dressing needs frequent renewals.

I wish to thank my senior colleague, Mr. H. L. Fuller, for allowing me to treat this case. The patient's recovery in the face of so many disasters was largely the result of the untiring efforts of Sister Holmes and her nurses.

Preliminary Communication

REDUCING SUBSTANCES IN CERVICAL MUCUS

DURING the follicular phase of the menstrual cycle healthy cervical mucus sustains the life and motility of spermatozoa for several days.[1] Since the survival of human spermatozoa seems to be conditioned by the sugar content of the medium,[2] it seems likely that healthy cervical mucus supplies this source of energy to spermatozoa. Pommerenke[3] reported that cervical mucus contained reducing substances (obtained by hydrolysis) which he said were demonstrable at any stage of the menstrual cycle. We also have found reducing substances, both free and conjugated, in experiments in which cervical mucus obtained with syringe or forceps was examined by Nelson's quantitative methods for the determination of sugars.[4] Our findings suggested a relationship between the phases of the reproductive function and the secretion of free reducing substances by the cervix. We have since found that this relationship can be demonstrated by a simple qualitative test.

Procedure.—The cervix is exposed with a dry speculum and swabbed with dry cotton-wool. A small tightly wound cotton-wool swab is next inserted into the cervical canal to a depth of about $^1/_2$ in. twisted several times so that a little mucus adheres, and then withdrawn. The swab is next dropped into a test-tube and covered with a suitable alkaline copper reagent—e.g., Somogyis reagent. It is then boiled for 60–90 sec., after which the tube is cooled under the tap and Nelson's phosphomolybdic acid reagent is added to the cooled liquid (about 1 ml. per 1 ml. of copper reagent).

Thorough mixing is effected. The presence of reducing substances is indicated by the immediate development of a deep blue in the fluid or upon the surface of the swab or in both fluid and swab. In the absence of reducing substances the swab and fluid become almost colourless. It is advisable to run a blank control swab in cases of doubt, and in any case until familiarity with the colour reaction has been acquired. The positive reaction is usually very pronounced, since the concentration of free reducing substances, if present, expressed as glucose, is usually high; it may amount to 550 mg. per 100 ml.—i.e., more than is present in other normal body fluids—whereas, on the other hand, the reaction is positive with a total concentration of 0·02 mg. equivalent to glucose on the swab.

Disturbing Factors.—If the swab is mounted on a wooden rod it may be left on this during the reaction. If a metal holder is used, the swab must be taken off

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2. MacLeod, J. *Endocrinology*, 1941, 29, 583.
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before being boiled. Cotton-wool may contain some reducing substances; so it should be tested before being used for making swabs. If the swabs are not subjected to the reaction immediately after collection, destruction of the reducing substances by bacterial action may have to be prevented by suitable precautions.

RESULTS

Ovulatory Phase.—Of 43 specimens collected from 38 women believed to be fecund during the presumptive ovulatory phase of the menstrual cycle, 32 gave a positive reaction, 3 a weakly positive reaction, and 8 a negative reaction. Of 6 similar specimens obtained during postcoital tests and heavily invaded by spermatozoa showing a high survival-rate, 5 also gave positive reactions. Two extremely densely invaded specimens showing a low survival-rate (isolated oscillatory spermatozoa only) gave a negative reaction, as if the free reducing substances had been exhausted by the invaders or had been deficient. The semen in these cases gave a positive invasion test with good survival.

Luteal Phase.—Of 23 specimens collected from 16 women during the luteal phase of the cycle, two to eleven days after the thermal shift from the low to the high waking temperature, 16 gave a negative reaction, 5 gave positive reactions of various degrees, and 2 were doubtful.

Early Pregnancy.—Of 18 specimens collected from 13 women during early pregnancy—i.e., before the end of the eighth week, 13 gave a negative reaction, 4 gave positive reactions of various degrees, and 1 was doubtful.

Secondary Amenorrhœa.—In 2 cases of secondary amenorrhœa with presumptive œstrogen deficiency the traces of mucus obtained gave a negative reaction. After injection of œstrone (1·5 mg. microcrystalline suspension) an appreciable quantity of mucus was secreted and a positive reaction obtained. Combined injection of œstrone crystals 1·5 mg. and progesterone crystals 3·5 mg. evoked secretion of mucus which gave a negative reaction. Conversely, in 2 cases of secondary amenorrhœa with presumptive high level of œstrogenic secretion (profuse clear cervical secretion; pronounced proliferation and cornification of the vaginal epithelium, with deposition of glycogen) the mucus gave a strongly positive reaction.

Endocervicitis.—The test was carried out in several cases of endocervicitis with purulent secretion during the ovulatory phase. The reaction was positive during this phase.

CONCLUSIONS

The results are compatible with the following tentative conclusions:

(1) The cervical glands tend to react to œstrogenic secretion with the production of mucus rich in free reducing substances, but these are not demonstrable in all specimens, even though the mucus may show the typical ovulatory appearance.

(2) If, however, the œstrogenic secretion is combined with progesterone (as in early pregnancy), the production of reducing substances tends to be inhibited.

(3) The inhibition probably depends on the relative amounts of œstrogen and progesterone secreted. These tend to vary during the luteal phase and in early pregnancy. During these phases dominance of œstrogens producing temporary falls in the waking temperature and passing "clarification" of the cervical mucus has been observed.[5] These variations (œstrogen surges) may explain the appearance of reducing substances in some specimens taken during the luteal phase or during pregnancy. It is also possible that in some cases mucus may be secreted in such quantities and of such a nature that conjugated reducing substances are liberated during heating of the swab. This possibility is being investigated.

The reaction may be of assistance in the understanding of endocrine conditions prevailing at any given time and in the examination of cervical mucus during postcoital or invasion tests, since survival of human spermatozoa appears to be associated with availability of reducing substances. The possible clinical application of the test is being investigated jointly with Dr. Mary Barton, to whom we are much indebted for the supply of specimens of cervical mucus.

5. Barton, M., Wiesner, B. P. (unpublished data). See also Greylich, W. W., Morris, E. S., Black, M. E. *Proc. Conf. Problems Human Fertility*, 1943, p. 37.

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Reviews of Books

Modern Methods of Infant Management

Before, During, and After Birth. Editor: W. R. F. COLLIS, M.D., F.R.C.P., pædiatrician, Rotunda Hospital. London: Heinemann Medical Books. 1948. Pp. 285. 17*s.* 6*d.*

DESPITE its small size, this is a remarkably comprehensive little book, in which two pædiatricians (Dr. Collis and Dr. P. C. D. MacClancy) have joined forces with Dr. Ninian Falkiner, an ex-master of the Rotunda, and Miss M. Moran, the sister in charge of the infants' department. It deals with antenatal care and the conduct of labour, the management of the newborn baby, problems of infant feeding, and a variety of abnormal conditions encountered in the neonatal period. The editor says in his preface: "No sentiment of any kind enters the question as to whether it [the infant] is going to thrive or fail, live or die. The rules are exact and clear and, if followed, one may reasonably expect a healthy thriving baby, if neglected disease and death." This may be a surprise to some of us who were inclined to wonder why so many mothers who placidly follow their instinctual way raise healthy children while others who conscientiously follow the "rules" are sometimes less successful. But it is certainly true that neonatal mortality can and should be reduced by better instruction of the doctor and midwife in the care of the newborn. In many ways Dr. Collis's book is well suited to the purpose, being well illustrated, and mostly non-controversial. Sometimes, however, the facts are oversimplified to the point of being misleading. Of pneumonia acquired at birth, or within the first week of life, one of the authors remarks: "The symptoms resemble those of pneumonia at other age periods: rapid respiration, high temperature, moist sounds in the chest with variable signs of consolidation. It is not a difficult diagnosis to make, though the examination of the infant's chest is a science in itself which the inexperienced can only acquire from practice." It would be interesting to know what proportion of pneumonias in the first week of life are in fact correctly diagnosed on the criteria given.

The Salicylates

A Critical Bibliographic Review. MARTIN GROSS, M.D., assistant professor, laboratory of applied physiology, Yale University; LEON A. GREENBERG, PH.D., associate professor at the university. New Haven: Hillhouse Press. 1948. Pp. 380. $6.

THIS is an exhaustive review of published work on the salicylates. If there is little new in the conclusions about the analgesic and antipyretic effects of these drugs it is nevertheless valuable to have the whole subject reviewed. The effects on the gastro-intestinal system are difficult to assess: large doses undoubtedly induce prothrombinopenia. Writing of rheumatic fever, the authors say that "suppression of the inflammatory process and prevention of undesirable sequelæ are best effected by a quickly established concentration of salicylate in the plasma." Coburn showed that a salicylate concentration of at least 35 mg. per 100 ml. of plasma was necessary to produce constant progressive subsidence

of rheumatic inflammation. A daily dose of 10–12 g. generally results in about this concentration, which Gross and Greenberg believe should be built up as rapidly as possible, intravenously if necessary. The use of salicylate derivatives in tuberculosis is mentioned, but the revived interest in this subject was only just bearing fruit as the book went to press. Like its companion volume on acetanilide, this monograph is careful and valuable.

The Question of Lay Analysis

An Introduction to Psycho-analysis. SIGMUND FREUD, foreword by ERNEST JONES, M.D. London: Imago Publishing Co. 1948. Pp. 81. 9*s.*

Professor Freud was always beguiling. In this book he leads us, in the Socratic manner, to the absurdities of antagonism to lay analysis—or psycho-analysis for that matter. His case is that lay psycho-analysts are competent to analyse, while doctors who are equally competent are rare. The need for psycho-analysis is still increasing, whereas the rate of increase of competent doctor psycho-analysts cannot be proportional. If a medical qualification is insisted on, the tendency will be for the psycho-analytic part of the qualification to become more and more a mere addition to a medical degree, and in the end the purity of the psycho-analytic approach will be swamped by the ordinary therapeutic approach of the doctor. This case is powerful, and any attempt to keep a great man's contribution to society pure should be respected, especially if that contribution really led to a revolution in thought, as Freud's did. Nevertheless, either medical culture must assimilate psycho-analysis or psycho-analysis must assimilate medical culture—a very improbable consummation. While the slow assimilation of psycho-analysis by medicine is in progress lay psycho-analysts can be valuable catalytic agents. At the same time we must remember that understanding of psychosomatic medicine is spreading rapidly, and the psychosomatic disorders can seldom be treated satisfactorily by practitioners who lack a medical qualification. The cases suitable for treatment by the lay analyst must be carefully selected; the selection becomes even more difficult when other systems of psychological thought and treatment, as respectable as Freud's, are taken into account. It is on the question of demarcating their sphere of activity that Professor Freud's thought is least adequate.

Problems of Fertility in General Practice

MARGARET HADLEY JACKSON, M.B., JOAN MALLESON, M.B., JOHN STALLWORTHY, F.R.C.S., KENNETH WALKER, F.R.C.S. With a foreword by Sir EARDLEY HOLLAND, F.R.C.S., F.R.C.O.G. London: Hamish Hamilton Medical Books. 1948. Pp. 248. 17*s.* 6*d.*

SUCH a book as this has long been needed. About a quarter of it is devoted to contraception, and besides much useful information on various methods this section contains valuable and sensible chapters on coitus interruptus and on the safe period. The greater part of the book, however, is concerned with the investigation and treatment of infertility; and here it seems that the authors have been too modest in their choice of title, for there is much to interest the consultant as well as the general practitioner. Nevertheless, consideration of the problem of a couple who consider themselves subfertile must always begin—and may end—with the family doctor, and he is perhaps too apt to refer them—or one of them—to a "specialist," thus placing their difficulties at once on the plane of the abnormal. Often all that is really needed is a careful history, a relatively limited examination including a postcoital test, and finally some sound and sympathetic advice. Hence the preliminary "statement of the problem" might well have been expanded to say how far the interested general practitioner is justified in carrying out investigations himself. Likewise the single chapter on abortion might have been extended, for it concerns the practitioner very closely. The woman who has miscarried, or threatens to do so, consults her doctor more readily than does the woman who has primary infertility, and she confronts him immediately with the question of direct treatment. In this connexion the value of progesterone is discussed rather too optimistically, and no mention is made of recent work on the possible value of the œstrogens; nor is there any reference to the common type of abortion (initial or repeated) associated with a defective fertilised ovum. Much hormone therapy has been wasted in attempts to treat as a "threat" an abortion which has been inevitable from the outset.

The authors are to be congratulated on their avoidance, in general, of dogmatic statements on controversial subjects, and special praise is due for the way in which artificial insemination is handled, and for the sensible and helpful chapter on coital problems, with its admission of, and useful advice on, the common difficulty of discussing such matters with the uneducated man and woman. In a book intended for general practitioners, more might perhaps have been said about the uses, and especially the abuses, of œstrogen therapy, and the reader may be left with rather too hopeful an impression of the value in general of hormone therapy both in male and female.

Additional features of interest are a short section on genetical problems, and an appendix with some data on existing contraceptive clinics and appliances of proved value, the technique of seminal analysis, and the organisation of a subfertility clinic.

Clinical Toxicology (2nd ed. London: H. Kimpton. 1948. Pp. 373. 22*s.* 6*d.*).—Prof. Clinton H. Thienes and Mr. Thomas J. Haley, PH.D., disclaim any originality in this American handbook, which endeavours to cater for the diagnostician and the analyst. In this country, of course, no one practising clinical medicine and requiring a working knowledge of toxicology ever analyses any substance, but the book will be of some use to the practitioner as a rapid reference in cases of poisoning; the skilled analyst will find in it a symposium of the identifying tests listed in textbooks of toxicology. A great deal of information is collated, and it is on the whole adequate to the restricted use for which it is intended.

Zinsser's Textbook of Bacteriology (9th ed. New York and London: Appleton-Century-Crofts. 1948. Pp. 992. $10). —This edition, of which Dr. D. T. Smith and Dr. D. S. Martin, of Duke University, are principal editors, retains the biological approach to bacteriology while it also caters for the public-health worker and the clinician. The rewriting of chapters on bacterial metabolism, immunology, and fungus and virus diseases, and the introduction of a new section on antibiotics have improved this standard American text. Bacterial ecology is given space, and the importance of spontaneous mutation in the study of bacteria is emphasised. The information is accurate and the many illustrations include excellent electron-micrographs.

A Short Practice of Surgery (8th ed. London: H. K. Lewis. 1948. Part I, pp. 224 and part II, pp. 195. 52*s.* 6*d.* the set of 5 parts).—This popular textbook of surgery by Mr. Hamilton Bailey and Mr. McNeill Love is now to appear in five volumes, with the object of keeping the material up to date. It is proposed to issue the parts at intervals of about two months. Part I of the 8th edition enhances the reputation which previous editions have gained for up-to-date information and beautifully clear illustrations. It comprises 224 pages of text and covers the same ground as the 7th edition in 8 fewer pages. It is good to see the section on the treatment of burns rewritten and to note that tying of the angular vein in carbuncles of the upper lip is not mentioned. Part II, covering the intestines, liver, gall-bladder, pancreas, and spleen, contains an extra chapter on peptic ulcer, to emphasise the importance of the subject. There are new paragraphs on Banti's syndrome and porta-caval anastomosis, and many lesser revisions of arrangement and illustration. Small points for friendly criticism are: the absence of all mention of the part played by the emotional state in producing peptic ulcers, in which context the work of Wolf and Wolff might receive brief attention; the diagram to illustrate excision of the head of the pancreas, in which the arrows should be reversed and the common bile-duct and pancreas anastomosed above the stomach; and the advocacy of cholecystgastrostomy for irremediable obstruction of the lower common duct, anastomosis to a defunctional loop of jejunum giving a better chance of excluding beer, porridge, &c., from the biliary tree.

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THE LANCET

LONDON: SATURDAY, NOV. 27, 1948

International Campaign Against Tuberculosis

INTERNATIONAL effort has not kept pace with the advances made in many national anti-tuberculosis schemes. In the United States the Federal government, the U.S. Public Health Service, the National Tuberculosis Association, and other voluntary bodies have banded together in a comprehensive attempt not merely to control but to eradicate the disease. In our own country legislation has not lagged behind, though much more could be done by better coördination between the various agencies concerned. In Scandinavia a lead has been given particularly in the application of tuberculin-testing and B.C.G. vaccination on a large scale. But these endeavours have had no international counterpart.

In recent months, however, steps have been taken to narrow the gap that has separated national and international enterprise. At last something is being done to bring national authorities closer together and to promote personal contacts which have previously been too few and far between. The leader in the intergovernmental field is, quite rightly, the World Health Organisation, with its headquarters at Geneva, and an account of the first year's work has lately been given by Dr. J. B. McDOUGALL.[1] Recommendations made by an expert committee and accepted at the first meeting of the World Health Assembly last July include the following:

(*a*) The provision of travelling fellowships to countries most in need, principally to train doctors in administrative, laboratory, epidemiological, and clinical work. The aim is to award about 50 of these fellowships in 1949. The candidates selected will be those who will be returning to responsible positions in the anti-tuberculosis campaigns in their own countries.

(*b*) The preparation from time to time of information for the use of physicians and others who may ask about recent developments. It is intended to provide textbooks and articles for circulation to countries which of late years have not had full access to the literature.

(*c*) The sending of demonstration teams, at the request of governments, to countries where new schemes are to be introduced. These field demonstrations are meant to show what the countries themselves might later do. They have already been undertaken in China, Greece, Poland, India, and elsewhere.

(*d*) The establishment of uniform procedures in such matters as the classification of tuberculosis, X-ray interpretation and mass radiography, laboratory diagnosis, and the evaluation of chemotherapeutic agents such as streptomycin. A subcommittee on streptomycin has already met.[2]

One of the most important functions of W.H.O. is to work with other international organisations, and accordingly a joint committee has been formed with the United Nations International Children's Emergency Fund (UNICEF) to consider policy in anti-tuberculosis work of an emergency nature. Much attention has been paid to B.C.G. vaccination, which is to be undertaken on an unprecedented scale, some $5 million having been set aside for the purpose. The actual field work has been undertaken by UNICEF and the Scandinavian group of countries, and already much has been done in Poland, Yugoslavia, Czechoslovakia, Hungary, and Finland. The principal object is to vaccinate negative reactors to tuberculin and to protect them by the intradermal injection of B.C.G., and an extension of the scheme into Asia (India, Ceylon, China, and the Philippines) and Africa (Tunis, Morocco, Algiers, and Egypt) is contemplated. Teams for this campaign will number at least 200 in Europe alone, and much credit must be given to the Danish Red Cross Society for the part it is playing. The personnel for the initial work has been supplied almost entirely by the Scandinavian countries, and Dr. JOHANNES HOLM, of Denmark, is the chief supervisor of the work, assisted by a member of the staff of W.H.O. It is proposed that W.H.O. shall continue this campaign as and when the emergency organisation (UNICEF) ceases its activities. Meanwhile, the joint committee has also been considering the sending of streptomycin to countries which ask for it; and, provided these countries are prepared to follow the routine of administration recommended by the W.H.O. subcommittee, supplies will be made available. Also staff and equipment will be sent to improve the laboratory side of the diagnosis of tuberculosis. Requests for laboratory aid and for streptomycin are now coming in from many countries.

It is good news also that the International Union against Tuberculosis (with headquarters in Paris) is likely to be reorganised in a manner consistent with its responsibilities in the voluntary field. Its constitution is to be revised; an executive director with wide powers is to be appointed; and it has been granted affiliation with W.H.O. This illustrates the way in which the various international units against tuberculosis are at last being grouped for a general offensive. If the International Union can bring the voluntary agencies together as successfully as W.H.O. is associating the governmental bodies, the anti-tuberculosis campaigns in many countries having undeveloped programmes will receive much-wanted support.

1. *Tubercle*, September, 1948, p. 208.
2. See *Lancet*, Oct. 16, p. 626.

Management of Hæmophilia

ON the present view hæmophiliacs suffer from a congenital failure to release thromboplastin when their blood is shed; so the first step in blood-coagulation—the formation of thrombin from prothrombin in the presence of ionised calcium and thromboplastin—is seriously hindered. It is agreed that both platelets and a plasma factor are concerned in the proper production of thromboplastin.[1] QUICK[2] contends that there is a plasma factor, thromboplastinogen, which, when activated by another factor released by disintegrating platelets, forms thromboplastin: in hæmophilic blood there is no thromboplastinogen, so the platelet activator has nothing to act on and clotting

1. *Lancet*, 1947, ii, 798.
2. Quick, A. J. *Amer. J. med. Sci.* 1947, **214**, 272.

does not begin. BRINKHOUS,[3] however, from very similar experimental observations, concludes that the missing plasma factor acts by releasing thromboplastin from the platelets, and he names the factor a "thrombocytolysin." For the purposes of the clinical management of hæmophilia we are therefore safe in assuming that it is a factor—be it thromboplastinogen or thrombocytolysin—present in normal plasma that is missing in hæmophilia; consequently if normal blood or plasma can be supplied to a hæmophilic patient his blood can be made to clot normally. This observation, originally made 43 years ago by SAHLI, explains the special value of blood-transfusion in hæmophilia in addition to any replacement of lost red blood-cells. In America a plasma fraction retaining this plasma factor was obtained in association with a globulin but free from fibrinogen and prothrombin.[4] This purified plasma factor could be dried, and a dose of 200–600 mg. given intravenously promptly reduced the coagulation-time of a hæmophiliac to normal; the effect was maintained for 5–8 hours.[5] Potent fractions such as these are still not generally obtainable, but it is possible to design a rational scheme for the control of hæmophilic bleeding by using whole blood or plasma, both of which are now readily available. And it looks as though we should relegate to obscurity the extracts of lung and spleen, the egg-white preparations, and the other materials that have been proposed for this purpose.

The patient with hæmorrhage due to hæmophilia is easily detected; bleeding from a minor injury or after a tooth extraction has gone on steadily for a long time, or he has hæmarthroses. Even a rough estimate of the coagulation-time of the blood is usually sufficient to confirm the diagnosis of hæmophilia: 1 ml. of venous blood is put into a small test-tube about 8 mm. in diameter, and in a normal person the blood will clot firmly within 4–10 minutes at room temperature, or 2–4 minutes at 37°C; hæmophilic blood will remain uncoagulated for longer (sometimes much longer) periods and the clot will be poor. This simple test will quickly distinguish the "bleeder" who suffers from recurrent hæmorrhage after tooth extraction because of defective capillary closure—patients often confusingly named "pseudohæmophiliacs"; and the test is particularly reliable since the only other condition that causes similar prolongation of coagulation is the extremely rare congenital afibrinogenæmia. Family history is not always reliable, since a positive history is not obtained in every case of hæmophilia—there are not a few apparently sporadic cases—and there may be a family history in the pseudohæmophilic group, though both sexes are usually affected. Having made sure that the condition is hæmophilia, the immediate treatment of hæmorrhage is transfusion of fresh blood—i.e., blood used within half an hour of withdrawal. Fresh blood must be used because the plasma factor is labile in whole blood.[6] Blood-transfusion must be repeated if the hæmoglobin and red-cell levels are low, and again at least every 72 hours since it has been shown that the coagulation-time of the blood returns to its previous level in about this time. Minor operations like tooth extraction can be undertaken in hæmophiliacs if proper precautions are taken. Before the extraction the dentist makes a mould to fit the jaw and keep a dressing firmly in the socket. The patient is transfused not more than, say, 5 or 6 hours before the extraction. The sockets are firmly packed and the mould used to keep the packing in place; suturing the gums is bad practice in these patients and often leads to troublesome ulceration. Further transfusions are given on alternate days until all oozing has ceased and healing looks firm. All this necessarily means admission to hospital, usually for 10–14 days.

In our present issue SCHILLER, NELIGAN, and BUDTZ-OLSEN, of Oxford, show that, when the necessity for frequent (almost daily) blood-transfusion is recognised, and full coöperation with the physician is maintained, even major surgery can be undertaken with a fair chance of success. There can be few more hazardous operations than the one they report, in which a subdural spinal hæmatoma was removed through a laminectomy wound. The postoperative progress of their patient, a little boy of 16 months, shows another difficulty that has to be faced in hæmophilia—slow healing of the wound. This complication was successfully met by the use of the modern absorbable hæmostatic materials, fibrin foam and oxidised cellulose; but the wound still took ten weeks to heal.

ALEXANDER and LANDWEHR [6] have now carried the treatment by the provision of plasma factor a step further. They gave regular infusions of normal human plasma to four severely affected hæmophilic patients and so kept their coagulation-time normal or nearly normal for long periods—10–20 months. JOHNSON [7] had done this before but only for 3 months, not really long enough for proper assessment. ALEXANDER and LANDWEHR did not use the stock plasma; they prepared a special plasma that was separated and frozen within half an hour of withdrawal so as to preserve the maximum antihæmophilic activity. An intravenous infusion of 150 ml. restores the coagulation-time to normal levels very quickly and it remains normal for 24 hours; the coagulation-time rises slowly during the next 24 hours and rises to its previous level within the third 24-hour period. Intramuscular injection was much less effective. All four patients could undertake more or less normal activities so long as they received these infusions three or four times weekly. Some hæmorrhagic episodes did occur, and an interesting point is that infections seem to have played a part and that they were controlled by penicillin, which has no clot-promoting activity.[8] This treatment is not, so far, available for hæmophiliacs in this country. Fortunately few of them are so severely affected as ALEXANDER and LANDWEHR'S four patients; most hæmophiliacs have long remissions when there are no spontaneous hæmorrhages and minor injuries do not have serious effects, so long as the larger blood-vessels are not damaged.

This kind of treatment again raises the question of the practical value of measures that involve

3. Brinkhous, K. M. *Proc. Soc. exp. Biol., N.Y.* 1947, **66**, 117.
4. Lewis, J. H., Tagnon, H. J., Davidson, C. S., Minot, G. R., Taylor, F. H. L. *Blood*, 1946, **1**, 166.
5. Lewis, J. H., Soulier, J. P., Taylor, F. H. L. *J. clin. Invest.* 1946, **25**, 876.
6. Alexander, B., Landwehr, G. *J. Amer. med. Ass.* 1948, **138**, 174.
7. Johnson, J. B. *Ibid*, 1942, **118**, 799.
8. Macht, D. *Fed. Proc.* 1947, **6**, 160.

such dependence on exceptionally skilled attention. So many of the new treatments are of this type; exsanguino-transfusion for acute leukæmia, supporting transfusions for aplastic anæmia, the special technique needed for nitrogen mustard administration—all these make great demands on the time of doctors that can hardly be met outside the special teaching hospital clinic. In the U.S.A. it is apparently possible to entrust these repeated intravenous infusions to the blood-bank nurse; it is doubtful if this would be allowed here. And what of the almost crippled hæmophiliac who is given, for some months, a taste of normal life at the price of absolute dependence on the special clinic facilities? For if he misses one infusion his hæmorrhages will recur. The preparation alone of the special plasma needed every 3 or 4 days must involve much labour. But similar difficulties were met, and solved, in the treatment of diabetes and Addison's disease; and perhaps now that we know the site of the missing factor in hæmophilia further progress will lead to simpler methods for the continuous control of the coagulation defect.

Vitamin-E Therapy

VITAMIN E (tocopherol) was discovered some twenty-five years ago during experiments on the effect of dietary restriction on the breeding-power of rats. Since that time many disorders not specifically related to reproduction have been attributed to its deficiency. In various animals these have included muscular dystrophy[1]; brown pigmentation of the uterus, skeletal muscles,[2] and adipose tissues[3]; exudative diathesis[4]; encephalomalacia[5]; renal abnormalities[6]; ceroid pigmentation of the liver[7]; and the uneconomical use of protein[8] and vitamin A.[9] Such findings suggest that the vitamin has a wide sphere of activity, exerting its powerful anti-oxidant action in many different biochemical systems.

Of vitamin E in man we know much less. Its presence in human tissues can certainly be detected by biological[10] and chemical[11] tests. There is evidence, too, that during gestation it is transferred from the maternal circulation to the fœtus.[12] But not everyone agrees even that vitamin-E deficiency is a significant cause of failure of reproduction—despite the encouraging first reports on habitual abortion.[13] Trials in muscular dystrophy and allied conditions have usually proved disappointing,[14] though it should be remembered that its administration has only limited success in dystrophic rats once these have become paralysed as the result of deficiency.[6] The surprising claim of MILHORAT and BARTELS[15] that in human muscular disorders the absorption of vitamin E is defective through its failure to conjugate with inositol has not yet been confirmed. The hope that vitamin-E medication may prove useful would indeed have receded but for the faith of EVAN SHUTE, in Canada, who has had long experience in the treatment of both pregnant and non-pregnant patients with wheat-germ oil concentrates and later synthetic tocopherols. While his early investigations indicated that vitamin E might be beneficial in emergencies such as abruptio placentæ[16] or premature labour,[17] he has concentrated latterly on its use in cardiac and vascular diseases.[18] From experience of 1500 cases of every type of heart disease he concludes that vitamin E is both effective and safe; that 80% of cases improve continuously; and that even in the worst cases the improvement may sometimes allow greatly increased activity. These beneficial effects he ascribes to the action of the vitamin in decreasing the permeability and increasing the dilation of the capillaries, in decreasing the anoxia of the cardiac muscle, in preventing further thrombosis and resolving existing thrombi, and in softening and relaxing scar tissue by invasion with fresh blood-vessels. He also claims that for the same reasons the vitamin is valuable in the treatment of indolent ulcers, arteriosclerotic gangrene, thrombophlebitis and phlebothrombosis, cerebral thrombosis, thromboangiitis obliterans, purpura, and even defective powers of vision and dark adaptation. Furthermore, BURGESS[19] has found vitamin E effective in collagenoses such as atopic dermatitis, granulomatous ulceration of the leg, sclerosis of the legs, and lupus erythematosus. On the other hand, other workers have been less successful in substantiating SHUTE's claims. Thus MAKINSON et al.,[20] after comparing vitamin E with phenobarbitone, aminophylline, and calcium lactate in 22 cases of angina pectoris, concluded that it has no value in this condition; and BALL[21] was equally unimpressed after tests on 10 cases. Similarly in 13 cases of angina pectoris, and chronic heart-failure secondary to myocardial infarction or chronic rheumatic valvular disease, LEVY and BOAS[22] found that massive doses of 200–800 mg. daily were ineffective, even when given for several weeks.

Since SHUTE himself is not disturbed by the lack of controls in his investigations, and even hints that ideas and controls may be incompatible, we might well hesitate before accepting all his conclusions, even if there were no contradictory results. At the same time it is well to remember the conclusive evidence from animal experiments that vitamin E does in fact participate both in maintaining the normal permeability of capillaries and in protecting heart muscle from degeneration. Thus in experiments with chicks DAM[4] found that deficiency of vitamin E causes "exudative diathesis," characterised by an undue fragility of the capillaries with a resulting tendency to œdema. In the rat MASON[23] found that partial deficiency of vitamin E causes vascular abnormalities of the fœtus, with variable degrees of dilation and thrombosis, hæmorrhage, and sometimes œdema. In dogs with experimental kidney injuries HOLMAN[24] found that vitamin E prevents

1. Olcott, H. S. *J. Nutrit*, 1938, **15**, 221.
2. Martin, A. J. P., Moore, T. *Chem. Ind.* 1936, **55**, 236.
3. Dam, H., Granados, H. *Science*, 1945, **102**, 327.
4. Dam, H., Glavind, J. *Nature, Lond.* 1938, **142**, 1077.
5. Dam, H., Glavind, J., Bernth, O., Hagens, E. *Ibid*, p. 1157.
6. Martin, A. J. P., Moore, T. *J. Hyg., Camb.* 1939, **39**, 643.
7. Victor, J., Pappenheimer, A. M. *J. exp. Med.* 1945, **82**, 375.
8. Dam, H. *Proc. Soc. exp. Biol. Med.* 1944, **55**, 55.
9. Davies, A. W., Moore, T. *Nature, Lond.* 1941, **147**, 794.
10. Evans, H. M., Burr, G. O. *Mem. Univ. Calif.* 1927, **8**, 61.
11. Emmerie, A., Engel, C. *Rec. Trav. chim. Pays-Bas.* 1939, **58**, 895.
12. Athanassiu, G. *Klin. Wschr.* 1947, p. 362.
13. See Bacharach, A. L. *Brit. med. J.* 1940, **i**, 890.
14. Fitzgerald, G., McArdle, B. *Brain*, 1941, **64**, 19.
15. Milhorat, A. T., Bartels, W. E. *Science*, 1945, **101**, 93.
16. Shute, E. *J. Obstet. Gynæc.* 1937, **44**, 121.
17. Shute, E. *Amer. J. Obstet. Gynec.* 1942, **44**, 271.
18. Vogelsang, A., Shute, E., Shute, W. *Med. Rec.* 1948, **161**, 83.
19. Burgess, J. F. *Lancet*, Aug. 7, p. 215.
20. Makinson, D. H., Olcesky, S., Stone, R. V. *Ibid*, 1948, **i**, 102.
21. Ball, K. P. *Ibid*, p. 116.
22. Levy, H., Boas, E. P. *Ann. intern. Med.* 1948, **28**, 1117.
23. Mason, K. E. Essays in Biology. Berkeley, 1943; p. 400.
24. Holman, R. L. *Proc. Soc. exp. Biol. Med.* 1947, **66**, 307.

the development of arteritis. LAMBERT [25] is enthusiastic over the value of the vitamin in the treatment of aged dogs and cats suffering from heart disease. Cattle deficient in vitamin E, according to GULLIKSON and CALVERLEY,[26] exhibit progressive electrocardiographic abnormalities, and are prone to sudden death. MASON and EMMEL [27] have reported myocardial lesions in rats deprived of vitamin E for long periods, while MOORE and his colleagues [6 28] hold that the pigment granules found in the dystrophic muscles of such animals strongly resemble those typical of brown atrophy in the human heart. SHUTE's surprising claims for the therapeutic value of vitamin E therefore become more plausible when all the known effects of experimental deficiency are considered. Further animal experimentation should indicate clearly the directions in which controlled clinical tests could profitably be undertaken.

For the present it is natural to ask whether vitamin E is deficient either in the average diet or in that of patients suffering from diseases said to respond to its administration. Clearly the doses said to be necessary for successful therapy are greatly in excess of those consumed in an ordinary diet. Thus BURGESS's patients with collagenoses were having doses of 100–600 mg. daily, while their food contained only the normal 15–30 mg.; and he concludes that defective absorption or utilisation must be involved. SHUTE points out that the increased incidence of angina pectoris in America during recent years has coincided with the milling of flour poor in vitamin E; but he emphasises that his patients have derived no benefit whatever from the vitamin in amounts equal to those found in ordinary diets, and he recommends 200 mg. as an average daily dose for the control and maintenance of most patients with heart disease, with up to 900 mg. initially, provided that this heavier dosage is not contra-indicated by chronic rheumatic heart lesions or severe hypertension. He believes that he is using vitamin E not as a food accessory but as a chemotherapeutic agent. Indeed LEVY and BOAS have noticed that massive doses sometimes cause headache and vertigo; but the clinical significance of these side-effects is still uncertain.

25. Lambert, N. H. *Vet. Rec.* 1947, **59**, 355.
26. Gullickson, T. W., Calverley, C. E. *Science*, 1946, **104**, 312.
27. Mason, K. E., Emmel, A. E. *Anat. Rec.* 1945, **92**, 33.
28. Moore, T., Wang, Y. L. *Brit. J. Nutrit.* 1947, **1**, 53.

Annotations

THE KING'S HEALTH

ON Tuesday a bulletin from Buckingham Palace announced that the King is suffering from obstruction to the arterial circulation in the legs, and that the defective blood-supply to the right foot causes anxiety. The bulletin, which is signed by Sir Maurice Cassidy, Sir Thomas Dunhill, Prof. J. R. Learmonth, Sir Morton Smart, and Sir John Weir, adds that "though His Majesty's general health, including the condition of his heart, gives no reason for concern, there is no doubt that the strain of the past 12 years has appreciably affected his resistance to physical fatigue." Accordingly his visit to Australia and New Zealand, which was to begin on Jan. 27, has been cancelled; but he will continue to carry out his normal State duties at the Palace, including audiences.

Those who appreciate the weight of the physical and mental burden imposed on Royalty by a tour of the kind projected must be glad that this illness has declared itself now rather than later. Its seriousness is all too evident, and is the more impressive because, in a life of service, the King has so seldom allowed himself to be deflected from any public task, whether great or small. Yet there is good hope that, provided the acute phase yields to rest and treatment, it will be followed by a return of health and strength; though possibly, like so many of his subjects at the same age, the King will have to purchase continuing health at the cost of some of his more strenuous activities.

PROCONSUL AFRICANUS

ADDRESSING the Geological Society on Nov. 17 Prof. W. E. Le Gros Clark, F.R.S., gave a short preliminary account of the fossil skull of a Miocene ape recently found on Rusinga Island in Kenya. The discovery was made by Mr. L. S. B. Leakey, PH.D., and Mrs. Leakey last September, during the second season of the British-Kenya Miocene Expedition. Though a number of remains of fossil Miocene apes have previously been found, not only in Africa but elsewhere, these remains have hitherto been almost entirely confined to teeth and fragments of jaws. This is the first occasion on which a skull of one of these early primates has been obtained.

The specimen belongs to a species *Proconsul africanus*, originally defined on the basis of the dentition by A. T. Hopwood of the British Museum. The greater part of the facial skeleton has been preserved—almost intact on the right side, but much crushed and distorted on the left. The frontal region of the brain-case is also present, and the mandible is complete. The whole of the dentition (of which the third molars had already erupted and undergone some degree of wear) is excellently preserved. Portions of the occipital bone with the articular condyles, and also fragments of the petrosal bones, are among isolated fragments which, because of lack of contacts, unfortunately cannot be placed with certainty in their relation to the main skull. From the general dimensions of this skull, it appears that *Proconsul africanus* was somewhat intermediate in size between a large gibbon and a small chimpanzee. It contrasts strongly with the chimpanzee and gorilla in the complete absence of a supraorbital torus; indeed, the supraorbital region has a rather curiously human appearance. This latter feature, however, does not necessarily betoken any special relationship with the Hominidæ, though it may perhaps be taken to indicate that the latter have retained (or regained) certain primitive features which are of much greater antiquity than had been supposed. The skull is markedly prognathous; but, as compared with the modern African apes, this may be partly illusory owing to the difference in the supraorbital prominence; it may also to a slight degree be exaggerated by post-mortem deformation. The contour of the nasal aperture resembles that of the catarrhine monkeys rather than the anthropoid apes, and in some endocranial features such as the presence of a large subarcuate fossa (for the petrosal lobule of the cerebellum), a broad vermiform fossa on the occipital bone, and indications of a relatively small frontal lobe, it appears that the brain was more primitive than that of the large apes of today. The whole skull is very lightly constructed, with a remarkably thin cranial wall.

The geological age of the deposits in which the specimen was found is judged, mainly on palæontological evidence, to be Early Miocene. Since the Miocene period is generally believed to have begun about 35 million years ago, and to have ended 15 million years ago, the estimate of an antiquity of at least 20 million years is probably somewhat conservative. Professor Le Gros Clark pointed out that, though this fossil skull is unique, it is only one of

a great many specimens of fossil apes (some very fragmentary) which have been collected by the British-Kenya Miocene Expedition during the last two years. One of the significant results of this expedition has been the demonstration that, so far back as Early Miocene times, an astonishing variety of primitive and generalised anthropoid apes were already in existence in East Africa —ranging from small gibbon-like forms to great creatures of gorilloid dimensions. Arising out of this remarkable diversity, it is of course possible that certain types appeared which, much later, led on by a process of evolutionary development to the Hominidæ. Certainly, the time factor required for such a transformation no longer seems a difficult problem. Apart altogether from such considerations, however, these fossil remains provide most important material for elucidating the relationship of the anthropoid apes to the cercopithecoid monkeys. They are thus in some measure complementary to the fossil ape-like creatures (Australopithecinæ) of which, incidentally, still more important discoveries have quite recently been reported in South Africa. For while the South African fossils—even though their precise status is still unsettled—have obviously an important reference to the problem of the origin of Man from an ape-like ancestral stock, the East African fossils provide evidence bearing on the origin of the whole anthropoid ape group (including, of course, the actual progenitors of the human family) from still more primitive forms. Dr. Leakey and his colleagues are to be congratulated on the results of their excavations in Kenya, the success of which is due to an unusual combination of great physical energy and high technical skill. It is to be hoped that funds will be forthcoming to make possible a continuation of the work of the British-Kenya Miocene Expedition next year.

SISTERS IN THE MAKING

THE King's Fund, always fertile in good ideas, and never afraid to try them, are going to start a preparatory course for staff nurses about to become ward sisters. In a memorandum,[1] just issued, the general plan of such a course is set out.

The studies of the Working Party, reinforced by opinion in many quarters, have shown how urgent is our need to build up the body of trained nurses in our hospital wards. Many newly qualified nurses leave the profession —in order to marry, to enter other branches of nursing, to take a midwifery course, or for many other reasons. The post of ward sister does not capture their imaginations as it should; yet in no other appointment does the nurse get such unequalled opportunities for the direct care of patients or the training of the young entry. Doubtless newly qualified nurses are influenced partly by an urgent need to escape from the maternal restrictions of the nurses' home, and doubtless, too, financial considerations have an effect; and these two causes of wastage must be corrected. Nevertheless, it seems that some girls really hesitate at the prospect of the responsibility, for which they feel they have been ill prepared. Others more ambitious, find that the post of ward sister does not at present offer them the same chance of distinction as other branches of the profession. The King's Fund course is being planned to give the doubting girl confidence, and to help the ambitious girl to appreciate the full scope and opportunities offered by ward work.

Students nurses are often annoyed and frustrated by the lack of ward teaching, and by the fact that their classroom work is not sufficiently related to their ward duties. Staff shortages make it difficult for the sister to teach as much as she should, and in many hospitals sisters are apt to leave all that side of their work to the tutors. A practical course in methods of teaching, the King's Fund believe, would help the ward sister to give clear explanations and instructions, to demonstrate methods of treatment, and to realise how much guidance the student needs before she is left to carry out nursing procedures alone. Staff management has been studied much of late in industry, and many of the lessons learned can be applied in nursing. "Young sisters," the King's Fund memorandum suggests, "may not have learned to carry authority, to give simple direct instructions, to correct impersonally, to delegate responsibility to their staff nurses." It is a commonplace that an ungracious manner in a sister can lose nurses to the profession; and if few are naturally good at managing other people, yet, as the memorandum notes, all can profit by training. Again, insight into business methods and the elements of general administration of a hospital would give a nurse a good background for running a ward; and the actual ward administration, it is suggested, can best be learned during a term of apprenticeship, the novice working with a sister in a well-run ward.

The curriculum is merely outlined in the memorandum, for it is to be allowed to evolve; but the course will last 15 weeks, half of which will be spent at the staff college, and half in selected hospitals where the students will work as supernumeraries. The project will prove of great importance if it has its intended effect of restoring to the post of ward sister much of its original status, and of introducing into many hospitals the practice of the best.

1. Memorandum to Hospitals on the Need for Courses in Preparation for Ward Sisters' Duties. August, 1948. King Edward's Hospital Fund for London, 10, Old Jewry, London, E.C.2.

AFRICAN PROSPECT

As the first Sims Commonwealth professor, Sir Hugh Cairns spent the first three months of this year in Australasia,[1] and he has now reported on a tour during August and September in Southern Rhodesia and the Union of South Africa.[2] This second tour proved very different from the first, for in Australasia the medical problems of an English-speaking white population differ little from those of Britain. In South Africa, however, Cairns found two of the medical schools to be bilingual, while the third is primarily Afrikaans-speaking; moreover, "varying shades of nationalism" find their way into medical affairs, and towering above all else is the problem of disease in the native and coloured population. Though he recognises that splendid work has already been done on behalf of the native Africans, often in the face of great difficulties, he regards their malnutrition and ill health as the most important medical problem in Africa today. He mentions that the incidence among them of bilharzia, hookworm, and other tropical diseases, and of venereal disease and malnutrition, is so high that it is hard to know how to begin to treat them with existing means. In Durban, at the King Edward VIII hospital for natives, there are 2000–2500 cases of amœbic dysentery yearly, with a 10% fatality-rate; at Makerere, in Uganda, with its native medical school, 100–150 cases of pneumococcal meningitis are admitted yearly, and the results of penicillin treatment are not yet satisfactory. There is evidently no universal body of opinion that this problem should be tackled forcibly, since Cairns notes that the need for more systematic attempts to solve it was expressed only "in some parts" of Rhodesia and South Africa. It is, unfortunately, closely linked with questions of economy and education. How can the natives become healthy, he asks, until they have enough food and use it intelligently? Many broad questions need answering. What is the state of health, and what the standard of intelligence, of natives in different parts of Africa? What systematic attempts are being made to survey and eradicate the various

1. A report of his first tour, in Australasia, was reviewed earlier this year (*Lancet*, 1948, 1, 760).
2. Report to the presidents of the Royal College of Surgeons of England, the Royal College of Physicians of London, the Royal Australasian College of Surgeons, and the Royal Australasian College of Physicians.

diseases? To what extent can natives from various tribes be trained as doctors, medical assistants, and nurses? Cairns suggests that some future Sims professor, preferably "at no distant date," should be an expert in tropical medicine, and experienced in the study of native Africans, and that he should confine his travels mainly to the African continent, visiting not only the British Colonies and the Union, but also French Equatorial Africa and the Belgian Congo, where native medical schools have developed on lines differing from ours.

He was much impressed by the great competence and devotion in caring for the natives shown by many doctors, some of whom undertake both the medicine and the surgery of their hospitals, see a large number of outpatients daily, and turn their hands to big-game hunting when elephant and buffalo are eating their patients' crops. He visited the three South African medical schools, at Pretoria and Cape Town Universities, and the Witwatersrand University at Johannesburg. Plans are being made for the founding of a medical school for native Africans at Durban; and the Cape Town and Witwatersrand schools admit a small number of native, coloured, and Indian students each year. Medical training for non-whites should clearly be provided on a much wider scale, since in the Union there are some 9 million native, coloured, and Indian people to 2·3 million whites. Cairns found surgery of a high standard among both Europeans and non-Europeans in South Africa, and was particularly impressed by surgical teaching in clinical diagnosis and case-presentation. At Johannesburg both practice and research in neurosurgery were of the highest order, judged by international standards, and he regrets that the work is not more widely known: it is sometimes as bad a fault to publish too little as to publish too much.

BOLTJES CONTRA PIJPER

SOME time ago[1] we commented on Pijper's theory that bacterial flagella were no more than shreds of "slime-envelope" (or capsule) trailed behind a bacillus which progressed by a helical movement of its curved body. It was plain that this iconoclasm would receive its answer, and orthodoxy has found her champion in Boltjes of Amsterdam.[2] Against the elegant experiments and patent logic of his antagonist he matches a wealth of reference and comparison, minute observation, and a beautiful example of electron-photomicrography. This last he claims to refute Pijper's argument that the flagellum is no essential structure, since there was no evidence that it traverses the cell wall; and if we had more experience of the method we might be in a position to agree with one or the other. *Argumentum secundum, tertium . . . octavum*—each in turn draws on experience and analogy to confute heresy, and if at the end we have any doubt remaining it is that in the discussion of physical properties of microscopic structures analogy with macroscopic and tangible bodies may lead to unjustified conclusions. For example Boltjes says: "The way in which a flagellum is pushed aside by swimming bacteria also shows that it is not rigid." Yet we push aside the branches of hazel and briar with similar effect; and they are of very different rigidity. Rigidity and stickiness are both measurable physical properties, and for such arguments to convince they must be measured. That this is so far beyond our technical powers is only a reason for not using these arguments. However, this part of Boltjes's paper is perhaps little more than verbal fencing. His coup-de-grâce lies in his observation that when the stranded bacillus is hard aground the flagellum continues to beat, which is indeed odd behaviour for the inert trailer towed by a moving body. There is an answer to this: that such movement is due to brownian agitation or convection currents: but no doubt Pijper can provide a better one. We hope he can, for in these earnest days it is heartening to witness wise men doing no more than pursue wisdom. Had the members of the senior common-room any time to spare from attending committee meetings, "Boltjes contra Pijper" would provide better postprandial argument than Russian genetics.

1. *Lancet*, 1946, ii, 871.
2. *J. Path. Bact.* 1948, **60**, 275.

THE NEW LEGAL SERVICE

UNDER the new Legal Aid Bill the English taxpayer incurs an unknown liability while the benefits are confined to persons whose "disposable" income does not exceed £420 a year or whose capital does not exceed £500. Members of the medical profession will have their own views of a social service thus arbitrarily limited in scope. Hitherto in criminal proceedings the legal interests of the "poor person" have been looked after tolerably well. The expense was borne by local rates, and, if the brief fees brought the young barrister no great wealth, at least he was content to gain experience and, for what it was worth, a modest but legitimate advertisement. The Rushcliffe Committee rightly pointed out that in civil proceedings (apart from divorce) the position was less satisfactory. Poor persons have had no help in county courts or other inferior courts; the income limits (where help was available) were too low, and the recipient had often to make some out-of-pocket payment. Under the new Bill the Exchequer will pay. There will be full-scale fees and costs in the county court, and 85% of the taxed fees and profit costs in the High Court, Court of Appeal, and House of Lords. Except in divorce work (where the Law Society's existing scheme will continue) the poor person will have the right to choose his own solicitors and counsel from the panel of volunteers. England and Wales will be divided into 12 areas, with local committees acting through "certifying" subcommittees. The only limit to the prospective benefit, it seems, is that actions in such matters as libel, slander, and breach of promise will for the present be outside the scope of the terms of service. Legal advice will be available at centres where whole-time solicitors will attend. There will be special arrangements for these legal clinics for members of the Armed Forces oversea. A similar Bill for Scotland is on the way.

We must wait for the arguments to be deployed and discussed. The legal profession, not yet nationalised, is to work a plan of State-paid legal service brought within the reach of persons who otherwise could not afford this luxury. Payment by the State is payment by the taxpayers. Will there not be disappointment that those who pay cannot all have the chance of the benefit?

NURSES AND THEIR PAY

LAST week we suggested that the salaries proposed by the council of the Royal College of Nursing for staff nurses and ward sisters were too small. We are glad to learn that the figures we quoted from the *Nursing Times* of Nov. 6 were incorrect. On Nov. 13 that journal published the following amended statement of the college's proposals:

> "The proposed salary for the staff nurse is to start at £260, with emoluments assessed at £130; after statutory deductions of £47 3*s*. 4*d*. have been made the net cash salary would be £212 16*s*. 8*d*. Annual increments of £15 will give the maximum salary of £320 in four years.
>
> "The proposed salary for the ward sister starts at £310 per annum, with emoluments assessed at £150, and giving a net cash salary after statutory deductions of £62 9*s*. 4*d*. have been made, of £247 10*s*. 8*d*. Annual increments of £20 will bring the salary to £430 followed after ten years by a further increment of £20 and after another five years by a final increment of £20 making the maximum salary of £470."

These scales would represent a real advance.

Reconstruction

THE UNIVERSITIES AND THE HEALTH SERVICE

J. HENRY DIBLE
PROFESSOR OF PATHOLOGY, UNIVERSITY OF LONDON

SOME time ago a question was asked in the B.B.C. Brains Trust: "Where do you think the greatest repository of wisdom is to be found?"—or words to that effect. The reply was "Among university professors"; the speaker adding, "because they only work half the year."

My purpose here is not to sustain the foregoing proposition, but to point out that present trends are wholly eliminating its supposed basis. There is today a progressive and ever-increasing burden of affairs, arising partly out of the evolution of medical science, but aggravated by the passing of the new Health Act, which is becoming absolutely intolerable and is removing every vestige of the precious leisure so important to the professors of medical subjects. It is a matter of urgency that the universities decide without delay what is to be their future policy; for if the present encroachment continues unchecked there can be little room for wisdom of any kind in the hurried life in which we are involved.

A professor is usually appointed on the basis of his contributions to his subject arising from his original investigations, for his reputation for learning, and to some extent on his ability as a teacher. These qualities accrue only through his having had a large measure of free time for thought and reading, as well as that spent in the actual prosecution of observations and experiments, and it is on this that his knowledge and reputation are built. Once he is appointed to a chair he has to assume considerable administrative responsibilities for the organisation of an institute or set of laboratories, to concern himself with the problems—scientific, technical, and personal—of his staff, and to play his part in the life and internal politics of the university to which he is appointed. These are all his proper duties and in the ordinary way they are not oppressive. But certain medical professors have, in addition to these, to carry a burden of responsibility for the care of patients, for the whole gamut of modern clinical diagnostic tests, or for the provision of a post-mortem service to a hospital. This additional work has to go on through the whole calendar year and is not eased in the least by the arrival of vacations. Such a burden of hospital routine may be, and often is, a crippling one; it absorbs the greater part of the professor's time and puts him in a very unfavourable position compared with his colleagues in, for example, anatomy or physiology, who carry no such responsibilities and can look forward to complete freedom for their own pursuits in their vacations.

If such a state of affairs is, as I submit, undesirable and burdensome, it threatens to become an impossible one as a result of the impact of the National Health Service. The universities are dragged in as participants, and this adds yet another load of administrative work to already laden shoulders. But an even more corroding action is the tendency to regard the professors of the subjects of the clinical years of the student's curriculum as "medical specialists," and thereby servants of the hospitals and through them of boards of governors and the Ministry, rather than as members of a university staff. The new administrative machinery makes large calls upon the time and energy of the university professors, who are expected to sit upon an increasing number of committees concerned with hospital administration and finance, as well as upon quasi-academic bodies called into being by the schemes which have been set on foot for the training by postgraduate instruction of the "specialists" of the future. Within the past week I have received the minutes and agenda from a hospital board of governors amounting to 58 pages, and papers from an educational institution amounting to 49 pages; and these represent the labours of only two of the considerable number of committees upon which circumstances are forcing me to sit. Much of this work is not in the remotest degree concerned with learning and the advancement of my subject, for which purpose I was appointed to my present position, and it can only be dealt with by the sacrifice of proper and presumably more useful interests. A great deal of this material is a recent fungous growth, much of it created by individuals who have been appointed to administrative offices which are new creations, and justify their existence by busy promotion of schemes which are of questionable value.

The second danger in our present position is the financial lure which threatens to draw the academic staff of our universities into the group of "hospital consultants." The Spens report has recommended salaries for clinical specialists which appear highly attractive, and this report the Government has accepted "in principle." The highest-paid specialists are to receive a salary of £5000 "in terms of the 1939 value of money" (it will be remembered that this proviso was also made in the ill-fated Goodenough report); and the simple-minded consultants have, it seems, swallowed the bait, each no doubt believing in his own heart that he will be one of the favoured worthies to whom the higher rewards will go. Now, when it comes to assessing merit, it may well be argued that the university professors, who have reached their eminence not by seniority or apostolic succession but by open competition in a nation-wide and often world-wide market, must have high claims for the major rewards; and, confident in this belief, they are exposed to the great temptation of allowing themselves to be classed as medical specialists—a status to which they have every claim on the basis of the hospital work for which they are responsible. On the other hand the universities must regard these astronomical salaries with alarm, for they have to consider the position of many professors in the faculties of arts, science, law, or engineering, and their income is relatively fixed. They may therefore be tempted to get out of a difficult position by moving on parallel lines and letting or even urging their medical professors to become in the main hospital specialists and only in a minor degree university professors in the true sense.

It is known that these problems are engaging the attention of the University Grants Committee and the Committee of Vice-Chancellors, but my general anxieties on the whole problem are aggravated by a fear that in their extremity these bodies may be driven to hurried decisions permanently damaging to the cause of medical science and teaching. At the same time I can appreciate the difficulty of their position in virtue of the responsibility I have towards my juniors. These are on the whole a selected group of medical men of high ability and not too well remunerated. To deny them the rewards offered by the public service to specialists would seem an act of disloyalty. For myself, however, the position is clear. If a choice is to be made between on the one hand the large financial gains offered to hospital specialists, with which must be coupled the conditions of service under the Ministry of Health, and on the other the status and emoluments of a professor with the traditional freedom and privileges of that office, even at a much lower salary, I should not hesitate to accept the second.

However necessary the vast expansion of laboratory services in hospitals of all types may be, it is surely a vital matter to ensure that there shall remain a *corps d'élite* of university professors, in whose lives there shall be time for thought, reading, and that exercise of an inquiring mind which often leads nowhere in particular, but is of itself a worthy pursuit and occasionally leads to unplanned results of transcendent importance to the human race. It is the duty of the universities at this juncture to ensure that this academic freedom shall remain.

Special Articles

SPECIFIC LABORATORY TESTS IN STREPTOMYCIN THERAPY OF TUBERCULOSIS

REPORT BY THE PATHOLOGICAL SUBCOMMITTEE OF THE STREPTOMYCIN IN TUBERCULOSIS TRIALS COMMITTEE, MEDICAL RESEARCH COUNCIL.*

In the two reports of the Streptomycin in Tuberculosis Trials Committee (Medical Research Council 1948a and b) reference is made to certain laboratory tests such as the determination of the streptomycin sensitivity of tubercle bacilli and the assay of streptomycin in body fluids. No details of the methods were given, and as streptomycin is becoming more widely used in Britain it was thought desirable to describe and discuss the tests together with the results obtained, particularly in relation to the streptomycin therapy of pulmonary tuberculosis.

It is not suggested that these methods are the best or most accurate techniques, but they were devised and adopted as most suitable to the resources of the coöperating laboratories.

STREPTOMYCIN SENSITIVITY

Isolation of Organism

Sputum from cases of pulmonary tuberculosis was treated either by the acid-peroxide-iron method of Jungmann or with 4% sodium hydroxide before inoculation on to two tubes of Lowenstein-Jensen egg medium, which must be made with fresh eggs and used as freshly as possible. When sputum was unobtainable, laryngeal swabs or stomach washings were used. The centrifuged deposit of cerebrospinal fluid was cultured on Dorset-egg as well as on the Lowenstein-Jensen medium; alternatively, or in addition, some of the deposit was inoculated into guineapigs. Cultures incubated at 36–37°C were examined weekly and were not discarded until at least 8 weeks' incubation, since positive cultures sometimes developed very late from material in which the tubercle bacilli were presumably scantily present. Microscopically positive specimens of sputum obtained before or during streptomycin treatment almost invariably gave growth of tubercle bacilli on culture, and a large proportion of microscopically negative specimens also yielded growth of the organism. All strains from pulmonary cases and all but one of the strains from cases of tuberculous meningitis appeared to be of human type as judged by cultural characteristics; confirmatory tests on animals were made with several strains.

Medium

A synthetic medium containing Tween 80 and bovine albumin (Dubos and Davis 1946) was used for estimating the degree of streptomycin sensitivity. It was prepared as follows:

Potassium dihydrogen phosphate (KH_2PO_4) ..	1·0 g.
Disodium hydrogen phosphate ($Na_2HPO_4 12H_2O$) ..	6·25 g.
Sodium citrate	1·5 g.
Magnesium sulphate ($MgSO_4 7H_2O$)	0·6 g.
Dissolve one at a time in glass-distilled water.	
Add:	
Tween 80 † 10% solution	5 ml.
Casein hydrolysate ‡ 20% solution	10 ml.
Glass-distilled water to	1000 ml.

The medium should have a pH of 7·2. It was distributed in 2·5 ml. amounts in 7 ml. screw-capped bottles (bijou bottles) and autoclaved at 10 lb. pressure for 10 min. A 9% solution of bovine albumin (fraction V, Armour & Co.) was prepared, seitz-filtered, and 0·1 ml. added before use to each 2·5 ml. of medium, giving a final concentration of 0·3% bovine albumin when the volume in each bottle was made up to 3 ml. This Tween-albumin medium was prepared at the Central Public Health Laboratory and distributed in bulk to the other centres. Later, some of the centres prepared their own medium.§ The advantage of this medium is that the tubercle bacillus grows quickly and diffusely from a small inoculum. The Tween 80 has a dispersive action on the ordinarily granular growth of the organism, and bovine albumin, besides promoting growth, is protective against substances that are toxic for the tubercle bacillus. Thus, with a young diffuse culture of tubercle bacilli, adjusted to an agreed opacity, it was possible to use inocula of some uniformity in the numbers of viable bacteria.

Inoculum

As soon as typical colonies of *Mycobacterium tuberculosis* became apparent on the egg medium, a large loopful representative of the growth was emulsified in 0·5 ml. of distilled water. After the grosser particles had been allowed to settle, about 0·2 ml. of the suspension was transferred to a bottle of the Tween-albumin medium, which was incubated for about 7–10 days. If growth in this first subculture was still rather granular, 0·1–0·2 ml. was transferred to a second bottle of medium, which was incubated for 7–10 days, when there was usually a good diffuse growth. This culture was adjusted when necessary to a density about equal to Brown's opacity tube o. 2, and 0·2 ml. of a 1 : 10 dilution was used as the inoculum. An 8-fold decrease in this inoculum had no effect on the end-point of the test, though a 4-fold increase might change the end-point by two or more tubes. Thus the adjustment to standard opacity of a strain which had not grown fully was not of great importance, whereas a heavy growth, which sometimes developed, particularly with the standard strain, could be readily adjusted.

Standard Strain

A standard virulent human strain of *Myco. tuberculosis* H37Rv. was obtained from the Depot of Standard Cultures of Tubercle Bacilli, Saranác Lake, U.S.A., and was maintained by subculture at 3-week intervals on the surface of Proskauer and Beck's synthetic medium (Steenken and Gardner 1946). Because of difficulties in maintaining growth on this medium the streptomycin sensitivity of a strain of H37Rv. maintained for a year on glycerol-egg medium was compared with the culture on Proskauer and Beck's medium and was found to be identical with it.

An inoculum of the standard strain was subcultured into the Tween-albumin medium, and a sensitivity test was set up in parallel with the isolated strains.

Sensitivity Test

A small volume (0·3–0·5 ml.) of the standardised solution of 1% streptomycin ‖ was diluted 1 : 10, and from this 0·1% solution 2-fold dilutions were prepared in 7 tubes of sterile distilled water to contain 30, 15, 7·5 . . . . units per ml.

* The following members have served: ROBERT CRUICKSHANK, chairman (Central Public Health Laboratory); P. D'ARCY HART, secretary (National Institute for Medical Research); J. W. CLEGG and D. A. MITCHISON (Brompton Hospital); G. B. FORBES and H. D. HOLT (Central Public Health Laboratory and Colindale Hospital); I. A. B. CATHIE and J. C. W. MACFARLANE (Great Ormond Street Hospital); F. L. JACKSON and R. REES (Guy's Hospital); MARY BARBER (Hammersmith Hospital); E. NASSAU (Harefield Hospital); J. M. ALSTON and A. MOHUN (Highgate Hospital); J. N. CUMINGS (National Hospital, Queen Square); ISABELLA PURDIE (Bangour Hospital, West Lothian); W. H. TYTLER (Sully Hospital, Glamorgan); G. L. MONTGOMERY (Royal Hospital for Sick Children, Glasgow); A. W. DOWNIE and A. C. T. VAUGHAN (Alder Hey Hospital, Liverpool); R. L. VOLLUM (Radcliffe Infirmary, Oxford).

† Obtainable from Messrs. Honeywill & Stein Ltd., 21, St. James's Square, London, S.W.1.

‡ Prepared as for casein yeast agar (Mackie and McCartney 1942). To 200 g. of commercial casein in a litre conical beaker add a mixture of 170 ml. of concentrated hydrochloric acid with 110 ml. of distilled water. Stir quickly with a glass rod to obtain a uniform suspension before the casein swells and becomes solid. Autoclave at 120°C for three-quarters of an hour. Cool and add 40% sodium hydroxide till neutral (about 180 ml.); cool again and filter through pulp on a Buchner funnel. Dilute to 1 litre, place in a Winchester quart bottle, and add 1% chloroform. Shake vigorously immediately and at intervals to emulsify the chloroform. Store in the dark.

§ The Tween-albumin medium is now being prepared for distribution by Dr. J. E. McCartney, Southern Group Laboratory, Park Hospital, Hither Green, London, S.E.13.

‖ The streptomycin used was batch no. 594 (Merck & Co.) issued in bottles containing the equivalent of 1 g. of the pure base. Tests at the Biological Standards Laboratory, National Institute for Medical Research, Hampstead, N.W.3, showed that this preparation did not differ significantly in potency from the Provisional British Standard Streptomycin. The contents of a bottle were made up to 100 ml. with distilled water, and samples of this 1% solution were sent out to the other laboratories from the Central Public Health Laboratory. After 6 months' storage at 4°C this solution, compared with a freshly prepared solution from the same batch of the powder, showed no diminution in potency (fiducial limits = ±7% for $P = 0{\cdot}05$). An assay of the streptomycin contained in a series of tubes of Tween-albumin medium used for a sensitivity test indicated that there was no loss of potency after 14 days' incubation at 37°C.

(1 : 33,000, 1 : 66,000, 1 : 132,000 . . . .) 0·2 ml. of each dilution was added to the appropriate bottle of Tween-albumin medium, so that, when 0·2 ml. of culture was added to make a final volume of 3·0 ml., the concentration of streptomycin for strains isolated before treatment ranged from 2·0 to 0·03 units per ml. Tests were usually performed in duplicate. The bottles were incubated upright with caps screwed tight. They were read after 10 and 14 days' incubation at 37°C, though it was unusual with the pretreatment sensitive strains for any change to occur in the reading at the later period. The sensitivity of the strain was expressed as the lowest concentration of streptomycin per ml. giving complete inhibition of growth. The relationship of this end-point to the end-point for the standard strain put up at the same time was also noted—e.g., "two times less sensitive than H37Rv."

When numerous tests were to be set up, it was found convenient to add albumin and streptomycin to a series of flasks containing larger amounts of the medium, say 180 ml., and to dispense these with aseptic precautions.

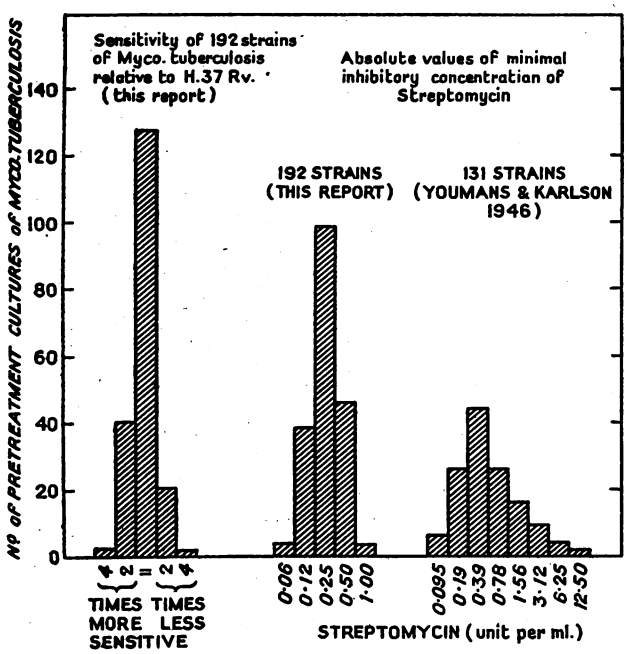
It is essential to adopt a safety technique in pipetting tubercle bacilli in this test. Great care should be taken, for example, to avoid blowing out the contents of the pipette either during the inoculation or before discarding.

RESULTS OF SENSITIVITY TESTS

Before Treatment

Altogether 520 cultures of *Myco. tuberculosis* from 13 centres dealing with cases of pulmonary tuberculosis and tuberculous meningitis have been tested for streptomycin sensitivity before treatment was begun or from untreated patients. These strains showed a range of sensitivity varying from 0·06 to 1 unit per ml. and were never more than four times less sensitive or four times more sensitive to streptomycin than the standard strain H37Rv. Most of the strains fell within a range of sensitivity of 0·1–0·5 unit of streptomycin per ml. A few bovine strains from other sources had the same degree of sensitivity.

As a check of the methods used and the results obtained at different centres, 192 pretreatment cultures, of which 100 came from other centres, were retested by Dr. D. A. Mitchison, using the same technique from March, 1947, to July, 1948. Results were analysed in terms of the degree of sensitivity relative to the standard strain (see figure). The analysis of variance indicated that, within the limits of the accuracy of this test, there is no real difference in the sensitivity of strains derived from different patients. The inherent error of the method is approximately one tube up or down from the true value in 19 out of 20 tests.



Sensitivity of pretreatment cultures of *Myco. tuberculosis*.

During Treatment

Cultures of cerebrospinal fluid and of sputum, or, where none was available, of laryngeal swab or stomach washings were made at regular intervals during treatment with streptomycin. The results as regards the development of streptomycin resistance have been described in the main reports (Medical Research Council 1948a and b).

Where a resistant strain of tubercle bacillus was expected, a higher range of streptomycin concentrations was used, with a maximum usually of 1000 units per ml. There appeared to be some risk of discrepancy in the reading of tests with resistant strains, since a few days' extra incubation sometimes allowed growth in one, two, or more tubes containing greater concentrations of streptomycin, especially where a resistant strain had only recently appeared. It is therefore particularly important in dealing with suspected resistant strains to read the results after 14 as well as 10 days' incubation.

Comparative Results

The comparative findings when 97 strains isolated and tested for their streptomycin sensitivity at Harefield Hospital, and 41 strains isolated and tested at the Central Public Health Laboratory, were retested at the Brompton Hospital Laboratory were as follows:

	Harefield Hospital	*Central Public Health Laboratory*
No. of strains compared	97	41
No. of patients from whom derived	25	14
Results in agreement:		
Range up to 1 unit per ml.	61/64	25/25
Range 1–4 units per ml.	1/4	2/2
Range greater than 4 units per ml.	26/29	13/14
Total	88	40
Results in disagreement:		
No. of strains	9	1

Details of strains in disagreement: Minimal bacteriostatic concentration of streptomycin (units per ml.)

Case no.	*No. of strains*	*Harefield Hospital*	*Central Public Health Laboratory*	*Brompton Hospital*
A	1	4		0·25
	2	4		0·25
B	1	50		1·00
	2	10–50		1000
C	1	2		0·25
	2	8		1000
D	1	0·3		0·06
E	1	0·7		0·06
F	1	0·7		0·06
G	1		12·5	1·00

Results are considered to be in agreement when there are not more than two tubes—i.e., a 4-fold—difference between the results obtained. Discrepant readings were obtained with 10 out of 138 strains, mostly among strains showing some degree of streptomycin resistance. The wide divergence in readings with a few of these strains might be explained as follows. Streptomycin resistance, as measured by this technique, may appear suddenly in the culture from any given patient, with the result that there is a sudden large increase in the concentration of streptomycin necessary to inhibit growth. Furthermore, during the next week or two there may be considerable fluctuations in this level. This may be explained by assuming that in such a culture there is a large population of sensitive organisms and a few relatively resistant variants which, purely by chance, may or may not be included in the sample removed from the culture for the sensitivity test.

ASSAY OF STREPTOMYCIN IN BODY FLUIDS

Blood Serum

The method adopted for routine use in estimating streptomycin in serum was based on that described by May et al. (1947). It is a capillary-tube method requiring very small amounts of serum, using a strain of Friedlander's bacillus (*Klebsiella pneumoniæ* 3) as the test organism, and a serum-glucose mixture as the indicator medium (1 part horse-serum, 1 part 10% glucose, and 2 parts distilled water, with a saturated aqueous solution of phenol red as indicator). The test is carried out as follows:

Boil 5 ml. of the indicator medium in a test-tube. Cool. Add 0·1 ml. of a 24-hour broth culture of *K. pneumoniæ* 3.

Prepare a standard serum containing 16 units of streptomycin per ml.

Flame the surfaces of two waxed slides divided into 10 compartments, and place nine separate volumes of sterile physiological saline solution in positions 2, 3, 4, 5, 6, 7, 8, 9, and 10 on the slides. Place one volume of the test serum ¶ in position 1, and add one volume of serum to the saline in position 2. Mix, and transfer one volume to the saline in position 3, and so on. After mixing in position 9, discard one volume so that 10 can be used as a control. Add one volume of indicator medium to the serum in position 1, to the serum dilutions, and to the saline control. Repeat this technique with the standard serum. The final dilutions of the test serum are thus 1/2 .... 1/512, and the final concentrations of streptomycin in the dilutions of standard serum 8, 4, 2, 1, 0·5, 0·25, 0·125, 0·06, 0·03, 0.

Draw up the mixture of serum dilution and indicator system into capillary tubes. Place the tubes horizontally in 'Plasticine,' leaving the ends unsealed. Incubate at 37°C for 24 hours.

Where full growth of the test organism has occurred the column of fluid in the capillary tube shows opaque clotted serum coloured uniformly yellow; where no growth has occurred the fluid remains red and transparent. The highest dilution showing no growth is taken as the end-point.

The reading obtained in the test serum is compared with that in the standard serum, and the concentration of streptomycin in the test serum is calculated from the formula $\frac{\text{T.E.}}{\text{S.E.}} \times 16$, where T.E. is the reciprocal of the test-serum end-point and S.E. the reciprocal of the standard-serum end-point—e.g.:

$$\text{T.E.} = 16 \qquad \text{S.E.} = 64$$
$$\frac{16}{64} \times 16 = 4$$

Therefore the unknown serum contains 4 units of strept mycin per ml.

An alternative and more accurate method (Mitchison and Spicer 1949), based on the agar-diffusion method of Stebbins and Robinson (1945), was used throughout at Brompton Hospital and for the most part at Harefield Hospital.

As intramuscular injections of streptomycin were given at 6-hourly intervals, it was agreed to test specimens of blood-serum at 1, 3, and 6 hours after the standard dose of 0·5 g. The results from the three main pulmonary tuberculosis centres are summarised in the accompanying table. Since assays were being made on

COMPARISON OF STREPTOMYCIN LEVELS (UNITS PER ML.) IN BLOOD-SERUM AT THREE CENTRES

Centre	No. of cases	No. of tests	Average streptomycin levels at		
			1 hour	3 hours	6 hours
Brompton..	11	18	22·2	14·9*	8·7
Colindale ..	11	32	19·4	14·3	6·6
Harefield ..	14	19	20·9	14·2	8·5

* Some observations included in this average level at 3 hours were made at 2 or 2½ hours after the injection.

The agar-diffusion method of assay was used at Brompton and Harefield Hospitals; and the capillary dilution method was used at the Central Public Health Laboratory, Colindale.

cases in the Brompton Hospital at shorter intervals than 1, 3, and 6 hours, the readings nearest 1, 3, and 6 hours were taken for comparison with the results obtained at Colindale and Harefield Hospital. The maximum and minimum levels recorded from these three centres at 1, 3, and 6 hours were respectively 42, 32, and 24 units, and 5·6, 4·0, and 1·0 units. There was thus a wide range of values, which was sometimes demonstrable in repeat tests on the same patient These variations are probably due as much to technical difficulties with the methods of assay as to variations in the absorption and excretion of streptomycin by different persons or in the same person at different times. The average results indicate that the level of streptomycin in the blood for the 6-hour period after injection of 0·5 g. is sufficient to have an inhibitory effect on the growth of streptomycin-sensitive tubercle bacilli, provided streptomycin is getting ready access to the bacilli in the infected tissue.

¶ Sufficient serum is obtained by collecting blood from ear prick or finger prick into a Widal tube. It has been usual to inactivate the serum by heating at 56°C for 30 min., but this may be unnecessary with the test organism *K. pneumoniæ* 3.

Urine

Serial 2-fold dilutions of urine and of a solution of streptomycin (1000 or 2000 units per ml.) were made in nutrient broth; the range of dilutions depended on the anticipated level of streptomycin in the urine, based on the calculation that 50–70% of streptomycin is excreted in the urine within 24 hours of parenteral injection. The dilutions of urine and of streptomycin solution were inoculated with a standard inoculum of *Staphylococcus aureus* Oxford (0·02 ml. of a 1/100 dilution of a 24-hour broth-culture) and incubated at 37°C for 24 hours. The highest dilutions which completely inhibited growth, as indicated by absence of turbidity, was taken as the end-point, and the level of streptomycin was calculated from the formula $\frac{\text{U.E.}}{\text{S.E.}} \times 1000$, where U.E. is the reciprocal of the urine end-point, and S.E. the reciprocal of the streptomycin end-point. When the urine was bacterially contaminated, the test sample was first heated at 60°C for one hour. The urine must not be sterilised by seitz filtration, which removes a considerable amount of streptomycin.

Assay of streptomycin excreted in 24-hour urine of 9 patients with pulmonary tuberculosis given streptomycin 0·5 g. 6-hourly was made by the test-tube dilution method described above and gave levels of 500–1500 units per ml.

Cerebrospinal Fluid

Assay of streptomycin in cerebrospinal fluid may be made by the capillary-tube method or by a test-tube dilution method using a standard medium of 1% 'Lab. Lemco' (pH 7·5) containing 1% glucose. The results obtained in tuberculous meningitis have already been described (Medical Research Council 1948a). The agar-diffusion method may also be used for assay of streptomycin in cerebrospinal fluid or urine.

DISCUSSION

Sensitivity Tests

The remarkable uniformity in the results reported from different centres of the sensitivity tests of strains of tubercle bacilli isolated from tuberculous patients before treatment with streptomycin suggests that the method adopted will give comparable results in the hands of different workers. This view is confirmed by the results of retesting a large number of strains at one reference laboratory, where the regional findings were usually corroborated.

The uniformity of results is, we believe, attributable in large part to the use of the new Tween-albumin liquid medium, which encourages diffuse growth of the tubercle bacillus and so allows the use of inocula of some uniformity. This medium has, however, been recently criticised by Fisher (1948a), who found that in 20 patients treated with streptomycin for 20 weeks resistant strains were demonstrable in only 5 cases when the strains were tested in a medium containing Tween 80, whereas in Youmans's medium, which contains no Tween 80, 11 of the strains were resistant. Using 3 resistant strains of tubercle bacilli, Fisher (1948b) later reported that the addition of Tween 80 or of glycerol had apparently an antagonistic effect on the organism and so increased the sensitivity of the test strains. This phenomenon was partly reversed by the addition of bovine albumin or plasma. The medium used in our investigations contained 0·3% instead of 0·2% bovine albumin, and casein hydrolysate instead of asparagin as in Fisher's medium, and seemed to be satisfactory for demonstrating the emergence of streptomycin resistant strains.

Certainly the proportion of resistant strains which developed during streptomycin therapy in our series of cases has been at least as high as in any series reported

from America. Youmans and Karlson (1947) have reported a greater scatter in the range of sensitivity of strains from untreated cases than we have found (see figure). It should be noted, however, that their inoculum was apparently greater than ours, and a large inoculum is more likely to contain variants that have some natural resistance to streptomycin (Yegian and Vanderlinde 1948). Pyle (1947) has found that sputum from untreated patients may contain variants of the tubercle bacillus that resist 5–10 units of streptomycin. Yet the great uniformity in our results with pretreatment specimens indicates that the proportion of resistant variants must be very small, and that the great bulk of strains are inhibited by 1 unit or less of streptomycin.

The disadvantages of this method of testing the streptomycin sensitivity of tubercle bacilli from patients before and during treatment are (1) the delay of 6–8 weeks before the result can be reported, and (2) the assay of streptomycin resistance on a qualitative rather than a quantitative basis.

It is important, when streptomycin is becoming more available and likely to be used much more extensively, that all strains of tubercle bacilli should be tested for their sensitivity to streptomycin before treatment is begun, so that the occurrence of fresh tuberculous infections with streptomycin-resistant or even streptomycin-dependent strains (Spendlove et al. 1948) may be detected. If possible, the test, besides being reliable, should be easily and rapidly carried out, since many small laboratories will be expected to collaborate, and clinical colleagues will want to know the result as soon as possible. The method described here is rather laborious and ill adapted to the small or overcrowded laboratory. An alternative method is to incorporate streptomycin in different concentrations in the medium used for primary isolation of the organism. Thus, American workers are using an egg medium containing 1, 10, and 100 units of streptomycin per ml. for primary culture or early subculture, and in this way they determine within broad limits the degree of resistance of the organism within 3–6 weeks (Karlson and Needham 1948, Steenken 1948).

The second objection is that resistant strains of tubercle bacilli, even when they constitute a very small proportion of the primary growth on a solid medium, will grow out when inoculated into the liquid medium containing streptomycin; hence a report of a strain resistant to say 10 or 100 units of streptomycin may simply mean that one variant out of several hundreds is resistant to that concentration of the drug. This would explain why some patients apparently respond to streptomycin after their infecting strain has been reported streptomycin-resistant, for in fact the bulk of the organisms may still at that stage be sensitive to streptomycin. The method of culturing sputum from patients under treatment on to plates of Herrold egg-yolk medium containing a range of streptomycin concentrations (Pyle 1947) may be used in an attempt to overcome this disadvantage, but it is not particularly suitable for a routine laboratory. The diagnostic oleic-acid-albumin-agar medium of Dubos and Middlebrook (1947), or modifications of it, may similarly be tried.

Assay of Streptomycin

Assay of streptomycin in body fluids is necessary at the commencement of an investigation with a prescribed size and rhythm of dosage in order to determine that effective levels of the drug are being obtained. When satisfactory levels have been demonstrated, routine assay of streptomycin in treated patients is not essential, and may be confined to cases where there is some evidence that the streptomycin is not being absorbed or excreted in a normal way—e.g., in patients with renal dysfunction. It has already been pointed out (Medical Research Council 1948a) that assay of streptomycin in cerebrospinal fluid, when patients are on intramuscular therapy only, may have some prognostic significance.

SUMMARY

The techniques for testing streptomycin sensitivity of tubercle bacilli and for assay of streptomycin in body fluids adopted by laboratories engaged in the Medical Research Council trials of streptomycin in tuberculosis are described and discussed.

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LEGAL COMMITTEE ON MEDICAL PARTNERSHIPS

THE report of the Legal Committee on Medical Partnerships, appointed by the Minister of Health, Mr. Aneurin Bevan, was published on Tuesday.[1] The committee, with Sir Gerald Slade as chairman, were asked to consider whether it is desirable, in order to secure an equitable result as between medical partners affected by the National Health Service Act, 1946, to amend sections 35 and 36 of the Act, either by clarification or by the extension of powers thereby conferred or in some other way.

The committee examined various types of partnership and make a series of recommendations which would require legislation to implement. Their main recommendation is that it should be declared that nothing in sections 35–37 of the Act shall "render unlawful the due fulfilment of obligations or due exercise of options in existing partnership agreements" existing on July 5, 1948. They propose, however, that where agreements do not expressly provide the manner in which compensation under the Act for loss of right to sell a practice is to be divided among the partners, there should in certain cases be modifications of the existing obligations and options.

Position of Partnerships.—Where all the members of a partnership have joined the National Health Service, and one member is under an obligation to sell a share of his goodwill to another, the committee recommend free transfer of that share. The partner making the transfer should then be entitled to draw immediately the State compensation payable in respect of that share in lieu of being paid the purchase price. Where some of the partners have joined the service and some have not, the committee recommend as follows:

If a partner *not* taking part in the service is under an obligation to purchase a share from a partner *taking* part in the service, this obligation should be converted into an option. If the option were exercised, the partner in the service should take the contract price and forego his share of State compensation in respect of such share.

If, on the other hand, it was a case of a partner who had *joined* the service purchasing a share in the practice from a partner who had *not* joined the service, then on paying the contract price he should be entitled to compensation out of a supplementary compensation fund which the committee propose should be set up.

Arbitration.—The committee believe their recommendations would in general enable an equitable result to be secured as between members of existing partnerships; but as the application of the principal Act and

1. Cmd. 7565: H.M. Stationery Office. Pp. 21. 6*d*.

of any amending Act might in certain cases produce special hardships which it is not possible to foresee, they propose arbitration machinery for dealing with such hardships if they arise. Such cases should either be referred (where the parties agree) to a single arbitrator to be nominated by, or on behalf of, the partners; or, failing agreement, to a committee of arbitration consisting of a legal chairman, a qualified accountant, and a medical practitioner. The first two members would be nominated by the Minister of Health and the third by the president of the British Medical Association.

The report makes a detailed study of difficulties which might possibly arise in relation to partnership agreements.

GENERAL MEDICAL COUNCIL

PRESIDENT'S ADDRESS

THE 174th session opened last Tuesday. Owing to indisposition, Sir HERBERT EASON was prevented from giving his presidential address, which was read by Prof. Sydney Smith, who, under section 9 of the Medical Act, 1858, had been chosen by the members present to act as president. In his address Sir Herbert expressed regret at the death of Sir George Newman, a former treasurer of the council and chairman of the public-health committee; and of Prof. J. K. Jamieson, who represented the University of Leeds from 1928 to 1936. Mr. J. C. Flood has resigned from the council and has been succeeded, as representative of the Apothecaries' Hall of Ireland, by Mr. J. J. O'Donnell.

Applications for registration under the Medical Practitioners and Pharmacists Act, 1947, now number just over 1600, and nearly 1050 applicants have been registered under the Act. The primary business of settling the position of practitioners who were temporarily registered during the emergency by virtue of Defence Regulation 32B has been substantially completed. Of just under 1100 applicants in this category nearly 950 have been registered under sections 1 and 2 on the receipt by the council of evidence of satisfactory service in a medical capacity while they were temporarily registered. Nearly 300 applications have been made by practitioners who were temporarily registered by virtue of section 5 of the Polish Resettlement Act, 1947. The number of applications under section 3, which relates primarily to persons who after Sept. 1, 1939, served in a medical capacity outside the United Kingdom in any of H.M. Forces, and also to persons whose war service in other circumstances was considered by Parliament equally deserving of consideration, is just under 140. There have been 95 applications under section 4, which relates to persons not within the scope of sections 2 and 3 who before Aug. 4, 1947, have been permitted to enter, or to remain in, the United Kingdom in view of circumstances attributable to war, and to certain other persons falling within provisions of section 5 of the Polish Resettlement Act, 1947. The number of applications lapsed, withdrawn, or refused as not being in conformity with the statutory conditions is 36; and after deduction of this number about 500 applications remain under consideration.

The penal cases committee have been concerned in the last year or two to note the number of cases reported to the council of convictions of practitioners for infractions of the Dangerous Drugs Acts and Regulations. While the council draw a distinction between the purveying of drugs by practitioners to addicts, and self-addiction, they feel that members of the profession should realise—to quote the words of a memorandum issued by the Home Office this year—that "in a number of cases doctors who had purchased drugs for the gratification of their own addiction have been convicted of the offences of unlawfully procuring and possessing these drugs." It is therefore clear that the self-administration of dangerous drugs for the gratification of addiction is not one of the necessities for practice for which alone practitioners are authorised to possess and supply such drugs; and the council feel it right to issue a warning that self-addiction on the part of practitioners may be considered as a grave lapse from the proper standards of professional conduct.

The draft Bill for the amendment of the Medical Acts which the council have submitted to the Government was not mentioned in the King's Speech at the opening of the present session of Parliament; but it may perhaps find a place among the other measures which will be laid before Parliament during the session if time permits.

Medicine and the Law

Nature of Statutory Adoption

AN unhappy experience of child adoption came before a Scottish court earlier this year. A married pair adopted a three-months-old boy after the adoption society had made the usual inquiries and reports which the statutory regulations prescribe. The health report stated that he had been medically examined and was fit and healthy. Presently, when it was found that he was not exhibiting normal development, another medical examination indicated that he was, and would always remain, mentally defective, owing apparently to a severe brain injury sustained at birth. The adopting couple then asked the court to cancel the adoption order, contending that it had been applied for in error induced by the information coming from persons acting on behalf of the boy's mother. What Scots lawyers call error *in essentialibus* might justify rescission of an agreement based on innocent misrepresentation if the mistake means that there has been a complete difference in substance between what was supposed to be supplied and what was in fact received. The Court of Session, however, refused to look upon the transaction as if it were a contract at all. Adoption under the statute, said the court, was a matter of status; it did not fit into the ordinary categories to which forms of action are assigned. It was not possible, since the statute made no provision for cancelling an adoption order, thus to invert the status of the child; the child had no part in the transaction.

It will be remembered that the Act of 1939 forbids the adopter to apply to the court for an adoption order until the end of a period of three months from the date on which the child is delivered into the care and possession of the adopter. During that period the adopter may notify the society of his or her intention not to adopt the child—in which case the child must be returned to the society within seven days. If no such notice has been given in the three-month period, the adopter must within another three months either apply to the court for an adoption order or notify the society of his or her intention not to apply for one. As for the information given by a society about the health of a child, the particulars about which the society must inquire and report include 23 questions, forming a medical report which must be signed by a duly qualified medical practitioner. Two of these questions ask whether the child's mental and physical development, and its behaviour, speech, and articulation, are normal for its age. It is hard to see what further precautions could be prescribed.

Explosion of Anæsthetic Machine

The Southend coroner has lately inquired into the case of a patient who died after an explosion had wrecked the apparatus from which he was being given a general anæsthetic. The anæsthetist gave evidence of having seen a flash at the side of the breathing-bag; the machine itself was wrecked and the connexions near the patient's face were blown apart. He suggested that ignition was due to a static electric spark. The patient died some five hours after the operation was completed, from massive collapse of the lungs as the result of pulmonary shock. The manufacturers said that, having reconstructed the machine, they found a leak between the breathing-bag and the bag joint. A verdict of death by misadventure was recorded.

In England Now

A Running Commentary by Peripatetic Correspondents

Now that air transport has brought the Colonial Empire within hours or days of London, specialists in every branch of medicine and surgery will soon be bringing to the backwoods and outposts the latest advances of the research laboratory and the newest techniques of the operating-theatre. After reading the Students' Guide one wonders how soon the specialist medical-student selector will be coming to give us a summary of the intelligence and a forecast of the future of the applicants for training in our embryo training schools. Perhaps he would advise us whether to accept or reject the candidate living a hundred miles away who writes thus:

Dear Sir,—As I have heard how famous your hospital is, I very much desire to apply a vacancy in it, to be trained as an assistant. The reason why is that if I shall not get anough points to go to a High School I shall want to be as you see above there. Very politely and without adoring myself I may tell you that I am a keen boy. I am in Form II now waiting to sit the Preliminary Examination in November, Sir. I should be very glad if you will allow me, as I am very interested in it. As I am in a discomposure I am going to conclude my letter, which I have written so abbreviately that I ca n't write more for the time being.—With much comity, I remain, Sir, Yours faithfully, . . .

* * *

Last week I took time off to assume the rôle of Dr. *Peripatékos* for an afternoon and wandered round the Royal Horticultural Society's hall where the London Medical Exhibition was being held. It was worth while, for I learned a bit, met many old friends not seen in years, and found plenty of material for speculation. The gentlemen on the stands—"reps" they are called in the trade—were most informative, and several soared way over my head into a chemical firmament where I could not follow. The structural formulæ of œstrogens and anti-histamine substances rouse no response in me. Clinically, however, the new ethinyl œstradiol sounded interesting. Procaine penicillin looked a nice preparation and an obvious advance on the oil-wax suspension. *p*-Aminosalicylic acid, a newcomer of promise in the tuberculosis field, was on exhibition, but the company are not releasing it yet except for carefully controlled trial—a very sensible policy I thought. There was a fascinating plastic gadget for giving penicillin-dust inhalations which appeared ingenious and efficient. (In a recent American journal I saw a reference to the use of this apparatus for administering adrenaline analogues as a dust in asthma.) Among the instruments the new heart-sound amplifier caught my eye as a useful adjunct for teaching and research as well as a diagnostic aid. This little list is of course, a personal one; a colleague would probably have come up with quite a different set of notabilia. I brought away a mass of commercial literature which (strangely enough, some might say) shall be kept. I find it useful, for it summarises a lot of journal reading I never have time to do anyway. Naturally it is partisan, but I make allowances for that, and anyway the Simon-pure scientific report is often enough pretty partisan in its presentation of the author's pet theory. But most of the firms seem to me to have a lot to learn about the production of commercial literature.

There seems to be a satisfying number of firms doing high-grade research. The new developments in both pharmaceutics and instruments should be not only useful in the therapeutic field but valuable assets in the export markets. This effort appears all the more meritorious when one considers the burden of taxation on research (which I believe is proportionately much less in America), the scarcity of highly skilled men, and the immense difficulty of getting new scientific instruments; for many of these a delay in delivery of one to two years is, I am told, quite usual. Here and there among the reps one found the odd line-shooter. A few firms were wrapping up the mixture as before by turning out the well-established favourites in slight disguise. Then the multiplicity of names for the same product exasperates; the new ethinyl œstradiol already has four proprietary names. It is time that this Babel of nomenclature was knocked down; but how this is to be done is another matter.

* * *

For some time there has been one criterion which showed whether the "chronics" among the women in this mental hospital were in touch with outside events. They might not know that the war was over or even that it had taken place, but they all knew that Princess Elizabeth was going to have a baby. On the morning after the announcement one ward got up early to have a celebratory round of tea, but most dramatic of all was white-haired Mary. She stops me on the stairs every day with a torrent of incomprehensible language. But that morning she took me to one side and whispered simply "It's a Boy!"

* * *

I [27 38 116] think that [46 75] this method [3 32 84 502] of citing references [8] to published papers [16 43 95 117] is rather overdone [21 74 110] by some workers, [91 143 405 512] particularly American authors [25 38 76 85 112 240 512] of review articles, et al.

* * *

The discussion in the mess centred on the detection of lead-swingers. Since ours is an intake centre this problem is not uncommon, especially after a long week-end. The value of the classical "number nines" was reviewed, and then the Atomic Physician proposed his revolutionary method. A tracer dose of radioactive lead is given to each suspect, and a Geiger-Muller counter is placed over the xiphisternum and connected to an x200 scaler in parallel with a cathode-ray oscillograph. As the lead swings there and back past the counter tube, the gamma-ray emission will be shown on the cathode-ray tube as a characteristic curve. We are now embarking on a controlled survey and we hope to obtain a series of graphs from which our physicist can deduce a formula, based on the amplitude and frequency, and giving the answer in units; one unit being equal to a day in the guardroom or a week's C.B. The scheme has now been submitted to the Service research establishment and we are sitting back expecting recognition in the form of promotion. It is, of course, possible that we shall be demobilised before an answer is received; or even that the higher-ups will mistake our idealistic motives and, assuming that we have too little to do, post one of our hard-worked M.O.s elsewhere.

* * *

My patient, Mr. Thingummyjig,*
Wears a fairly inobvious wig.
He wasn't seeing as well as he might,
But a pair of spectacles put that right.
Deaf as an adder, he makes the grade
Now that he has a hearing-aid.
After the usual grim adventures
His teeth were drawn and he now wears dentures.
His chest and guts were, of course, X-rayed
But all in vain; the films betrayed
No gastric or duodenal lesion,
Not so much as a mere adhesion.
Enteroptotic and far from svelte,
He had to have an abdominal belt;
And his hernia caused a fearful fuss
Till caught and controlled by an adequate truss.
Till cased in a silk-elastic stocking
His varicose veins ached something shocking.
Time marches on and as on it marches
He'll need supports for his fallen arches.
And it won't be long till he asks, I feel,
For a bag to carry his hydrocele.

Some may consider that Mr. T.
Is less of a man than a Christmas-tree.
But thanks to being an O.A.P.
To the dentist, to Mr. Bevan and me,†
All shall be added unto him—free.

* This line is wholly fictitious.
† Not to mention the backroom boys.

Letters to the Editor

CHRISTMAS GIFTS

SIR,—At Christmas, 1947, each of our regular beneficiaries received a Christmas gift of £5 from the Royal Medical Benevolent Fund, and these gifts gave great pleasure and help to all. Christmas, 1948, is now near at hand, but the response to my appeal made in October has not yet reached the sum required. I feel sure that no-one would want the amount of the gift to be reduced, and therefore I beg those of your readers who have not sent a contribution to do so as soon as possible. Contributions should be marked "Christmas Gift" and sent to: Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15. They will be gratefully acknowledged.

WEBB-JOHNSON
President, Royal Medical Benevolent Fund.

HOSPITAL MANNERS

SIR,—Though the correspondent writing on Two Hospitals in your issue of Nov. 13 seems to have been singularly unfortunate in the choice of her first hospital, there is certainly an element of truth in her criticisms, many of which are entirely due to the lack of the necessary staff and equipment. Our hospitals have been handicapped in their progress for the patient's comfort by two world wars. It is devastating to compare our wards and their equipment with those of countries such as Sweden and Switzerland.

I would agree as to noise and the lack of privacy. I have striven to obtain a quiet atmosphere and small wards for my patients for over twenty years. I have not been frustrated in my efforts by my board of management at any time, but merely by lack of money, and in recent years complete inability to provide cork and rubber floors, smooth running wheels on trolleys, &c., &c. But I am confident that I have provided a happy, friendly, and sympathetic nursing staff to whom the patient is of paramount importance.

Now I am glad I am near the age of retirement. Quite soon, good nurses will be a thing of the past. The constant adverse criticism of the matron and ward sisters, the large percentage of whom are wise and kindly administrators, with a few difficult ones thrown in as in all other professions and walks of life, will drive out all the senior members and prevent new recruits coming in. The modern student nurse will disappear. At present she is a happy young woman, has an eight-hour day, and is keen on her work. Most hospitals provide a comfortable home for her, with only those rules and discipline imposed such as she would observe in her parents' house, and a firm, but wise and kind control of her actions on the sick wards, this being part of her education, to ensure that she will eventually develop into a nurse able to meet the demands of the sick person in her charge, and to ensure that she will be a capable and responsible woman able to deal with matters pertaining to the recovery of the patient, and who if she is not disciplined and efficient may cause the death of a patient.

How long will these young students come forward when responsible people like Lord Crook in the House of Lords accuse the matron or ward sisters of the hospitals of tyrannising over the nurses? I venture to think that Lord Crook would be the first to complain were he unfortunate enough to have a serious illness, and his nurses were not calm, efficient, and disciplined.

Recruitment is being seriously affected by this idle ill-informed chatter about those in authority in hospitals. Every week as I interview prospective candidates, 99% tell me: "Of course, everyone tries to persuade me that I am crazy to think of nursing, it is a hard and irksome profession, and my father is very upset that I have chosen it." At present, I thank God that there are strong-minded girls who will not be put off by their fathers, and those others who know nothing of the real joy of our work and who care nothing for the service to mankind which our nurses desire to render. The general public and the fathers are the first to cry for nurses when ill, and the first to grudge the nurse a day off if she happens to be nursing them.

Let us have some support and encouragement in our work, so that we shall be able to improve conditions for our patients, so that there may be no element of truth in complaints such as registered by your correspondent of Nov. 13. I would like to reply to her criticisms one by one, only a few of which I think are applicable to my own hospital, but I feel you will not allow me the space in your journal.

I would only add that I see "the writing on the wall," and unless we are given more credit and help for the work which we are striving to do against heavy odds, soon there will be no efficient nurses to do even the bare essentials for the patients, not to mention all the improvements which hospital routine so badly needs.

University College Hospital, London, W.C.1. E. O. JACKSON Matron.

SIR,—The article on Two Hospitals, and your editorial, should be read by all hospital workers. Maybe none of us can fully appreciate the patient's position until we too have been patients, but we can try to do so. I have recently tried to find out patients' views by follow-up letters, but these are notoriously unreliable. Many patients are averse to writing and complaining, and I had to send 195 letters to get 100 replies. Other methods such as sitting incognito among the outpatients and talking to visitors in the bus queue yielded some useful suggestions.

These problems are not confined to our own hospitals. Here is a notice I came across on the wall of an office in an American hospital:

Hotels have accumulated fortunes by astutely commercialising the biblical injunction "A soft answer turneth away wrath." Hospitals have not yet learned this lesson.

Daily contact makes it easy to forget that a body diseased often means a body disordered. Many patients suffer from anxiety. Some are actually in danger and know that death is within the range of probability; pain and distress are usually accompanying features. Surely such patients find small comfort in the coldness and indifference often encountered in places that claim to be organised for the purpose of promoting health and consequently happiness. These remarks apply with double force to a child snatched from the arms of a loving mother and placed in a hospital ward with not a familiar face in sight. Hospital attendants are seldom positively cruel. Many often exhibit this tendency in a negative sense expressed by inattention.

Physicians and nurses particularly should adopt the hotel plan of service and incidentally comprehend the fact that hospitals were organised primarily for the treatment of sick persons and not to provide places for the staff.

Hospital attendants should maintain an inexhaustible supply of kindness, consideration and forbearance, especially the latter, ready for instant use.

An aptitude for debate or a natural or cultivated taste for recrimination have no place in the armamentarium of a doctor or nurse.

A mind small enough to interpret as a personal affront the peevish or unreasonable complaint of a sick individual means that its possessor is totally unfit to practice the healing art or care for those distressed in mind or body.

Chase Farm Hospital, Enfield. C. ALLAN BIRCH.

SIR,—I write to you as a recent patient in two London hospitals. In the first I was in a large ward, and I noticed the discomfort suffered by patients through not being told of their condition, their progress towards recovery, and the kind of treatment being used, or proposed to be used. As your correspondent says, "They don't tell you anything."

I was photographed with X rays and could not obtain from doctor, sister, or nurse any information at all of the condition shown by the photograph. The teaching specialists hardly ever said a word to me or listened to my remarks or questions. I did, after some weeks' delay, get my regular visiting doctor to listen to me and explain to some extent the treatment I was receiving and the progress of my disease; but he always treated me as a person not really to be considered in the matter.

Though nurses were always ready and willing to do—as quickly and efficiently as conditions allowed—anything a patient required, they had always to be asked.

No nurse, in my 14 weeks in two hospitals, ever asked me if she could do anything for me, or if I needed anything: and there are people who do not like to ask overworked women to do anything. On the other hand, I shall never forget the kind and sympathetic help and attention received from all the nurses who ministered to my needs in my weakness.

What is needed to produce perfect service in hospitals (apart from human sympathetic care which is there in abundance) is more doctors and nurses, and more mechanical appliances. A patient under present conditions soon finds out that the doctors and nurses are too few to provide that personal individual care which would be the ideal condition to achieve rapid healing. They now have not the time to get acquainted with the varying needs of patients, and their different ailments and dispositions.

London, W.C.2. B. W. YOUNG.

SIR,—I am at the moment attending as an outpatient at one of the London teaching hospitals. A deep-rooted aversion to hospitals made me apprehensive for days before I first went.

The appointment clerk gave me a friendly smile and told me to go and sit down, but I was so nervous that I could not turn the pages of a book. A doctor then came up and asked whether he could do anything, and on receiving a negative reply he stayed and talked to me for a minute, putting me at my ease. I then went into the surgery and sat down and waited, noting with some surprise that this seemed to be a combined consulting and waiting room, the patient only going behind a screen for examination. I was lucky; there was nobody else waiting and no students. The doctor was charming; considering there was practically nothing the matter with me he could not have been more sympathetic. Going back the next day I was surprised that my records were given to me to hold, and I studied them with interest. The doctor seemed to have mislaid his pleasant manner, and appeared to be showing off to the two students now present. However, he passed me on to the orthopædic department, and the appointment clerk whom I now saw treated me as if my convenience was of far more importance than the time of the hospital staff. Here again the waiting and consulting room were combined—an arrangement which I consider extremely bad.

Lastly I was referred to the physiotherapy department. Here again the good manners of doctors, nurses, physiotherapists, and the student who took my case-history, were all very much appreciated and did more than I can say to overcome my horror of hospitals.

AN OUTPATIENT.

SIR,—Some while ago I was sent with a note from my doctor to the outpatients' department of a London hospital—he wanted me to have an X ray for a suspected bone injury.

I duly presented the note, and listened to an argument between two clerks as to whether my case was medical or surgical. They apparently decided on the former, and I was made to wait four hours in a draughty corridor with lavatories on one side and on the other cubicles and a sort of dressing-station. When the four hours were up I expostulated with a sister (who was extremely kind and most apologetic: she was the only one who showed the slightest concern for the outpatients), saying I had to get back to my work. I was then taken in to see the house-physician, who for some minutes sat grandly at his desk ignoring me and reading whatever was written on my card and in my doctor's note. Irritatedly I said that I thought I had come for an X ray only. He seemed astounded that I should speak at all, and made some remark to the effect that "the patients were doing the diagnosing now!" After a few questions I was told to disrobe and waited another ten minutes in a room—the before-mentioned dressing-station—covered with a blanket on which there was a large and recent bloodstain. The physician then came back and proceeded to do the usual chest-thumping and knee-tapping. Finally I was allowed to go and have the X ray, which was what I had come for and which took exactly seven minutes. Was it necessary to waste my time and the doctor's and nurses' with a medical examination which could have been done beforehand by my own doctor if necessary?

I was instructed to come again in a few days and see the surgeon. On that occasion I waited five hours among a packed crowd of others, some of whom no doubt waited longer than I. Why could it not be arranged for people to come at, say, half-hourly intervals, so as to avoid part, at least, of this endless waiting?

UNDER TREATMENT.

SIR,—Your leading article of Nov. 13 put me in mind of a story which I heard as a student in Edinburgh many years ago and have never forgotten. It refers to an earlier age when Latin was more freely spoken among doctors than it is now. A certain lecturer concluded a bedside dissertation to his class with the words "Fiat experimentum in corpore vilo"; to which the patient quietly replied, "Pro hoc corpore vilo Jesus Christus mortuus est"—a rebuke which might well be borne in mind by the present generation of teachers and housemen.

London, W.1. W. A. LETHEM.

SIR,—Your correspondent's article in the issue of Nov. 13 should be a salutary reminder to the medical profession of our neglect of Hippocratic wisdom in this scientific age.

> "Life is short, the art is long, opportunity is fleeting, judgment is difficult, and experience is fallacious. It is the duty of the physician not only to do that which immediately behoves him, but to secure the coöperation of the patient, of those in attendance, and all external agents."

The first part of Hippocrates's first aphorism is well known, but the second part might be practised more often. In appreciation of my old teacher, Russell Howard, who stressed the value of the Hippocratic lore, I sign myself

OLD LONDONER.

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SIR,—Since the recent excellent article on this subject by Mr. Cohen [1] did not refer to accidental intra-arterial administration of soluble thiopentone mixed with curare, the following case is of interest.

A fit man, aged 45, thought to have a carcinoma of the colon, was brought to theatre for laparotomy. A solution of 15 ml. of 5% soluble thiopentone was mixed with 1·5 ml. of the Duncan Flockhart preparation of *d*-tubocurarine chloride, containing 15 mg. The median basilic vein of the right arm was chosen. After a little difficulty in venepuncture was overcome, what appeared to be venous blood was withdrawn into the syringe and slow injection was begun. The patient, asked whether the injection caused any discomfort, said it did not.

When 6·5 ml. of the mixture had been given, about ten seconds after the start of the injection, he complained of intense pain in the forearm and hand, and he screwed up his face with pain. He likened the sensation to that of an electric shock to the arm. The needle was at once withdrawn, 10 ml. of soluble thiopentone was injected into another vein, and anæsthesia was maintained with cyclopropane and oxygen. Almost coincident with the complaint of pain, the whole forearm and hand became intensely flushed. The radial pulse appeared equal on both sides.

Anterior brachial-plexus block was performed, after an interval of ten minutes, with 40 ml. of 2% procaine without adrenaline. The blood-pressure was then 90/40 mm. Hg. During laparotomy the arm was kept extended on a pillow, and the patient was returned to the ward with the arm in this position, with instructions for skin temperatures of both forearms to be taken every quarter of an hour. The readings obtained showed little variation.

Palpation of the antecubital fossa showed that the brachial artery ran a superficial course and lay immediately beneath the median basilic vein.

Convalescence was uneventful, no further complaint of pain in the arm was made, and there was no sign of thrombosis in the vessels of the forearm.

Comroe and Dripps,[2] in their experimental work on the intra-arterial injection of tubocurarine in man,

1. Cohen, S. M. *Lancet*, Sept. 4, p. 361.
2. Comroe, J. H. jun., Dripps, R. D. *Anæsthesiology*, 1946, 7, 260.

reported the production of huge weals and flares, which they thought were due to a histamine-like action of curare. In the present case the tubocurarine may have reduced or antagonised the spasm-producing properties of the thiopentone.

I wish to thank Dr. P. M. Edwards, senior anæsthetist to the West Middlesex County Hospital, for her help and advice.

Isleworth, Middlesex. F. R. RUSSELL.

GASTRIC ACIDITY

SIR,—The concentration of acid in the gastric contents, as determined by a fractional test-meal, is usually greater in patients with duodenal ulcer than in patients with gastric ulcer or normal subjects. The following factors operating singly or together might account for the increased concentration of acid:

1. *Supranormal rate of emptying.*—In patients with duodenal ulcer emptying is often hurried after a radiopaque meal, and the emptying-time of a gruel fractional test-meal is shortened. The gastric secretions are correspondingly diluted by a smaller proportion of test-meal.

2. *Supranormal volume of gastric juice.*—The volume secreted during a test-meal has not so far been measured, but it is known that patients with duodenal ulcer tend to secrete larger volumes in response to histamine and insulin than do normal subjects.[1]

3. *Supranormal concentration of acid.*—No reliable measurements of the concentration of acid in the juice secreted during a meal have yet been made, but the concentration in the juice of patients with duodenal ulcer after the injection of histamine or insulin is probably representative of the juice secreted during a meal. Such secretion is generally believed to have a supranormal concentration of acid in patients with duodenal ulcer. For example, Hollander[2] wrote: "Concentration of acid and pepsin in *gastric juice* [my italics] . . . the range for gastric ulcer coincides with that for normal individuals, whereas for duodenal ulcer it reaches a distinctly higher limit. Correspondingly, the average also is greater in duodenal ulcer patients."

Ihre,[1] however, concluded that the concentration of acid in the gastric juice of patients with duodenal ulcer was lower than that in normal subjects. He stimulated secretion first with histamine and then with insulin, avoiding contamination by continuous aspiration of the duodenal contents. He collected gastric juice from 24 normal subjects (mean age 23), from 20 patients with gastric ulcer (mean age 45), and from 20 patients with duodenal ulcer (mean age 41). The

MEAN CONCENTRATION OF ACID IN THE GASTRIC JUICE [MILLI-EQUIVALENTS/l (CLINICAL UNITS)]

—	Patients		Normal subjects		
	Gastric ulcer	Duodenal ulcer	Ihre	Bloomfield and Keefer	
Mean age ..	45	41	23	20	40
Mean conc. of acid	81·5	87·6	122·8	75	64
Standard error of mean	±4·7	±5·4	±1·8	..	..

mean concentrations of acid and their standard errors, computed from Ihre's results for each group, are shown in the accompanying table. The mean concentration of acid in the juice of normal subjects is 35 milli-equivalents per litre greater than that in patients with duodenal ulcer, and 41 milli-equivalents greater than that in patients with gastric ulcer.

Although these differences are statistically very significant they do not warrant the conclusion that peptic ulcer is associated with a gastric acidity lower than that of normal subjects, since the mean age of the normal subjects is 20 years less than that of the patients with peptic ulcer. Bloomfield and Keefer[3] found in a mixed group of hospital patients that the mean acidity of gastric secretions after the injection of histamine declined with age. To show the importance of age, the mean acidity in such a group aged between 15 and 25, and in another group between 35 and 45 from Bloomfield and Keefer's material, have been included in the table. Probably because they were examining hospital patients, Bloomfield and Keefer recorded a much lower mean acidity for the group with a mean age of 20 than did Ihre. The difference between the group with a mean age of 20 and the group with a mean age of 40 was 11 milli-equivalents per litre. This is one-third of the difference between Ihre's normal subjects and his patients with duodenal ulcer. Thus probably a group of normal subjects, aged 40, examined by Ihre's technique, would show a mean acidity higher than that shown by his patients with duodenal ulcer. This is contrary to general impression. Detailed examination of Ihre's figures suggests that this reduced acidity in patients with peptic ulcer is due to an increase in the proportion of non-acid fraction of the gastric secretion.

Thus it seems that the increased concentration of acid in the gastric contents of patients with duodenal ulcer results from rapid emptying and an increased volume of secretion; it is not caused by the secretion of a gastric juice containing acid in concentration higher than normal.

I am indebted to Dr. Ihre for permission to use his figures.

Guy's Hospital Medical School, London, S.E.1. J. N. HUNT.

GROUP MEDICAL PRACTICE

SIR,—The writers of the report in your issue of Nov. 6 are, I think, not doing justice to the idea by making sweeping statements based upon experience of only two years. The comment by "Consultant" on Nov. 13 is sound. I would like to emphasise that however valuable group medical practice may be in an association of general practitioners, there are disadvantages when this group coöperation is transplated into their specialist services in a neighbouring small hospital. The difficulty is graphically illustrated by the example they give of the group's coöperation and organisation. While all five partners in the group were intimately concerned in the hazards of a major general surgical operation, an area of approximately 80 square miles with a population of 25,000 was deprived of five-sevenths of its general-practitioner service; and that is the real trouble of a small group working under the conditions described, for the conscience of the specialist cannot be squared with the conscience of the general practitioner.

Group general-practitioner-specialist services are still necessary in very remote parts of this country, but in these circumstances it is to be hoped that the terms of service provided by the Ministry of Health will be such that the general-practitioner consultants can be encouraged to give up the greater part of their general practice and to become more and more whole-time consultants, where their qualifications and experience permit. The only way in which group medical practice of the type described in the article of Nov. 6 can be conducted is where the firm comprises a bigger proportion of pure general practitioners and where the town and the local hospital are big enough to contain other groups so that coöperation of the specialist services within the hospital is conducted in such a way as to be divorced from the financial advancement of a closed corporation and free from any interference with the general-practitioner service.

In the original report, mention is made of orthopædic services; and therefore I should say that my experience of one such group medical practice is that the tendency is to call in orthopædic consultants late rather than early, because—owing to the nature of the commitments of such a group—the recognition of difficulties and of possible complications is not given the continuity and concentration of thought and care which such cases, particularly accident problems, require.

ORTHOPAIS.

1. Ihre, B. J. E. Human Gastric Secretion. London, 1938.
2. Hollander, F. *Surg. Clin. N. Amer.* 1947, **27**, 265.
3. Bloomfield, A. L., Keefer, C. S. *J. clin. Invest.* 1928, **5**, 285.

THE GENERAL PRACTITIONER

SIR,—Thirteen years ago I decided to enter general practice. Married, with a young family and a substantial overdraft, I had to borrow, by means of insurance policies and a personal guarantee, a further £1200 at 4½% interest. Such limited resources confined my choice not only of locality but also of size of practice and house. After a protracted search I found what seemed the only suitable practice on the market—an old-established one in the north, half urban and half rural, whose owner was retiring owing to ill health. All the usual inquiries failed to reveal any flaw. The agency was an old and trusted one, the accounts had been checked by an accountant, and a discreet personal inquiry was convincing.

Alas, my disillusionment was soon complete. The vendor had been an alcoholic for years, and I soon found that he had a mild Korsakoff's syndrome, for which I had to cut abruptly short the personal introductory period. The next few years were even harder for my wife than for me; but the practice grew, and each year the income showed a steady and reassuring increase. It had perhaps been worth while after all, but I would not have gone through with it had I seen the difficulties at the beginning. Nor would I advise anyone else to undertake a like venture. The National Health Service Act appeared to be a solution of all such future difficulties for those who, like myself, had no money—all who were lured into assistantships "with a view," "no premium required," and "pay out of income." How many assistantships ever matured to partnerships? Not many, I believe.

But again what disillusion this Act has brought with it. Now I have, at a modest estimate, lost one-third of my income; the hope of moving to a more salubrious district is receding, and the prospect of compensation is remote. Worst of all is the fact that I cannot increase my income except at the expense of my fellow practitioners; only by enticing their patients can I extend my practice. The most successful, if judged by earnings, will be those who adopt the attitude of the obsequious shopwalker, whose maxim is that the customer is always right. My practice had not grown by extending the number of my panel patients, these have remained fairly constant; the population is stable, and the people mostly loyal. Nor had it grown by any great increase in the number of private patients, though of course they became somewhat more numerous, especially during the first few years. The practice prospered mainly by my use of the skill gained from fifteen years of hospital experience; this was something more than the average general practitioner could offer.

Now the zest has gone; my hospital experience has been dearly bought. Almost anyone can write a prescription copied from the *National Formulary*, and fill up a form or send the patient to hospital. It is quantity that counts today, not quality. How much better if this cut-throat competition, so beloved by the B.M.A., had been entirely eliminated by paying us a salary compatible with our experience and years of practice. Happy indeed are those young and healthy enough to emigrate.

G.P.

COMME ON FAIT SON LIT ON SE COUCHE

SIR,—The attention focused on rheumatism in consequence of recent bequests for research leads one to hope that an important aspect of this matter has not been, and will not be, overlooked. I refer to the effect, if any, of exposure to damp on the incidence and course of rheumatic affections. I have already drawn attention in my inaugural lecture at this college to our national apathy in this connexion by reference to a familiar domestic example, in the following words:

> "Advances in our knowledge of the chemistry and physics of textile fibres point without a shadow of doubt to the fact that the right time to make a bed is within ten minutes of getting out of it. Yet the housewife (God bless her!) has been brought up in the belief that a bed must be thoroughly aired for at least an hour before making, preferably by an open window. This, in a country whose atmosphere for more than six months of the year has a relative humidity of more than 50%, is a shocking misuse of opportunities, which has to be paid for in agonies of human suffering in terms of neuritic and rheumatic affections for which these islands have been famous from time immemorial. Expressed in man-hours of work lost to industry it is even more alarming. And yet the facts are known, and have been known for years; the water-absorbing properties of cotton and wool have been quantitatively assessed, and the number of calories you lose when, by your body heat, you dry out your bed every night can be calculated with terrifying accuracy."

University College, Leicester. L. HUNTER.

ASTHMA

SIR,—May I be allowed to congratulate your correspondent on the perfect description he gave last week of his symptoms as an asthmatic. His description was applicable in every detail to many patients who suffer with asthma from allergy and superimposed microbic infection.

But has he been properly treated? I rather doubt it. He makes no mention of house dust or feathers—the two commonest causes of allergic asthma. The correct treatment in my estimation is to find out by skin tests to which proteins the patient is sensitive, and then to be desensitised to them by a long course of treatment. Where a microbic element is present the vaccine must be given by the small-dose technique: this is essential.

The various medicaments, down to the latest antihistamine drugs, do nothing to cure the complaint; they merely alleviate the symptoms. Breathing exercises should be directed, not to the accessory muscles in the neck, but to the diaphragm, over which so few people have the slightest voluntary control. One has found that those unfortunate people who were gassed, particularly with mustard gas, are always more difficult to help; possibly the lung tissue has sustained some permanent injury.

In brief, then, in my opinion the prime causes of asthma are allergy and microbic infection. All such influences as mental shock and overfeeding (especially at night) being secondary causes of relatively little import. However gloomy the prognosis given by your correspondent in his own case, this is not so in general. Hundreds of cases can be cured if properly treated, and one would like to see it a part of the N.H.S. to provide asthma and allergy clinics for all and within easy reach of all, up and down the country.

London, W.1. FRANK COKE.

THE VOCATION OF MEDICINE

SIR,—Lord Horder's address published on Nov. 6 contains the following passage:

> ". . . . it is possible to break away from the straight line of doctoring at a number of points in the course of training, a fact which should be borne in mind when any one of you begins to doubt if you are sufficiently interested in your human fellow creatures to make a good doctor. You can teach in the preclinical subjects; you can take up X-ray or radium work; you can be a clinical or an academic pathologist; you can engage in public health."

We do not think that Lord Horder can mean what these words imply—that poor doctors, lacking in human feeling, are well placed in the public-health service. If any such persons do seek employment let it be elsewhere than in social medicine; for that discipline asks for a degree of professional skill and a wealth of understanding at least as great as those demanded in other branches of medical work.

Imagine a mentally ill-equipped unsympathetic doctor in charge of services to raise living standards, to secure care and aftercare of sickness, to do the field work of epidemiology; worst of all, imagine such a man in charge of administration, where courtesy, sympathy, and imagination make all the difference between good work and a mechanical routine, adapted for nothing human or humane.

Social medicine can offer testing and rewarding work to the best men the medical schools can produce. Medical

officers of health are not all Simons or Southwood Smiths; there are even black sheep amongst them—what flock is without them?—but we have our standards, our ideals, and our traditions. We are justly proud of them and it is to these, in all humility, that we would ask our recruits to look.

C. FRASER BROCKINGTON
County Medical Officer, West Riding of Yorkshire.
D. P. LAMBERT
Medical Officer of Health to Sedbergh, Settle, and Bowland Rural Districts, and Divisional Medical Officer.

ANONYMITY

SIR,—May I protest against the pernicious habit of journals of publishing anonymous letters, to which the medical press, too, is becoming increasingly addicted. In the past I have understood that the tradition of journalism was to allow anonymity only rarely and exceptionally. Now almost every week one sees anonymous broadsides or retrograde stabs, as exemplified by three in last week's LANCET. May I plead for a return to the older and healthier tradition.

London, W. 1. DAVID H. PATEY.

*** Some letters lose most of their force and persuasiveness if unsigned. But anonymity has its use if it permits Radiologist, Income-tax Payer, or Ex-Convict to relate an experience, state a point of view, or present an argument without repercussions among his associates. The desire to detach a subject from personalities is sometimes legitimate and even praiseworthy; and English literature and public life owe much to the writings of "Anon." Nevertheless we share Mr. Patey's general preference for signed letters, and we are obliged to him both for his warning and for his example.—ED.L.

COST OF THE N.H.S.

SIR,—In your last issue (p. 831) you state that employed persons are paying 8½*d.* per week towards the cost of the National Health Service. While this is quite correct on paper it does not follow that the money is coming out of their pockets. Those employed persons, and there are many thousands of them, who since July 5 have secured a rise in wages on the plea that they could not afford to pay their N.H.I. contributions are no longer paying anything. Their contributions are being paid by their employers with the inevitable result—increased costs of production.

You dispute the statement of "Chirurgicus" that "the average individual is paying £10 a year in National Health Insurance." What he obviously meant was that the average individual is paying that amount FOR National Health Insurance. Whether the payment takes the form of insurance contributions, direct taxation, or indirect taxation is quite immaterial. The money must be found. The latest of the growing estimates of the cost of the health service is £230 million (Minister of Health, *Hansard*, April 8, 1948). Allowing for the further increase which is inevitable, and reckoning the number of those who contribute to the Exchequer in one form or another as 30 million the statement of "Chirurgicus" as above amended is not far wrong. At the moment, however, not one of us is paying a penny for it. It is a gift from that great capitalist country across the Atlantic.

Cambridge. FF. ROBERTS.

*** When "Chirurgicus" referred to "the average individual . . . paying some £10 a year in National Health Insurance," we naturally supposed that, like many other people, he thought that the whole of the weekly contribution (4*s.* 11*d.* for an employed man) goes to the National Health Service, whereas in fact the portion devoted to this object is only 8½*d.*

Assuming with Dr. Roberts that the N. H. S. will cost over £10 per head of population per annum, is this necessarily too much to pay? The estimated cost of medical care in the United States in 1947 was $6500 million,[1] which for an estimated population of 143 million works out at about $45 per head. Whether we choose to pay for health services privately, by charity, by contributions, or by taxation is a matter of internal bookkeeping. It would of course be possible for the medical services, by excessive development or by waste, to claim so much of the nation's man-power and other resources that they hindered industrial production instead of promoting it, and Dr. Roberts has done well to warn us of this danger.[2] But only if our health services became a handicap to production could the Americans be said to be indirectly paying for them; and the steps taken since July 5, in the hope of ultimately increasing the efficiency of these services, can hardly have converted them into a pure luxury. In so far as they are not a luxury, Dr. Roberts's concluding jibe is unjustified.—ED.L.

BASIC SALARY

SIR,—Today, at a local British Medical Association meeting, the secretary of the local medical committee demanded more precise criteria by which to judge applications for basic salary. Being the excellent men they are, his committee will undoubtedly do their drastic pruning with immaculate justice; but it is still an undeniable fact that the more applications they grant the less money they themselves will earn—a situation embarrassing both to them and to the applicants, and one which should not exist.

However, this is not my main point. Later, elaborating the difficulties of the task, the secretary was moved to cry despairingly, "Everyone has applied!" If everyone has applied, it is apparent that the general opinion amongst G.P.s is that the basic salary is desirable and justifiable, regardless of the appreciated fact that it reduces the income of men with large lists. I do not defend the method which allows basic salary to reduce the amount in the kitty—it should come from a separate fund. But, in implying that applicants for the £300 are disloyal to their colleagues, B.M.A. official policy is obviously once again out of touch with the feelings of the rank and file.

Whitchurch, Hants. BENJAMIN LEE.

TESTING ANALGESICS

SIR,—We wish to comment on the points raised by Dr. Bernard Kenton in his letter of Nov. 13. Our preference for maintained ischæmic muscle pain as a background for testing analgesic drugs is simply explained. In conjunction with Dr. F. Prescott and Dr. R. H. Thorp of the Wellcome Foundation, we originally set out to compare the analgesic properties of 'Physeptone' with those of morphine and pethidine by means of the heat-radiation method of Hardy and Wolff; but we found that, although the control threshold values were very constant, the responses to the drugs were extremely irregular and inconsistent. Indeed only 1 of 12 subjects tested (student volunteers) gave appropriately graded responses to different doses of the three drugs; one subject, in response to two separate injections of 10 mg. of physeptone, showed on one occasion a rise of 77%, and on the other a rise of 8%, above the threshold. It is difficult to account for such variability even on the basis of the distracting factors discussed by Wolff and Goodell,[3] who found that psychological influences alone could raise the heat pain threshold by 30% or more.

We therefore sought a method both more reliable and perhaps more closely related to the conditions of disease, and we found that properly controlled use of the subjective estimate of intensity of ischæmic muscular pain gave consistent and reproducible results, except for the increase in sensitivity over long periods of time, which we discussed in our paper.

We agree that the modes of action of analgesics are complex, and that the therapeutic effectiveness of drugs in the relief of pain must include reactions impossible to simulate in normal healthy individuals. As to whether analgesic and euphoric effects can be separated, all that can be said at the moment is that the very extensive work on phenanthrene derivatives, and the

1. Cost and Quantity of Medical Care in the United States. By Frank G. Dickinson, PH.D. American Medical Association Bulletin no. 66. 1948.
2. *Brit. med. J.* 1948, i, 485.
3. Wolff, H. G., Goodell, H. *Ass. Res. nerv. ment. Dis.* 1943, **23**, 434.

studies of newer chemical compounds such as pethidine and physeptone, have not yet produced drugs which can relieve severe pain without their also being liable to produce euphoria and addiction.

A. J. H. HEWER
C. A. KEELE.

Department of Pharmacology, Middlesex Hospital Medical School, London, W.1.

FELLOWSHIP FOR FREEDOM IN MEDICINE

SIR,—You were good enough to print a full account in last week's issue of the formation of this Fellowship, under the chairmanship of Lord Horder. May we ask you to state that all inquiries, including applications for membership, should be made to the hon. secretary, 40, Westminster Palace Gardens, Artillery Row, London, S.W.1?

G. H. ROSSDALE
E. C. WARNER
Hon. Secretaries.

APPLICATION FOR HOSPITAL POST

SIR,—Encouraged by the letter of "A.B." in your issue of Nov. 6, I should like to cite a similar experience in which the five applicants for an advertised appointment were asked to attend for an interview at 5 P.M., by telephone during the morning of the same day. At the time I was working in the country some 200 miles from London, where the interview was held.

The actual interview—a mere formality as so often happens—lasted two minutes, and the post was given to a man already working in the hospital. In these cases, where no further information is sought during the interview, is it necessary to waste applicants' and committee-members' time for the sake of formality?

I should also like to draw attention to the humour of the A and B2 classification of posts. Here those of us relatively recently qualified are competing with holders of higher qualifications with much more experience. Yet we are told that B2 and B1 posts exist in order to provide training or experience necessary before sitting the M.R.C.P. or F.R.C.S. examinations.

NON ÆQUANIMITAS.

Parliament

QUESTION TIME

Royal Commission on the Death Penalty

Replying to a question Mr. CHUTER EDE, the Home Secretary, said: On July 22 I informed the House that the question whether there were practical means of limiting the death penalty would be explored. The Government have given careful consideration to the question how this can best be done, and have decided to recommend the appointment of a Royal Commission. The terms of reference and membership of the Royal Commission are still under consideration and will be announced in due course. At this stage I can only say that the scope of the inquiry will be the questions whether liability under the criminal law in Great Britain to suffer capital punishment for murder should be limited or modified, what alternative punishment can be substituted, and what are the changes in the law and the prison system involved by any alternative punishment. The commission will be invited to take account of the position in those countries whose experience and practice may be of value in considering these questions.

Distribution of Doctors

Sir HENRY MORRIS-JONES asked the Minister of Health what recommendations he had received from the Central Medical Practices Committee on the question of maldistribution of medical practitioners; and if he would give this matter his consideration.—Mr. ANEURIN BEVAN replied: None so far. The committee are obtaining comprehensive reports on the adequacy of the medical services throughout England and Wales by Dec. 31. I shall naturally give most careful consideration to any recommendations the committee may see fit to make to me in the light of these reports.

Hospitals and Charges to Patients

Mr. PETER FREEMAN asked the Minister what charges, and under what conditions, hospitals controlled by his department might impose on patients; and whether they were informed on admission of such charges.—Mr. BEVAN replied: Patients may go into pay-beds, at full cost. Otherwise they can only be charged for extra privacy in single rooms or small wards, for the extra cost of certain expensive appliances, and for renewal of appliances through negligence. They are informed on admission.

Tuberculosis Patients' Benefits

Mr. T. W. BURDEN asked the Minister of National Insurance if he had considered a request from the National Association for the Prevention of Tuberculosis respecting the hardships imposed on the tuberculosis patients who had had their sickness benefits reduced to 5*s*. per week under the National Insurance (Overlapping Benefits) Provisional Regulations: and what reply had been sent to the association.—Mr. JAMES GRIFFITHS replied: I have received a letter from the National Association about the application of the Overlapping Benefits regulations to tuberculosis patients in hospital and have passed it for consideration to the National Insurance Advisory Committee. The regulations, so far as they relate to patients in hospital, are still under consideration and I understand that the committee is prepared to receive further evidence bearing on this part of the regulations from responsible persons or bodies.

Public Health

Foods

BY the Transfer of Functions (Food and Drugs) Order, 1948, the Ministry of Food is now the central department concerned with the composition, description, and inspection of food, and with hygiene conditions in the food trades. The Ministry's responsibilities will be discharged by three divisions:

1. The food standards and labelling division, which is responsible for the promotion of food standards and exercises the central department's functions in relation to those sections of the food and Drugs Act dealing with the composition and description of food, the Defence (Sale of Food) Regulations, and the Labelling of Food Order. It handles all technical correspondence with chemists.

2. The food hygiene division, which is responsible for the promotion of measures to improve hygiene conditions in the food trades, and exercises the central department's function in relation to those sections of the Food and Drugs Act dealing with food inspection and hygiene.

3. The liaison division (food standards and food hygiene), which provides for the two other divisions a liaison with local authorities and with the public, other than manufacturers and traders. It deals with all inquiries from local authorities regarding day-to-day administration, including applications for the Minister's consent to prosecutions, public analysts' appointments and reports, and applications under sections 15 and 16 of the Food and Drugs Act, 1938. It is also responsible for liaison with local-authority associations and professional bodies.

The address of all three divisions is 47, Portman Square, London, W.1 (Tel.: Welbeck 5500).

FOOD STANDARDS COMMITTEE

The Ministry's food standards committee has appointed a subcommittee to consider the effect of ingestion of foods contaminated with minute traces of metal and other injurious elements, and the possibility of prescribing limits for such contamination. The committee itself is at present considering the possibility of prescribing standards for ice-cream, processed cheese, iodised salt, edible gelatin, and preserves.

CATERING-TRADE WORKING PARTY

Dr. Edith Summerskill, parliamentary secretary to the Ministry of Food, announced in the House of Commons last week the appointment of a working party to recommend precautions for securing cleanly conditions in the catering trade. The chairman is Sir William Savage, M.D., and members include Dr. W. A. Lethem (Ministry of Food), Dr. A. L. Shinnie (medical officer of health for Westminster), Dr. E. L. Sturdee (Ministry of Health), Dr. I. M. Sutherland (Department of Health for Scotland), and Dr. Robert Sutherland (medical adviser and secretary, Central Council for Health Education).

Obituary

STUART McDONALD

M.A. DURH., M.D. EDIN., F.R.C.P.E., F.R.S.E.

Dr. Stuart McDonald, emeritus professor of pathology in the University of Durham, died in Edinburgh on Nov. 15.

He was born at Castle Douglas, in the Stewartry of Kirkcudbright, and educated at Dumfries Academy, where he was one of a notable band of scholars which included Sir William Wright Smith and the late R. W. MacKenna of Liverpool. In 1896 McDonald graduated M.B. at Edinburgh, and after postgraduate study at Freiburg he was appointed lecturer in pathology and bacteriology at the Edinburgh Extramural School of Medicine. He was also for a time pathologist to the Birmingham General Hospital. In 1907 he was awarded the gold medal for his M.D. thesis.

He went to Newcastle as the first whole-time professor of pathology in the University of Durham, and almost at once he was appointed pathologist to the Royal Victoria Infirmary. This dual appointment gave him opportunities which he was quick to seize, and it was not long before he had built up a fine department. But the 1914–18 war interrupted this side of his work. Troubled times faced the Newcastle school, and in the reorganisation period he was translated to the deanship, whose duties seriously interfered with his more congenial activities. But as dean he was most helpful to each and every student, and many men have reason to be grateful for his advice. During these busy years he also took charge of wards in the 1st Northern General Hospital and proved himself a capable if rather critical clinician.

Prof. Grey Turner writes: "McDonald was imbued with the Edinburgh tradition and soon showed himself a most competent morbid anatomist and histologist so that his work was of great value to the clinicians. He also inherited a tradition of responsibility as a teacher and he took infinite pains to develop that side of the work. Always eager to help his juniors with their problems, in his early days at Newcastle he started the Pathological Club, which consisted of members of the staffs of the college and infirmary, of all brands, with a sprinkling of the keenest of the general practitioners. The result was a delightful body and the rather informal and friendly meetings, always held latish on in the evening, were distinguished by the enthusiasm and enjoyment of the members. Discussion was free and unhampered and often we sat late, but never too late for McDonald! In his experimental work on meningococcus infections in monkeys and in other problems he always insisted that we should get 'back to the soil,' for he had constantly in mind the reactions of the body to pathological invasions.

"He had many sorrows to bear. When most beset he found solace in music, and he often used to treat himself to gramophone recitals alone and with the lights out. Poetry also made a great appeal to him, and almost our last correspondence, only a few weeks ago, concerned the life story of Ada Smith, the Northumberland poetess, whose poem *In City Streets* he often quoted:

> 'My eyes an ache to see the brown burns flowing
> Through the peaty soil and tinkling heather-bells.'"

McDonald was one of the few remaining original members of the Pathological Society of Great Britain and Ireland. He was long a most faithful attender at the biennial meetings of the society, and in days when these meetings were smaller and more convivial no-one was more warmly welcomed, especially as a post-prandial raconteur.

"In earlier years," Prof. Matthew Stewart recalls, "he made some notable contributions to pathological science, two of the chief being those on subacute liver atrophy with Lindsay S. Milne and on malakoplakia of the bladder and kidneys with W. T. Sewell. I believe he was the first person to observe asbestos bodies in the lungs of an asbestos worker. I was present when the late W. E. Cooke showed McDonald the sections from his pioneer case—the second on record—of pulmonary fibrosis occurring in an asbestos worker. This case had already been reported in 1924 by Cooke, who had figured and described 'particles of mineral matter . . . of various shapes' and having sharp angles, in sections of the lungs; but while he had regarded this foreign material as 'asbestos particles' he had failed to notice the 'peculiar bodies' to which McDonald now drew his attention.

"Those of us who knew him well in the years gone by recall a friend whom it was always a delight to meet, and a pathologist with whom it was a pleasure as well as an illumination to discuss problems of common interest. Year by year McDonald returned to Galloway to fish for trout in, I think, the twin lochs of Bargatton and Glentoo in the parish of Balmaghie. On retirement from his chair, he went to live at Broughton, where he was able to continue his enjoyment of the contemplative man's recreation."

Mrs. McDonald died in 1921, and their only son, another Stuart McDonald, in 1946, within a year of his appointment to the St. Andrews chair of pathology.

Diary of the Week

NOV. 28 TO DEC. 4

Monday, 29th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. R. M. B. MacKenna: Dermatology in its Relation to General Medicine. (Part II.)

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Sir Cecil Wakeley: Pancreas and its Relations.
5 P.M. Dr. L. E. Glynn: Liver-function Tests.

Tuesday, 30th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. E. B. Strauss: Psychoneuroses and their Treatment.

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. Brian Schofield: Digestion.
5 P.M. Prof. J. Z. Young: Injury and Repair of Peripheral Nerves.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

BRITISH ASSOCIATION OF PHYSICAL MEDICINE
5.30 P.M. (Royal College of Surgeons.) Lord Horder, Dr. Francis Bach, Dr. F. S. Cooksey: Domiciliary Physiotherapy.

Wednesday, 1st

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Dr. Schofield: Digestion.
5 P.M. Professor Young: Injury and Repair of Peripheral Nerves.

UNIVERSITY COLLEGE, Gower Street, W.C.1
5.15 P.M. Dr. J. W. Trevan, F.R.S.: Statistics from the Standpoint of the Pharmacologist. (First of two lectures.)

Thursday, 2nd

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. W. E. Lloyd: Pleurisy and Pleural Effusions. (Part I.)

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. James Whillis: Hip-joint and its Movements.
5 P.M. Dr. R. G. Macfarlane: Hæmorrhagic States.

INSTITUTE OF NEUROLOGY, Queen Square, W.C.1
5 P.M. Dr. Raymond Garcin (Paris): Contractures.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. G. B. Dowling: Scleroderma.

CHADWICK LECTURE
4.30 P.M. (St. Mary's Hospital medical school, W.2.) Dr. Charles Secley: Preventive Medicine and Clinical Medicine in Relation to Public Health. (Malcolm Morris lecture.)

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. *Medical Group.* Mr. R. F. West, Mr. C. C. Redman: Medical Photography and the Publisher.

Friday, 3rd

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. W. H. Sheldon: Steatorrhœa in Childhood.

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. Whillis: Intrinsic Muscles of the Hand.
5 P.M. Dr. Macfarlane: Hæmorrhagic States.

MAIDA VALE HOSPITAL, W.9
5 P.M. Dr. H. E. Dimsdale: Case demonstration.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. R. A. Beaver: Anæsthesia for Thoracotomy.

Saturday, 4th

BIOCHEMICAL SOCIETY
11 A.M. (Middlesex Hospital, W.1.) Short papers.

Notes and News

N.H.S. FIGURES

FACTS and figures about the National Health Service were given by Mr. John Edwards, parliamentary secretary to the Ministry of Health, in opening the Public Health and Municipal Engineering Congress in London on Nov. 15. Despite the immensity of the administrative effort in getting the service ready to start on July 5, the Ministry of Health staff involved was, he said, little more than 800, including every clerk and typist. The work included setting up 138 executive councils, each with 25 members—a total of 3450, of whom 552 were appointed by the Minister himself. Existing hospital accommodation had to be surveyed to decide what premises and property were transferable; areas for the grouping of hospitals had to be defined; and the Ministry had to set up 14 regional hospital boards, with about 380 members, and 36 boards of governors of teaching hospitals with over 1000 members. In all, 2587 hospitals were taken over, with 388,000 staffed beds, and 236 hospitals, were disclaimed. On the mental-health side, 108 mental hospitals had to be designated; 130 public-health and public-assistance premises were also designated for use as mental hospitals; 218 institutions were "directed" to be used for mental defectives; and 190 premises were designated for use for emergency mental cases. Nearly 1200 schemes put forward by local health authorities for reorganising and extending their health services had to be examined, adjusted where necessary, and approved by the appointed day. Over 250,000 staff had to be transferred to the new bodies running the health service and brought into a coherent superannuation scheme, and terms and conditions of service had to be settled—temporarily at first. Finally the health scheme had to be explained to the public—by the household leaflet, by press advertising, and by posters and films.

Now coöperating in the service in England and Wales, Mr. Edwards said, are 18,165 general practitioners out of 21,000, 8519 dentists out of 10,000, 5000 ophthalmic opticians and dispensing opticians, and 14,000 chemists. There are over 40,000,000 people on doctors' lists. Prescriptions are being dispensed at the rate of over 140 million a year—about the rate expected. About 1,700,000 people have already had dental treatment and about 1,500,000 have been supplied with spectacles.

DENTAL ASSISTANTS

WHEN, in the middle of last century, dental education was concentrated in training schools, dental surgeons had to look elsewhere for the help they once had from pupils; and since then women assistants have been largely employed. They work as secretaries, receptionists, or chairside assistants, and sometimes as all three.

A joint committee, representing the various dental associations, has now reported [1] on the training and conditions of service of these assistants, and particularly of the chairside assistants. In 1946 these numbered some 6000 among the the 12,000 dental surgeons in private practice, with a further 1000 to the 1000 surgeons in the public service. Inquiry showed that hardly any of these assistants left their employment except to marry, and the average length of service was about five years. Thus there is little ground now for the glum pronouncement of the author who some years ago suggested that the assistant chosen should be "one old enough to have a serious view of her work, or one financially poor enough to value the opportunity." Among the chairside assistant's duties are: to attend on the patient; before the operation to lay out the appropriate instruments and dressings; during the operation to assist the surgeon and to prepare materials for fillings or impressions; and afterwards to clean and sterilise instruments and tidy the surgery. Usually a knowledge of general-anæsthetic apparatus is required, and in specialist practices there are further duties.

The committee suggests that ultimately every busy practitioner should employ one woman solely on chairside work; but it expresses itself completely opposed to any extension of the assistant's present range of work. Training, to begin after the 17th birthday, should, in the committee's view, last one year and consist of two parts, each of six months; the first half year would be spent at a training-centre and the second in paid employment. Moreover, "a reasonable efficiency in typing and some fundamental knowledge of bookkeeping is highly desirable. . . . A knowledge of first-aid and home nursing is also valuable." At the end of training the successful trainee should be awarded a standard certificate of proficiency; those already employed as assistants should be given the opportunity of gaining the certificate, either by attending a part-time course, or, if they have been doing this work for over three years, by taking the week's refresher course recommended for student assistants at the end of their year's training. The committee also suggests that the successful candidate should be permitted by regulation to call herself "dental nurse."

The report holds that no special general-educational certificate should be required of an entrant. It emphasises, however, that she should have had a good general education, and that she should conform to the description given by one of the witnesses who appeared before the committee: "Clean, alert, and neat in her dress; of pleasant countenance; healthy looking teeth; pleasant voice; ready smile; confidence of manner and having a ready wit." The recommended salary for certificated assistants ranges from £3 at the age of 18 up to 5 guineas at 25, with weighting for those employed in the London area and additions for specialist work. At present values this does not seem an extravagant reward for assistance without which "the efficiency of the dentist and his capacity for work are both seriously handicapped and the strain of practice is materially increased."

1. British Dental Association, Incorporated Dental Society, Public Dental Service Association: Report of the Committee of Inquiry into the Training, Wages, Conditions of Service, and Title of Women Assisting Dentists in Public or Private Dental Service. Obtainable, price 1s., from the secretary of the committee, 13, Hill Street, Berkeley Square, London, W.1.

FILMS FOR THE CITIZEN

MOST people grumble when it comes to paying the rates; few stop to think how much they get for their money. The Middlesex county council are effectively tackling this civic churlishness by showing informative films about the services which their ratepayers own. *Taken for Granted* describes the West Middlesex main sewerage scheme which for less than 2*d.* a head per week deals with all the waste effluents of nearly 1/2 million people. In *Good Health* we see something of the work of the hospitals which the county council have been able to hand over to the appropriate regional boards with pride and a little natural regret. A nurse and an almoner speak for their professions; appointments are honoured by doctors and outpatients with unwavering punctuality; and a mass-radiography unit rapidly surveys a queue of volunteers. The Metropolitan Water Board is responsible for a third film of this kind. *Every Drop to Drink* follows London's water-supply from its sources—the Thames, the Lea, and Sir Hugh Myddleton's elegant New River—to the familiar tap in the kitchen.

RESEARCH ON ARTIFICIAL LIMBS

IN a recent parliamentary reply attention was drawn to the work of the research unit at Roehampton, under the direction of the Standing Advisory Committee on Artificial Limbs, which has included the following practical results and improvements: (1) a number of new arm appliances have been added to the existing list and others are being redesigned and improved; (2) six trial orders for a new artificial arm of improved design have been placed, and should these prove satisfactory the arm will go into general production; (3) a new method of suspension of an artificial leg by suction socket is under trial by patients and the trials are most encouraging; (4) a socket of new design for above-knee amputation is under trial by over 100 patients; (5) two new mechanical hands have been submitted by the contractors to the Ministry of Pensions and are under trial; (6) an apparatus is under experimental test for measuring comparatively the thrust which walking imposes on both the artificial and the sound limb. Work is proceeding on the improvement of crutches.

A NEW HEARING-AID

THE first noticeable feature of the 'Monostat' hearing-aid is its outward elegance. The actual circuit and microphone are concealed, but the batteries are easily disclosed by a press-button weighted lid. It is driven by a special type of low-tension cell with a long life, costing about 1/2*d.* per hour of use. The high-tension battery, apparently of a standard size, costs 3*s.* and has a life with intermittent use of 350 hours. The running cost of this instrument is claimed to be lower than

that of any other instrument of comparable size. One novelty is automatic volume control, by which high magnification is possible without the shock of extra loud sudden noises such as the banging of a door; and intelligibility is greater than with "peak clipping," which cuts off all sound above a certain voltage and thus introduces serious distortion. The makers say that the instrument can be set for "combined maximum output and amplification control to the user's particular requirement and he need not touch it again all the time the instrument is in use. . . . The amplification is raised and lowered entirely automatically to cope with the different levels of sound. Even shouting right into the instrument does not make any difference." For this reason it marks some advance in the design of hearing-aids. Unfortunately, at an estimated price of 37 guineas, it is very expensive.

The aid is manufactured by Messrs. Multitone Electric Co. Ltd., 223, St. John Street, London, E.C.1.

University of Oxford

The honorary degree of D.SC. is to be conferred on Lieut.-General Sir William MacArthur.

University of Cambridge

On Nov. 13 the following degrees were conferred:

M.D.—J. N. Agate, H. W. Balme, Frances C. Naish, M. B. Paul.
M.B., B.Chir.—T. B. Anderson,* Ellen M. Bennett, W. T. C. Berry,* Kathryn H. Cohen, Brenda M. Eley, Phyllis M. Glasspole,* Ruth M. Lloyd-Thomas, I. K. R. McMillan, F. G. Patrick,* Hermione B. Roxburgh,* Betty J. Spedding, Margaret H. Whitby.

* By proxy.

University of London

Dr. E. R. Boland has been elected dean of the faculty of medicine for 1948 to 1950.

The title of reader in experimental pathology has been conferred on Dr. P. A. I. Gorer in respect of the post held by him at Guy's Hospital medical school.

At recent examinations the following were successful:

M.B., B.S.—Elizabeth Bennett, Paul Chadwick, K. M. Citron, Brian Creamer, A. A. Eley, H. J. A. Hahn, Cherry D. Heath, Joan E. Jermyn, G. D. Starte (with honours); M. S. M. Adams, Maureen B. Adams, C. P. T. Alexander, A. M. Angel, Marion M. Ashforth, R. N. H. Askham, D. S. G. M. Bailey, J. R. Ballantyne, T. W. Barnes, Barbara Baxter, S. J. Beales, M. D. Begley, Silvio Benaim, G. C. Blake, Hazel C. Blomfield, W. R. Bodenham, Edda L. I. Boesen, J. M. N. Boss, J. H. Boydell, Margaret L. M. Bridges, Ethel A. V. Brooks, P. D. Bryant, Rachit Buri, F. P. Cassidi, Ivor Chance, J. A. Cheese, D. W. Clark, P. S. Clarke, I. H. Colley, A. A. Collis, A. J. P. Crowden, Mary E. Curling, H. W. D. Davies, J. H. Davies, T. D. L. Davies, L. R. Davis, E. L. Dawe, D. C. Deuchar, Daphne M. Dowlen, E. M. Edwards, Evelyn S. Elliott, Hilary J. Elphick, D. M. Evans, Emrys Evans, D. C. Faull, K. J. Fisher, D. G. Fleck, C. A. Foster, P. B. Foxwell, Kenneth Froome, G. G. Garlick, Phyllis A. George, A. M. Goldthorpe, K. C. D. Gordon, D. B. Goss, R. L. Gothilf, E. W. Graham, A. H. Griffith, M. W. J. Grummitt, D. B. Gunasekara, June M. S. Harrington, D. F. N. Harrison, R. D. C. Hart, G. E. Haward, P. W. Head, J. L. Herbert, D. A. Hodgson, E. R. Hodgson Todd, H. D. A. Hope, Pamela C. B. Hopkins, D. A. Howell, F. H. D. Hutter, A. H. Jack, D. W. James, Barbara J. Jeffrey, F. H. W. Johnson, C. R. Jolly, D. H. Jones, E. F. Jones, J. S. Jones, Cyril Joseph, D. H. Judson, Gerald Kaufman, R. A. Keable Elliott, Zoë T. Kelly, Hari Ratan Ker, Mohammad Rafiqur Rahman Khan, F. R. S. Knight, Percy Lancer, B. H. Lawrence, J. C. S. Leverton, D. C. Lindley, R. H. Lougton, G. N. Lumb, Bernard Lytton, W. E. Macbean, R. P. C. MacDonald, Thomas McKendrick, David Mendel, R. L. Mendez, Leela Menon, Marie D. Merchant, D. K. Morgan, Elizabeth M. Mostyn, J. G. Neville, Margaret C. Newmark, P. B. O'Neill, M. W. Partington, Jacqueline I. C. Payne, G. W. Piper, D. G. Price, E. R. Price, K. J. P. Price, V. G. Radclyffe, George Selvaraja Ratnavale, Isidore Redstone, E. G. Rees, W. J. St. E. Rhys, B. W. Richards, H. R. C. Riches, Janet P. Rickard, P. P. Rickham, Douglas Rossdale, D. P. Rough, D. G. Rushton, M. V. Salmon, A. C. E. Sandiland, Benjamin Schwartz, M. L. J. Segall, J. C. Sherris, B. P. Skinner, J. F. Skone, G. B. Smith, D. B. Spanton, Diana H. Spears, Rosemary Stephens, Schler Sternberg, M. T. Sweetnam, Hilda Joan Tanner, D. G. Taylor, Thomas Taylor, Anita J. Thomas, O. G. Thomas, J. V. Thurston, P. H. Tribe, A. A. Turner, R. J. Vale, John Vance, P. R. Wagner, Daphne M. L. Walters, Mary B. Watson, F. E. Weale, Joan C. Wells, Margaret M. Whitaker, Horace Williams, W. J. Williams, M. B. Wingate, Mary I. Wray, John Zamler.

British Council Scholarships

Some 60 British Council scholarships out of a total of 359 awards for 1948–49 have been given to scholars studying medical subjects. These subjects cover the whole field of medicine as the following examples show: an Australian woman doctor is studying at the Institute of Child Health, London; a Brazilian doctor is taking a course in pædiatrics at Glasgow University; the Royal College of Nursing is arranging a programme in administration for a nurse from Guatemala; and two radiologists from Poland are studying, one at the Postgraduate Medical School of London, and the other at the Christie Hospital, Manchester.

Royal College of Surgeons of England

The honorary fellowship of the college has been conferred on Dr. E. D. Churchill, John Homans professor of surgery, Harvard University. The diploma was presented to Professor Churchill by Lord Webb-Johnson, president of the college, after the Buckston Browne dinner of fellows and members on Nov. 11.

Pay Beds in Liverpool Region

The Liverpool regional hospital board have recommended to the Minister of Health that, under section 4 of the National Health Service Act, 147 beds in their region should be reserved for patients who wish to pay a small extra charge for amenities, and that, under section 5, 252 beds should be reserved for patients who agree to pay the full cost of maintenance. The board have further recommended to the Minister that the charge for beds set aside under section 5 should be reduced by the average cost per patient in an open ward. The board are also making representation to the Minister for the equalisation of charges for pay-bed accommodation throughout the region.

Blood Donors

More donors gave blood to the National Blood Transfusion Service during the June quarter of this year than at any time since the war. They numbered 98,055, including 24,075 new donors. In the same period 30,497 people joined the service—the highest number since March, 1947—bringing the total strength to 377,304 for England and Wales. During the quarter 77,148 bottles of blood were issued—a rise of some 21,000 over the same quarter of last year, and of 31,000 compared with the same quarter of 1946. Of dried plasma 15,849 bottles were issued, compared with 14,959 in the corresponding quarter of 1947, and 13,906 in the corresponding quarter of 1946. It is estimated that another 142,000 donors are needed in England and Wales.

Sir Arnold Stott has been appointed an extra physician to the King's Household.

Dr. D. R. Lewis has been nominated a sheriff for Brecon-shire in the King's Bench division of the High Court of Justice.

Dr. C. H. Andrewes, F.R.S., has left for Hungary, where he is lecturing on behalf of the British Council.

On Nov. 10 Dr. J. Trueta was presented with the prix Labourie by the Académié de Chirurgie de Paris for his contribution to the progress of surgery. He later addressed the assembly on the renal circulation and its pathology, with particular reference to the research which he and his colleagues carried out at the Nuffield Institute, Oxford.

CORRIGENDUM: *Myanesin in Tetanus.*—In the article last week by Dr. Edwards and Dr. Wood, the 4th and 5th lines of the section on treatment (p. 807) should read: "so myanesin, 1 g. in 10 ml., was diluted with an equal quantity of water . . ."

Births, Marriages, and Deaths

BIRTHS

BRENAN.—On Nov. 14, at Cosham, Hants, the wife of Dr. A. H. W. Brenan—a daughter.
CARR.—On Nov. 18, in London, the wife of Dr. R. U. Carr, M.B.E.—a daughter.
FELTON.—On Nov. 17, at Preston, the wife of Dr. W. F. Felton—a daughter.
GARROW.—On Nov. 13, at Southsea, the wife of Dr. D. H. Garrow—a daughter.
LESLIE-SPINKS.—On Nov. 18, in London, the wife of Lieut.-Colonel A. J. Leslie-Spinks, R.A.M.C.—a son.
RENDLE-SHORT.—On Nov. 12, the wife of Dr. John Rendle-Short—a daughter.
SQUIRE.—On Nov. 13, at Oxford, the wife of Mr. C. M. Squire, F.R.C.S.—a daughter.
THOMSON.—On Nov. 15, at Bournemouth, the wife of Dr. R. W. Thomson—a son.
TROWER.—On Nov. 15, the wife of Dr. G. S. Trower—a son.

DEATHS

CROSS.—On Nov. 17, at St. Neots, Hunts, Edward John Cross, T.D., M.D. Durh., D.P.H., aged 83.
PICTON.—On Nov. 19, at Holmes Chapel, Derbyshire, Lionel James Picton, O.B.E., M.A., B.M. Oxfd, aged 74.
ROZELAAR.—On Nov. 21, in London, Abraham Levie Rozelaar, M.R.C.S.
VINCENT.—On Nov. 12, at Reigate, Herbert Edmund Vincent, M.D. Lond., aged 84.

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CONTENTS

SCIENTIFIC CONSTRUCTION OF THE NORMAL CHILD'S DIET *

ALAN BROWN
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PROFESSOR OF PÆDIATRICS IN THE UNIVERSITY OF TORONTO

IT is our belief, and I speak for the department of pædiatrics of the University of Toronto, that the proper supervision of the child's nutrition is one of the most effective means of maintaining good health. It should not be assumed that we neglect other factors such as the supervision of hours of sleep, the amount of exercise, fresh air, and sunshine obtained, and the treatment of foci of infection; but of all the means at the disposal of the present-day physician interested in preventive pædiatrics none gives greater health dividends than the proper supervision of the child's nutritional requirements.

Ebbs, of our department, has recently shown that the progress of an infant during its first six months of life is greatly affected by the mother's diet during the prenatal period (Ebbs et al. 1942). In this extensive study, which was carried on in collaboration with the department of obstetrics, the prospective mothers were interviewed three or four months before term. They were instructed to keep an accurate record of all the food they ate for a week. This was carefully checked by a dietitian, and on the basis of these records the women were divided into two groups—those on poor diets and those on good. Half of the mothers on the poor diets were provided with the following supplementary foods per day: 30 oz. of milk; 1 oz. of cheese; 1 egg; 1 orange; 4½ oz. of tinned tomatoes; 2 tablespoonfuls of a special preparation of wheat germ which contained added iron (about 6 mg. per tablespoonful); and a capsule containing 2000 I.U. of vitamin D in the form of viosterol. Capsules containing plain corn oil were given to the mothers remaining on the poor diet, to reduce any psychological effect. The mothers given the supplementary food developed much fewer and less severe complications during the prenatal period, labour, and the succeeding six weeks than those remaining on their usual poor diet; 86% of the mothers given the supplementary food were nursing their infants six weeks post partum, whereas only 59% of the mothers on the poor diet were doing so.

The comparison of the records of the infants during the first six months of life is equally impressive. The babies born of the mothers eating the poor diet showed a much higher incidence of respiratory infections (colds, bronchitis, and pneumonia), rickets, tetany, dystrophy, and anæmia. The provision of an adequate food-supply for the child even before birth is therefore very important. Stuart and his collaborators, in Boston, have also reported that the prenatal course of the mother and the condition of the infant at birth reflect the type of diet eaten during pregnancy (Burke et al. 1943).

Despite the great advances made in the artificial feeding of infants I am still convinced that breast-milk produced by a healthy mother is the best of all feedings. The general public do not seem to be fully aware of this fact, and we physicians should bear some of the blame for this state of affairs. The part that excellent prenatal diets play in the establishment and maintenance of successful lactation has been emphasised by Ebbs et al. (1942). The Ministry of Food has been well aware of this fact, as is evident from the increased rations allotted to pregnant women. Regular adequate care of the nipples during the latter half of pregnancy is also important. During lactation the mother's needs are even higher than during pregnancy. If you glance through the recommended daily allowances drawn up by the Food and Nutrition Board of the National Research Council in the United States (1945) you will note that in every essential, except calories, the lactating woman's allowances are higher than at any other period in her life.

Another aid to successful lactation that is often neglected is the provision of nurses skilled in handling the "nursing couple" during the first two weeks or so after the infant's birth. Waller (1938) and Middlemore (1941), here in England, have done outstanding pioneering work in this field, as have also the Maternal and Child Health Services in New Zealand. Certainly on our continent we have not applied this knowledge, and as a result many infants are denied the physical and psychological advantages of breast-feeding. By all means we should see that there are enough specially trained nurses in our obstetrical wards, so that every mother will receive the necessary help in the early stages of lactation. Evidence is also accumulating that the giving of supplementary milk feeds during the first few days lessens the mother's chance of establishing adequate lactation. The use of dilute lactose water is preferable, at least until it is evident that the maternal milk-supply is inadequate. The advantages of having the baby with the mother has also been investigated (Jackson 1946). In this case it is usual to restrict visitors to one member of the family to save the newborn from the risk of infection, and to provide means for the mother to wash and disinfect her hands before handling the baby. A normal mother can undertake a good deal of the care of the baby from the second day on, and having her infant in close proximity seems, in most cases where the mother wishes it, to be helpful to her. Here in Great Britain, I believe you have kept up this practice in many of your hospitals. Allowing the infant to nurse when it is hungry, even though this may entail frequent feeds in the first few weeks, stimulates lactation.

The self-demand schedules in breast-feeding are an interesting development (Gesell and Ilg 1937). At a relatively early age the infant usually settles down to a fairly regular schedule, and in most cases the number of feeds is reduced automatically earlier than when the usual schedule is followed. The increased freedom that the mother has in the management of her child produces a less tense mother and a more contented baby. This type of régime is well worth looking into and may provide a means for increasing the incidence of breast-feeding. At any rate the days of rigid schedules are past. Nowadays, when a normal breast-fed infant wakes an hour or so before his feeding-time, the nursing mother is advised to feed him right away rather than leave him to exhaust himself by crying. Conversely, if he oversleeps his feeding, the mother is no longer advised to wake him. However, a complete self-demand schedule is a great deal more difficult to follow in the case of the artificially fed infant and, for the present, this system probably should be undertaken only by intelligent mothers anxious to adopt it.

HUNGER AND COLIC

One of the most frequent diagnostic mistakes regarding the nutrition of the newborn infant is the error of confounding colic with hunger—newborn infants suffer nowadays not from overfeeding with breast-milk but from lack of it. For every case of overfeeding we probably see 99 cases of so-called hunger colic. Practically all young mothers, overtaxing their strength in their eagerness to be up and about after their long confinement, harried by tales told by old maids and barren women and by conflicting advice of well-meaning neighbours,

* An Ingleby lecture delivered at the University of Birmingham on May 18, 1948.

secretly afraid of her new baby, and frightened that he is going to die at every squirm and grunt and yawn, run short of milk toward the end of the day.

Milk production is milk production, whether in woman or in the lower animals. A Jersey cow, if frightened or teased about her calf, will give perhaps a quart of milk at the next milking instead of the expected one or two gallons. Even a hog or a dog that drives her from the pasture, or a strange milker, will affect the quantity of her milk. A woman is much more susceptible to nervous reactions. Milk production in all our minds is associated with green meadows, still nature, and kind-faced old cows standing in quiet streams (not listening to a hockey game or a prize fight over the radio). A modern educated woman is not a kind-faced stolid milk-machine, and so she always at some time or other runs short of milk. And the baby cries. And when the baby cries his stomach hurts him. Have you ever thought how the whole world is obsessed with the idea that every time a baby cries his stomach hurts him? The pædiatrist has added ears to the list of places which can hurt a baby; but, when the ears are examined and found normal, then he too usually says the baby's stomach hurts him. So night after night, when the tired worried mother runs short of milk, the baby cries. He cries, he screams, he gets red in the face and doubles up; he kicks and straightens out, and rears back in a perfect paroxysm of "rage"; he gnaws at his fist and his mother's face; he tries with every way he knows to show he is hungry, but still he has the stomach-ache. Finally, when he is comfortably full of hot water or medicaments he goes to sleep, and he awakens the next morning as if nothing had happened. But the next evening, late, when the tired family wants to go to bed, he "pulls another party." He is a smart-looking baby, he holds his head up well, and his back seems strong. He is preternaturally bright, and the neighbours all say they never saw such an intelligent-looking little baby. He is a light sleeper, and the whole family has to be quiet to keep from waking him. Occasionally a young father, untrammelled by old women's tales, will have a lucid idea and say "If that were a puppy, I'd say he was hungry and feed it." And there is no better appeal to their understanding than the illustration of the hungry puppy. The signs of hunger in other animals are usually recognised, because they are not hedged about with a mass of superstition and empirical nonsense. The hungry puppy is wakeful. He wakes with the slightest scrape of the foot on the floor. He gets up every few minutes and hunts for a softer place to lie. He is the smart dog who handles himself well, and, in begging for food, is all a-wiggle as if his muscles were of rubber. He is preternaturally smart and bright. Usually he is the runt who is crowded away from the breast by the stronger puppies, and because he appears smarter he is considered the pick of the litter. The full puppy is lazy, stupid, and relaxed.

The full baby is a stupid little animal. One who is easily waked, who is especially smart and intelligent-looking, one who handles himself too well for his age, is a hungry baby. You can walk into the nursery take one look at such a baby, and diagnose the cause for your visit just as you can stand at the foot of the bed and see rapid respirations with a flushed face and an expiratory grunt and know the baby has pneumonia.

RICKETS

Rickets and scurvy are now extremely rare in the Hospital for Sick Children in Toronto. In 1947, when we had 11,748 admissions to the hospital and 63,741 attendances at the outpatient department, only 5 cases of rickets and 5 of scurvy were diagnosed. I presume that clinical rickets is now very rare in Britain also. The provision of cheap or, if need be, free fish-liver oil by the Ministry of Food has no doubt helped in this achievement. We believe that a fish-liver-oil preparation which meets the infant's needs for vitamin A as well as for vitamin D is superior to a preparation containing vitamin D only (Robertson 1945). Also we recommend that the fish-liver oil be started when the infant is about 2 weeks old. The concentrated fish-liver oils, in which the dose is measured by drops, are easier for the mother to administer, since they may be dropped directly into the side of the infant's mouth. In Canada this type of medication is usually discontinued during July and August, and the mother is instructed to give the infant daily sun-baths of gradually increasing length so that his body becomes completely tanned. The administration of concentrated oils can be begun again in the autumn without any difficulty. These oils should not be given on a dry spoon or put in the feeds, because they adhere to the spoon or the feeding-bottle and the child does not receive the prescribed dose. If regular cod-liver oil is used, it is customary with us to prescribe half a drachm at the age of 2 weeks. A few weeks later this is increased to a drachm daily. Later on it is increased to two doses of a drachm daily. Since it is often difficult to restart cod-liver oil after it has been discontinued, it is preferable to continue administering it daily until the beginning of the infant's second summer.

As mentioned above, it is much more difficult for the mother to give the larger doses of cod-liver oil to the infant. This was very evident in a study made by several members of our staff (Drake et al. 1934) in which 500 healthy infants living at home were examined for rickets, both clinically and by X rays, at intervals during the five winter months. The infants were divided into several groups, and each group was given a different source of vitamin D. Despite the fact that two exceedingly competent nurses, trained in public-health work, each visited the mothers at least once a month, and the babies were examined by a physician once and sometimes twice a month, three infants who were supposed to be receiving 2 and 3 teaspoonfuls daily of biologically tested cod-liver oil developed moderate and well-marked rickets. Certainly greater care was taken to see that these infants received the prescribed amounts of cod-liver oil than would be the case in ordinary medical practice, but nevertheless the infants were apparently not getting it. Incidentally the nurses inspected the bottles of oil to check the consumption. Of the infants receiving cod-liver oil, 8% had to be dropped from the study because it was given very irregularly. In contrast to this, only 2% of those given a concentrated preparation were discarded for the same reason. In this same study the antirachitic effect of irradiated milk was also assessed. None of the 92 babies receiving it developed moderate or well-marked rickets. Two of them showed mild rickets, which was diagnosed by X rays. Therefore it seems advisable to prescribe irradiated evaporated milk rather than the non-irradiated type, when this kind of formula is desired. In addition, another source of vitamin D should be prescribed.

Rickets was formerly considered to be a disease of infancy. The report of Follis et al. (1943), of Johns Hopkins Hospital, shows that it occurs in older children also. These investigators found in a series of 230 consecutive necropsies, performed on children aged 2–14 years who had died from various acute and chronic diseases, that 46·5% of them showed microscopical evidence of rickets in the middle ribs which could not be diagnosed clinically. Since moderate and severe rickets was found in many of the children who died of acute disease, these workers state that it is valid to infer that up to the age of 14 years "rickets is of frequent occurrence in healthy appearing children." Though they suggest that their work should be repeated by other clinics, there is absolutely no reason to doubt the accuracy of their findings, and as a matter of fact they have been confirmed here

in Birmingham, where histological evidence of rickets in the same age-group has been found in 37·8% of the children examined (Parsons 1947).

DENTAL CARIES

Several investigators, including Lady Mellanby (1934), working in Great Britain, and Agnew and his colleagues working in our department (Anderson et al. 1934), had previously shown that the addition of vitamin D decreased the incidence of dental caries. In the latter study two groups of children, aged 5–15 years, were observed for a year. The diets for both groups were exactly the same, except that one group received additional vitamin D daily. Radiograms were taken and instrumental examinations of the teeth were made without any knowledge of which group the children belonged. When the examinations were completed the results were tabulated, and it was found that the number of markedly progressive cavities and the number of new cavities were twice as frequent in the children aged 5–10 years who did not receive an adequate supply of vitamin D as in those who did. Therefore, to prevent rachitic changes in the bones and to reduce the amount of dental caries, it is wise to continue the daily administration of a good source of vitamin D, such as fish-liver oil, during the eight or nine colder months of the year throughout the whole of the growing period. The daily dose should be about 400 I.U.

INFANTILE SCURVY

Infantile scurvy is probably as rare in Great Britain as it is in Canada. Here again we admire the resourcefulness and energy with which the Ministry of Food, with the assistance of many private citizens, provided vitamin C in suitable forms for your infants during the late war.

A great number of food samples have been assayed for vitamin C in our nutritional laboratories (Johnstone et al. 1946, Truscott et al. 1946). For example, orange juice obtained from the oranges bought by the hospital was assayed weekly for a year, and the figures were averaged. The average amount of vitamin C in orange juice was found to be three times that found in tomato juice. Therefore orange juice is the preferable antiscorbutic for the infant. Some years ago Snelling and Jackson (1939), of our research staff, reported that the plasma vitamin-C levels of infants under the age of 3 months not receiving any additional vitamin C were very low. Though frank scurvy is not seen until the age of about 6 months it develops slowly, and we believe that such low levels of vitamin C in the blood are unphysiological. Therefore small doses of orange juice should be started when the infant is about 3 weeks old. The amount is increased gradually so that by the age of 3 months the infant is receiving 2 oz. of orange juice daily, diluted with half as much boiled water. More of the vitamin is retained if it is given in divided doses. The same procedure is recommended for breast-fed infants.

Tests in our clinic have shown that ascorbic acid given in the form of orange juice is much more effective than synthetic ascorbic acid in the treatment of infantile scurvy. This is thought to be due to the presence of other factors, one of which has an antihæmorrhagic effect, in the orange juice. It has also been found that synthetic ascorbic acid has not so favourable an effect on the repair of scorbutic changes in guineapig's teeth as has orange juice. Vitamin C is very soluble in water, and if a diet very low in this vitamin is eaten, the body is rapidly depleted of it.

It is generally accepted that as small an amount as 5–7 mg. of vitamin C will prevent the development of scurvy, but at least from 4 to 6 times these amounts are recommended for optimal growth and health. In fact, a considerable body of evidence indicates that even higher amounts are preferable. The following study in which several members of our staff (Linghorne et al. 1946) took part supports this last statement.

A group of otherwise healthy Air-Force ground-crew men with mild or moderate gingivitis were given local treatment which cleared up or markedly reduced the condition. They were then placed in four groups and kept on constant daily intakes of vitamin C. One group received 10 mg. a day, the second 25 mg., and the third and fourth 75–80 mg. Except in the third group the vitamin C was obtained from foods. These diets were eaten for eight months. The men receiving 75–80 mg. a day showed definitely less recurrence of the gingivitis than did those receiving 10–25 mg. a day. In addition to carefully examining and recording the condition of the gums at monthly intervals, the plasma-vitamin C level was also determined and vitamin-C assays on about 25% of all the food served were carried out with due care.

Frequent food analyses have shown that relatively few common Canadian foods contain high or even moderate amounts of vitamin C. These superior foods include citrus fruits, raw or canned; the cabbage family; turnips; potatoes; and tomatoes. Immediately after harvesting, potatoes were found to contain 20–30 mg. of vitamin C per 100 g. Two months later the amount had dropped to 15–20 mg. per 100 g., and from then on it gradually decreased to about 10 mg. per 100 g. Tests on the effect of cooking showed that the use of the minimum of boiling water, the shortest period of cooking consistent with maximal palatability, and the avoidance of mashing or keeping warm after cooking minimised the loss of this vitamin. Leaving the skins on while cooking the vegetable was an advantage, as was also the reduction of cutting by boiling the vegetable in wedges instead of in shreds. Most of the loss was due to the leaching out of the vitamins into the cooking-water.

Raw cabbage and the other members of the cabbage family are very rich in vitamin C, providing 60 mg. in $3^1/_2$ oz.—i.e., in about one cupful. Strawberries, raspberries, currants, and cantaloups are also good sources of this vitamin. Unfortunately apples, pears, peaches, plums, and grapes are low in vitamin-C content. Many palatable Canadian diets were found to contain less than 5–7 mg. of vitamin C a day (Truscott et al. 1946).

VITAMIN-B COMPLEX

We have never observed specific symptoms, in an infant or child, that could be ascribed to deficiency of any member of the vitamin-B complex. However, in experiments on animals subnormal weight gains precede the development of specific deficiency symptoms. It may be that some of the poor weight gains that are seen during infancy are due to an insufficiency of these factors. Five of the B vitamins have been demonstrated to be essential for man: thiamine, riboflavine, nicotinic acid or nicotinamide, pyridoxine, and choline. Probably the other identified members of the B complex will eventually prove to be essential also, and it is likely that there are other such factors which have so far eluded discovery. Therefore, when you wish to administer the vitamin-B complex, it should be given in some form that contains not only the known members but also the unknown ones.

Another problem undertaken by our laboratory was that of developing a cereal mixture suitable for use in infancy and containing an abundance of the B vitamins and iron but not having the undesirable laxative effect of the usual whole-grain cereals. A mixture of farina, oatmeal, and cornmeal, with added wheat germ, dried brewer's yeast, dried alfalfa meal, and bone meal, was devised which met these requirements (Tisdall et al. 1930). Tests carried out on infants showed that it was well tolerated by them even at the age of 4 weeks (Monypenny 1940). Other tests (Snelling 1938) showed that, when fed from the age of 3 months on, it prevented

the development of the low hæmoglobin levels that Parsons (1936), in Birmingham, and Mackay and Goodfellow (1931), in London, have shown to be the rule in normal infants aged 3–6 months. In addition, when it was substituted for the usual cereals and breadstuffs in the diets of children of school age, who were living in an institution where the meals were similar to those eaten by low-income families, it led to improved growth. This increase in growth was shown to be only partially due to additional B vitamins present in the cereal. Parallel with the improved growth was an improvement in the hæmoglobin level.

During infancy, when solid foods are being introduced, it is important to add these foods in small quantities and one at a time. The amounts should be kept small until the child has learnt to accept the new food. If he objects violently to the new food, another similar food should be substituted. After a short period the rejected food, preferably prepared in a somewhat different manner, should be offered again. Coaxing, bribing, and forcible feeding should never be tried, since these methods usually lead to the development of feeding problems, though occasionally in an acquiescent child the last method may lead to obesity and eventually to serious emotional problems.

Owing to the introduction of long-extraction flour here in Great Britain during the past war, your citizens are no doubt eating considerably more thiamine than is the average Canadian. If these restrictions are lifted and the demand for white bread again arises, you will face the same problem that we are now facing. The Americans are meeting this difficulty by adding synthetic thiamine, riboflavine, nicotinic acid, and iron to their white flour. This method is not beyond criticism, for some investigators feel that the addition of only three of the B vitamins, rather than all of them, is an unphysiological procedure. During the war a new type of white flour, described as "Canada-approved vitamin-B white flour" was evolved as the result of a coöperative effort between our nutritional research laboratory, the Dominion Department of Agriculture, and some of the milling companies (Tisdall et al. 1941). By making minor changes in the milling techniques much more of the germ and the scutellum round it and some of the bran were incorporated in the flour. The resultant white flour was equivalent to whole-wheat flour in its thiamine content, though it was less well supplied with riboflavine and iron. Since milk is the main source of riboflavine in a well-chosen diet, and since there are many other foods that provide iron, these relative lacks in the new flour were felt to be of no serious consequence. Unfortunately the millers and bakers did not support this innovation wholeheartedly, partly because of their preference for the fortification method in practice in the United States. Consequently this type of flour is not generally available in Canada at present, but its use seems to be based on better physiological and economic principles than is the use of partially fortified white flour.

Cereals or porridges can also add appreciable amounts of thiamine to the diet, and some years ago the thiamine content of the common Canadian cereals were determined in our laboratory (Jackson and Malone 1943). It was found that the best and cheapest cereal was rolled oats, which provided 0·18 mg. of thiamine per oz., which is a generous serving. A fine granular wheat cereal containing wheat germ, or rolled or cracked wheat, was nearly as rich in thiamine (0·15–0·12 mg. per oz.). In contrast to this the fine white granular wheat cereal made exclusively from the endosperm, which we call farina, contained only a sixth as much thiamine as the rolled oats. It was also found that even protracted cooking of the porridge did not reduce its thiamine content.

The pre-cooked cereals, which unfortunately are commonly used in Canada, were also assayed. The best of these were the shredded-wheat products and the bran flakes, but they only contained about a third as much thiamine as rolled oats. Corn flakes, the puffed cereals, and the ready-to-eat cereals made from rice were entirely devoid of thiamine. Besides being poor nutritionally all these pre-cooked cereals cost from three to seven times as much per serving as rolled oats.

You would be wise to urge your patients to take one serving of a whole-grain cereal daily and, if possible, liver once a week. Other foods containing whole-wheat flour should be recommended also. It is an excellent plan to incorporate at least a tablespoonful of wheat germ in the daily diet. This can be added to cooked cereals, or in amounts of 25% to flour which is to be made into muffins, tea biscuits, &c. When wheat germ is cooked in this way, some 20% of the thiamine is destroyed, but even after that loss a great deal still remains. A tablespoonful of wheat germ contains about 0·3 mg. of thiamine, which is almost a quarter of the recommended daily amount of this vitamin for a child of 12 years.

Thiamine plays many rôles in the body. It is necessary for normal growth, though it is not unique in this respect. When diets low in this vitamin are eaten, anorexia and intestinal hypotonia often develop. It has also been shown that on such diets the body is unable to metabolise carbohydrates completely. Instead of being broken down to carbon dioxide and water, the carbohydrates stop at the pyruvic-acid stage. There is evidence that this accumulation of pyruvic acid is harmful, and it is plain that under such conditions the body is wasting some of its food. Several investigators have demonstrated clearly that people living on low-thiamine diets lack physical energy, are quickly fatigued, and suffer from mental depression and apathy.

Children should not be allowed to sprinkle sugar on their breakfast cereal or porridge. Sugar has a high satiety value and takes the edge off the appetite. It is our poorest food, since its only constituent is carbohydrate. Often, when the porridge is generously "sugared," the child refuses the latter part of his breakfast, which is much superior to the sugar in food value.

Milk is a particularly valuable source of riboflavine. In fact unless a pint of milk is taken daily it is very difficult to meet our needs for this factor. This vitamin is readily destroyed by light; therefore bottles of milk should not be kept in a light place.

VITAMIN A

We very seldom encounter evidence in Toronto of a deficiency of vitamin A. In the Hospital for Sick Children during the last 21 years we have had only 3 cases of xerophthalmia. None of these patients was receiving whole-milk dilutions or whole milk. This is what would be expected when one considers the wide and abundant distribution of vitamin A. It is present in the fat of dairy products, liver, kidney, and egg, and its precursor, carotene, is present in outstandingly large amounts in coloured vegetables and fruits.

Actually we can change only about 40% of the carotene that we ingest into vitamin A, but the green and orange vegetables are so rich in this substance that they usually constitute the major source of our vitamin A. As a general rule the more orange or green the vegetable, the more vitamin-A value it has. Carotene is a bright orange substance, but in the green vegetables this colour is masked by the intensely green chlorophyll. It is recommended that two vegetables besides potatoes be eaten daily. The raw and coloured ones are especially valuable.

CALCIUM

Milk provides about 80% of the child's intake of calcium. We are convinced that pasteurisation is necessary

to render this extremely valuable food safe. In support of this claim we can state that we have not had a single case of milk-borne infection (including bovine tuberculosis) since 1915 in a child who had lived in the City of Toronto and used no milk that has not been pasteurised (Brown 1943). In the preschool child, who normally grows slowly, a pint of milk a day is usually all that can be given with advantage as a beverage. If the mother allows such a child to drink a pint and a half of milk, he is often unable to eat sufficient amounts of the other essential foods. Cooking the milk does not materially reduce its food value, but it has the advantage, especially for these younger children, of evaporating some of the water and thus rendering it less bulky. High-fat milks, such as Jersey milk, often are not well tolerated by children and lead to digestive upsets. Their use is therefore unwise. The advantages of using evaporated half-skimmed milk in formulas for newborn and older infants was investigated by Snelling (1943), of our department. This type of feeding was found to give superior results in many of these infants. The lesser amounts of vitamin A present in this partially skimmed milk are of no consequence if the infant is being given fish-liver oil. It is generally believed that children under the age of 12 years retain the maximum of calcium if their intake is about 1 g. a day. This is provided by one and a half pints of milk (30 oz.). It seems likely that the rapidly growing older child should receive about 1·5 g. of calcium a day. Many of these children do not take that much, partly because of the appeal of the ubiquitous soft drink, and partly because of the girls' fear of becoming fat. Our teen-age girls are often short of calcium.

The availability of calcium in spinach has been the subject of two investigations in our laboratory (Tisdall et al. 1937, 1938), and in both of these tests, which were carried out on rats, it was found that, when large amounts of spinach were fed, the retention of calcium was much decreased. This effect is probably due in part to the oxalic-acid content of the spinach. It is well known that calcium oxalate is insoluble. Other investigators (Sherman 1947) have reported similar results. Therefore it is not wise to use spinach frequently in the diets of children, since their calcium requirements are high. Beet tops and chards are also unsuitable. The following greens, which belong to other botanical families are preferable: broccoli, loose-leaf cabbage, collards, dandelion greens, kale, mustard greens, turnip tops, watercress, and loose-leaf lettuce.

DEFICIENCY OF IODINE

In many areas, in both Canada and Great Britain, there is extremely little iodine in either the soil or the water. Consequently the diets of people living in these areas contain very little iodine. Children and pregnant and nursing women living in such areas, especially where the calcium content of the water is high, are prone to colloid goitre. To prevent this deficiency we recommend the use of iodised salt, and experts in this field assure us that no untoward effects follow its use. In other words, the amount of iodine taken in the salt is not sufficient to cause an increase in the symptoms even of a patient who already has a toxic goitre. In 1947 a bill was introduced in the United States House of Representatives designed to make the iodisation of table salt compulsory. On our continent sea foods are not used generously or universally and therefore they do not provide a reliable supply of iodine.

CONCLUSIONS

We have obtained no evidence that the average Canadian child receiving a diet at all reasonable suffers from a lack of protein. It is usually considered that 15% of the calories supplied should be in the form of protein, and 50% of this protein requirement should be grade-A protein—i.e., protein obtained from such foods as milk, meat, fish, eggs, and cheese. The requirement of grade-A protein will almost be fulfilled if the child receives 30 oz. of milk daily.

If the child receives 30 oz. of milk daily containing 3·5–4% fat, along with 1 oz. of butter, his fat requirements for normal nutrition will be fulfilled.

We have never found any evidence of a child receiving a diet containing too small a percentage of carbohydrate. The ease with which we obtain purified carbohydrates in the form of sugars and flours explains this. In fact the greatest error which we find today is an excess of purified carbohydrates. In some Canadian diets 30–50% of the calories are in the form of purified flours and sugars, which as a result of their purification are deficient in most of the minerals and vitamins.

It is recommended, whenever possible, that for normal children the daily diet should contain:

(1) About 30 oz. of milk.

(2) One, or preferably two, generous servings of a food rich in vitamin C—e.g., orange or grapefruit or their canned juices, tomato juice, or raw cabbage—and two vegetables besides potato, including coloured or raw vegetables.

(3) One serving of a whole-grain cereal or porridge, preferably with wheat germ added. Only whole-wheat or vitamin-rich white bread should be used.

(4) One serving or more of meat, fish, egg, or fowl; eggs three or four times a week or oftener; liver or kidney once a week.

(5) Iodised salt (this should be used exclusively).

(6) One regular dose of a good source of vitamin D during at least the six colder months of the year.

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SURGERY OF PORTAL HYPERTENSION

AN ACCOUNT OF 16 CASES

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THIS paper records our experience of 16 patients subjected to operation in the hope of relieving the symptoms of portal hypertension, either by constructing venous shunts, or, when the portal obstruction was limited to the splenic vein, by splenectomy alone. Before 1945, isolated attempts had been made by different surgeons to fashion in man communications between portal and systemic veins, usually on the principle of the Eck fistula often used in animals in the study of the metabolism of the liver; but the techniques available were unsuitable and consistently unsuccessful. In 1945, the work of Blakemore and Lord [1] provided a promising method of anastomosing veins and led to a renewal of interest in the surgical treatment of portal hypertension.

The patients included in our series were referred to the wards of one of us (J. R. L.) because of hæmatemesis, ascites, or both; they are conveniently classified as follows:

	No. of cases
Group I: lienorenal venous anastomosis ..	9
Group II: splenectomy (lienorenal venous anastomosis judged impossible)	3
Group III: laparotomy only	1
Group IV: splenectomy for splenic thrombosis	3

GROUP I: LIENORENAL VENOUS ANASTOMOSIS

In each of the 9 cases in which the splenic and renal veins were anastomosed some degree of hepatic cirrhosis was present. In 3 hæmatemesis was the only symptom; in 3 ascites had been present at the beginning of the illness but was absent or minimal when hæmatemesis occurred; and in the remaining 3 both ascites and hæmatemesis were present. One patient has only recently been operated on and is not included in the discussion; 2 died after operation; during the meeting of the Association of Surgeons in Edinburgh in May of this year it was possible to review the remaining 6 cases after postoperative periods ranging from four to twenty-three months, and to present them to our visitors. Though the longest interval is much too short for any estimate of ultimate prognosis, in none of the 6 had hæmatemesis recurred, though before operation copious and repeated hæmatemesis had occurred in 4, and during the week or so before operation 2 patients had had three and two almost fatal hæmorrhages. Moreover, we were much impressed by the improvement in the general condition of these patients: all had returned to full work, sometimes laborious; all had put on weight (in one case 20 lb. in eighteen months); and all felt and looked well. This general improvement was the more remarkable when it had taken place in patients who had shown unmistakable evidence of disturbance of hepatic function before operation, confirmed by histological examination of a portion of liver removed at laparotomy.

1. Blakemore, A. H., Lord, J. W. jun. *Ann. Surg.* 1945, 122, 476.

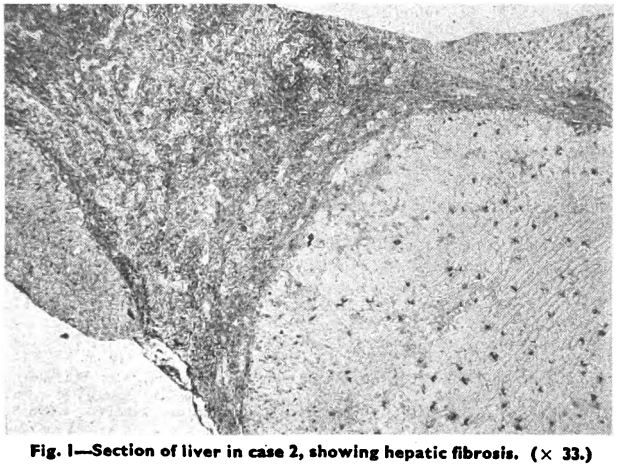

Fig. 1—Section of liver in case 2, showing hepatic fibrosis. (× 33.)

Case 1 (Dr. W. A. Alexander).—A boy, aged 15, with hepatolienal fibrosis, had had repeated hæmatemesis for 12 months. Well-marked œsophageal varices were present, the spleen weighed 440 g.; the liver showed diffuse cirrhosis. The portal pressure was 320 mm. water. After 23 months there was no further bleeding. The patient is now on full work in a distillery and plays football.

Case 2 (Dr. R. D. Lawrence).—A woman, aged 27, had had toxic hepatitis 4 years previously, glycosuria for 3 years, severe hæmatemesis on four occasions in 9 months. Large œsophageal varices and gross hepatic fibrosis (fig. 1) were present. The spleen weighed 470 g. The pressure in the splenic vein was 120 mm. water. After 18 months there was no further bleeding. The patient is now on full office and house-work, and has gained 20 lb. in weight.

Case 3 (Prof. L. S. P. Davidson).—A woman, aged 46, with hepatolienal fibrosis had had hæmatemesis for 36 months. Her spleen weighed 180 g., and there was diffuse hepatic fibrosis. After 14 months there was no further bleeding. The patient now does house-work.

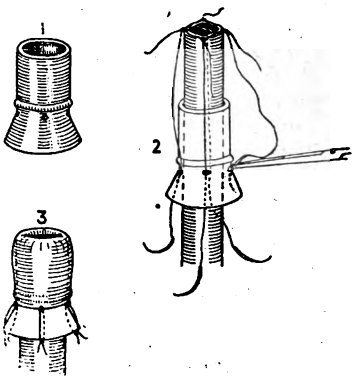

Fig. 2—(1) Vitallium tube with holes bored in flange; (2) and (3) method of everting and securing splenic vein over vitallium tube.

Case 4 (Dr. R. W. D. Turner).—A man, aged 27, who had had hepatitis (? infective) 2½ years previously and hæmatemesis for 18 months. His spleen weighed 940 g., and there was gross hepatic fibrosis. The pressure in the splenic vein was 250 mm. water. After 10 months there was no further bleeding. The patient now does normal work and plays games, except rugby football.

Case 5 (Prof. Charles Wells).—A woman, aged 53, with hepatolienal fibrosis had had hæmatemesis for 18 months and three copious bleedings while awaiting operation. Her spleen weighed 420 g., and she had diffuse hepatic fibrosis. After 6 months there was no further bleeding. The patient has returned to office work.

Case 6 (Dr. C. N. Armstrong).—A man, aged 32, had had infective hepatitis in 1943, and hæmatemesis for 6 months. His spleen weighed 340 g., and he had diffuse hepatic fibrosis. After 4 months there was no further bleeding.

Deaths after Operation

Case 7 (Prof. J. W. McNee).—A woman, aged 46, with hepatolienal fibrosis had had ascites and hæmatemesis for 24 months. She had diffuse hepatic fibrosis, and her spleen was very adherent and weighed 720 g. She died, without regaining consciousness, 12 hours after operation. Necropsy was not performed.

Case 8 (Mr. R. D. Rowlands).—A man, aged 48, with hepatolienal fibrosis had had ascites and hæmatemesis for 6 months. His spleen weighed 240 g., and he had advanced hepatic fibrosis. Anastomosis proved difficult. Death took place

32 hours after operation, clinically from pulmonary congestion and œdema. Necropsy showed advanced hepatic fibrosis and pulmonary œdema. The anastomosis was patent.

GROUP II: SPLENECTOMY (ANASTOMOSIS JUDGED IMPOSSIBLE)

In this group our intention to perform a lienorenal anastomosis had to be abandoned, usually because the available veins were unsuitable (see below).

Case 9 (Prof. L. S. P. Davidson).—A woman, aged 54, with hepatolienal fibrosis had had hæmatemesis for 24 months, with nephritis. At operation diffuse hepatic fibrosis was found, and splenectomy was carried out. Her poor condition precluded a lengthy operation. She died 26 days after operation, clinically of progressive hepatic failure. No necropsy was done.

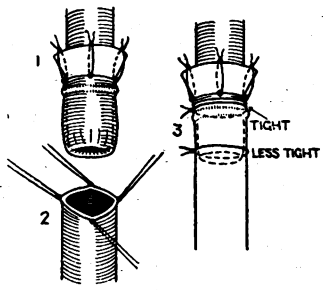

Fig. 3—(1) Splenic vein prepared for anastomosis; (2) stay sutures inserted in renal vein; (3) anastomosis completed.

Case 10 (Dr. A. Rae Gilchrist).—A man, aged 27, with hepatolienal fibrosis had had gross ascites for 16 months. Diffuse hepatic fibrosis was found. At splenectomy the splenic veins were found to be in numerous small branches. After 2 months the patient's condition remained unchanged.

Case 11.—A man, aged 29, had had infective hepatitis 6 years previously, and hæmatemesis for 3 months. Diffuse hepatic fibrosis was found. The spleen weighed 490 g. At splenectomy, the splenic artery and vein were found to be in numerous small branches. After 2 months the patient's condition remained unchanged.

GROUP III: LAPAROTOMY ONLY

In one patient, in whom ascites had been present for two months, laparotomy only was performed.

Case 12 (Dr. W. A. Alexander).—A woman, aged 23, had had hepatitis 3 years previously. She had extreme cirrhosis and gross ascites and her condition was judged to be hopeless. She died 28 days after operation, clinically of progressive liver failure. At necropsy there was severe postnecrotic scarring of the liver, and the spleen weighed 350 g.

DISCUSSION OF GROUPS I, II, AND III

Selection of Patients for Operation.—It is necessary to determine by clinical and laboratory examination that the hæmatemesis and ascites are the consequences of hepatic cirrhosis. This investigation includes tests of hepatic function to exclude hypoprothrombinæmia as the cause, or a contributory cause, of hæmatemesis, and to exclude inability of the liver to produce albumin as the cause of ascites. If these deficiencies exist they must be rectified as far as possible by dietetic treatment. We do not recommend liver biopsy by puncture, because in 2 patients, and on two occasions in one of these, material obtained in this way was normal, though at laparotomy cirrhosis was evident. It must be demonstrated by intravenous pyelography that both kidneys are present, that the function of the right kidney is normal, and that the left kidney is normally situated and not part of a horseshoe kidney.

Operation

Dr. John Gillies, reader in anæsthesia in the University of Edinburgh, induces anæsthesia with thiopentone and maintains it with cyclopropane and oxygen given through a cuffed orotracheal tube, using controlled respiration. As the peritoneum is incised, 15 mg. of *d*-tubocurarine is given. In our experience at least two hours, and usually longer, is required to complete the procedure. The patient is placed on a gall-bladder rest and tilted towards the right side. A drip transfusion of blood is started before operation.

A diathermy needle is used to divide the posterior leaf of the lienorenal ligament. When the spleen is large and numerous collaterals link it to the abdominal wall, a useful plan is to begin at its lower pole by dividing the gastrosplenic ligament, and to insinuate a pack upwards behind the spleen, where a relatively avascular plane may be found. This pack is worked outwards, until it can be displayed by the diathermy needle, along the convexity of the spleen. When the spleen is mobilised, the vessels in its hilum must be dissected to ascertain their size and disposition. If, as has happened on two occasions, the splenic veins are numerous and small, we now think that it is probably wisest to abandon the operation without splenectomy, and to close the abdomen. In more favourable circumstances the longest and largest, and if possible the lowest, terminal branch of the splenic vein has been chosen for the anastomosis. The splenic artery is divided between ligatures, and the blood in the spleen is returned to the circulation by faradic stimulation of the splenic pedicle distal to the point of division of the artery. The veins are clamped close to the spleen, which is removed. All tributaries joining the vein selected for anastomosis are secured with fine silk as close as possible to the parent vein, and it has usually been necessary to dissect the splenic vein proximally along the upper border of the pancreas for about 10 cm., to add to its length and mobility. When ascites has been present, the tail of the pancreas is swollen and hard, and at this stage it should be opened out by gentle blunt dissection to provide a "straight run" for the splenic vein towards the renal vein; if this is not done, the final anastomosis tends to be angled over the tail of the pancreas.

The splenic vein is next controlled with a rubber-shod bulldog clamp, applied to it in the grasp of curved artery forceps, and moistened with sterile liquid paraffin to prevent it from adhering to the vein. Four fine black silk sutures are passed through the wall of the vein at equidistant points, brought through a 'Vitallium' tube of suitable size (diameter about 0·7 cm.), and passed through small holes in the flange of the tube so that traction on the threads everts the vein; the threads are tied over the flange (fig. 2). The empty segment of vein is washed out with sterile isotonic sodium citrate solution and laid aside under cover of a swab moistened with the citrate solution.

The incision through the peritoneum of the posterior abdominal wall is next continued downwards over the hilum of the left kidney, where its direction changes towards the median line, to enable the renal pedicle to be brought anteriorly without angulation. The kidney is isolated, and the ureter divided between ligatures. The renal vessels are followed to their entrances into the kidney; if the renal vein is branched, the largest and longest, and if possible the uppermost, branch is chosen. The renal artery is divided between ligatures, the veins are clamped close to the hilum, and the kidney is removed. The renal vein is dissected medially, care being taken to preserve the suprarenal vein, which joins its upper border, and the spermatic or ovarian vein, which joins its lower border. The suprarenal vein is often large, because of its communication, direct or indirect, with the engorged splenic vein. The renal vein is controlled with a bulldog clamp and washed out with citrate solution, and four stay sutures of fine silk are inserted in its open end (fig. 3). These sutures are used to draw the open end of the renal vein over the everted splenic vein supported on its vitallium tube, care being taken not to twist either vein. The anastomosis is completed by tying a medium silk ligature firmly round both veins proximal to the flange on the tube, and a second ligature less tightly near the apex

of the tube, to prevent separation of the intimal coats of the veins by a layer of blood (fig. 3). The bulldog clamp on the renal vein is first removed, then that on the splenic vein; we have usually been able to confirm the direction of blood-flow from splenic to renal vein (fig. 4). It is possible to construct the anastomosis by circular phleborrhaphy (case 4), but it is our impression that the vitallium tube acts as a useful splint, especially when the two veins do not lie quite in the same plane. The area of operation is reperitonealised by suturing the lateral edge of the incision in the lienorenal ligament, and its continuation over the kidney, to the medial edge of the opening in the gastrosplenic ligament. The abdomen is closed in layers without drainage.

We have had no personal experience of end-to-side lienorenal anastomosis, with preservation of the kidney, or of any other type of portacaval shunt.[2]

After-treatment.—The foot of the bed is raised on blocks for the first twenty-four hours to encourage a rapid flow in the vena cava. After six hours enough heparin is added to the drip to keep the clotting-time at 12–15 min.; after twenty-four hours the heparin is discontinued.

Results

This report, it must be emphasised, is a preliminary one and includes only our small personal experience. Moreover, we are not in a position to compare the results of lienorenal anastomosis with those of other procedures designed to provide portal-systemic shunts, either directly (portacaval anastomosis) or indirectly by increasing the number of collaterals (Talma-Morison operation and its variants). In any large series of cases of portal hypertension, of whatever ætiology, cases will be found to fall into three groups [3]:

(1) An *acute* group, in which the obstruction is rapidly produced or widespread, or hepatic failure is so rapid, that collateral vessels do not form and the condition ends fatally after a short illness. In this group the question of surgical treatment does not arise.

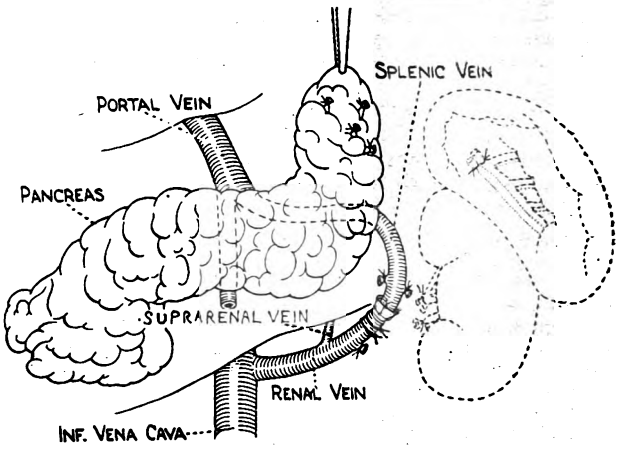

Fig. 4—General arrangement of structures after lienorenal anastomosis (after Blakemore and Lord [2]).

(2) An *episodic* group, in which the obstruction is less rapidly produced or less complete. Symptoms and signs abate as the collateral circulation takes over the venous load, and there may be long intervals, measured even in years, before an increase in portal obstruction surprises an inadequate collateral circulation and symptoms recur, possibly to disappear again if the collateral circulation can respond to the increased demand on it.

(3) A *chronic* group, in which initial ascites may have to be tided over by one or more tappings of the abdomen, or hæmatemesis, by one or more blood-transfusions after which the collateral circulation is sufficient to reduce the increased portal pressure. In this group the anatomical disposition of the collaterals may be such that, though ascites does not recur, hæmatemesis may be a danger.

The chronic group appears to offer the most promising indications for lienorenal anastomosis, and indeed—though this may be fortuitous—all our successful cases belonged to it. We cannot say with certainty that the anastomosis remains permanently open; in the fatal case which came to necropsy (case 8) it may be significant that in spite of a failing circulation the anastomosis was completely patent after thirty-two hours. This point can be clarified only by the examination of the site of operation at necropsy after much longer intervals. Nevertheless, we have been impressed by the considerable improvement in general health, including improvement in metabolism as indicated by increase in weight, which has been uniformly found in our small series. It is tempting to hope that, besides dealing with the hæmatemesis (though radiographic evidence of œsophageal varices may persist), we have made a physiological readjustment which has improved hepatic functions though we cannot offer even a tentative explanation of this process.

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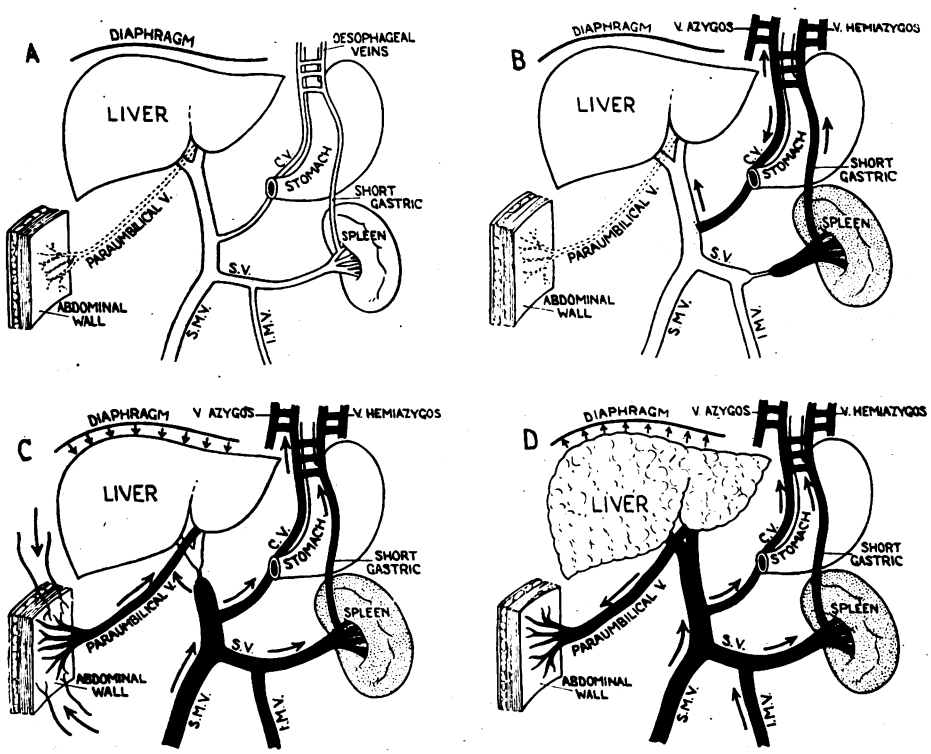

Fig. 5—A, Normal portal circulation; B, circulation in obstruction of splenic vein; C, obstruction of portal vein outside liver; D, intra-hepatic portal obstruction.

GROUP IV: SPLENECTOMY FOR SPLENIC VENOUS THROMBOSIS

In this group of cases the obstruction to the portal circulation is in the splenic vein, and the presenting symptom is hæmatemesis, the hæmorrhage being from grossly dilated collaterals about the cardia which connect the vasa brevia to the systemic circulation and to the left gastric vein (fig. 5B). In our experience the liver has been normal and ascites absent; the history has been characteristically episodic, incidents of bleeding, beginning even in infancy, being separated by long intervals of health. Splenomegaly is the rule.

Case 13 (Prof. L. S. P. Davidson).—A girl, aged 16, had had three episodes of hæmatemesis between the ages of 6 and 16 years. Her spleen weighed 400 g., and her liver was normal histologically. The pressure in the splenic vein was 200 mm. water. The collaterals at the cardia were enormous. After 17 months the patient was on full work on a farm.

Case 14 (Dr. Ian Gordon).—A girl, aged 6 years, had had several episodes of hæmatemesis in two years. Her spleen weighed 340 g., and her liver was histologically normal. The pressure in the splenic vein was 190 mm. water. After 8 months there was no further bleeding.

Case 15 (Dr. D. N. Nicholson).—A girl, aged 9 years, had had several episodes of hæmatemesis in two years. Her spleen was much enlarged, and her liver macroscopically normal. The pressure in the splenic vein was 140 mm. water. After 6 months there was no further bleeding, and the patient was very well.

DISCUSSION OF GROUP IV

Operation.—Splenectomy alone is required. Great care is necessary in mobilising the upper pole of the spleen, where we have seen the dilated collaterals hanging like a bunch of black grapes. All vessels in the splenic pedicle should be secured as close to the spleen as possible, to avoid the communications between the splenic vein(s) and diaphragmatic, œsophageal, and pancreatic collaterals.

Results.—In this small series the immediate results have been uniformly good.

SUMMARY

In 16 cases we had an opportunity of treating the effects of portal hypertension by surgical measures. It is emphasised that the series is small, the intervals since operation are short, and the methods used are restricted.

In 6 of 8 patients who survived lienorenal anastomosis there has been no further hæmatemesis after intervals varying from four to twenty-three months, and their general condition has been much improved.

In 3 patients suffering from hæmatemesis due to thrombosis of the splenic vein splenectomy has been a safe and so far satisfactory immediate method of treatment.

J. R. L. is greatly indebted to those colleagues in Edinburgh and elsewhere who entrusted these patients to his care.

"... There is no end to the fears initiated by trifles, but they are not necessarily trifling fears. ... Again and again patients discharged from hospital, when asked what the doctors have told them, say, 'Oh, they didn't tell me anything.' Often they have spent long periods in the ward and been elaborately investigated, all the time waiting and wondering and uninformed. Could anything be more conducive to the initiation or aggravation of anxiety than experience of this kind? Probably the divided responsibilities which obtain in institutions and the inexperience of house-officers are partly to blame, but the mechanistic, objective character of modern investigations also tends to distract the doctor's from the patient's thought and to direct attention away from private sensibilities and present needs. I have even watched air-raid victims being admitted, examined, X-rayed and transfused without a word of comfort or reassurance being given to them by those concerned. ..."—Prof. J. A. RYLE, *J. ment. Sci.*, January, 1948, p. 11.

HÆMOPHILUS INFLUENZÆ MENINGITIS

FOUR CASES TREATED WITH STREPTOMYCIN

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THE rarity and highly variable clinical course of *Hæmophilus influenzæ* meningitis render difficult the statistical evaluation of any new form of treatment. Reports from the United States (National Research Council 1946, Alexander et al. 1946, Alexander and Leidy 1947b) show that, although many cases can be cured with streptomycin alone, resistance to this remedy may prevent success. In the review by Wilson (1948) of 43 cases treated in this country 7 of the 9 failures reported appeared to be attributable to drug resistance. Of these same 43 cases 12 have been fully reported by Smythe (1948). A further 4 are reported here.

The dosage used was that recommended by the Medical Research Council committee—i.e., six daily intramuscular injections of 20 mg. of streptomycin per lb. of body-weight, together with an initial intrathecal dose of 50 mg. followed by 25 mg. daily. This dosage was continued until the cerebrospinal fluid (C.S.F.) had been sterile for at least seven consecutive days. Streptomycin hydrochloride (Merck) batch no. 565 was used throughout. All solutions for injection were prepared in sterile physiological saline solution. Each intramuscular dose was contained in 1 ml.; the daily intrathecal dose for cases 1, 2, and 3 was contained in 5 ml., and for case 4 in 2·5 ml. No local or generalised toxic effects from streptomycin were observed.

CASE-RECORDS

Though the 4 patients were all admitted to Addenbrooke's Hospital within the short space of seven weeks, they were otherwise unconnected, coming from widely separated districts of East Anglia. None had a history of recent contact with any case of infection of the upper respiratory tract. The cases are summarised in table I.

Case 1.—A boy, aged 21 months. Apart from a cold on the chest for the previous fortnight he had appeared well until Oct. 13, 1947, when he cried and vomited on waking after his siesta. In the evening he seemed dazed, did not recognise his mother, and vomited several times more. Though better next day, he had some neck stiffness on Oct. 15 and vomited frequently. He was admitted to the local hospital, where the C.S.F. was examined and *H. influenzæ* meningitis was provisionally diagnosed. Penicillin 20,000 units intrathecally and 10,000 units intramuscularly, and sulphadiazine 0·5 g. by mouth, were given, and that evening he was transferred to Addenbrooke's Hospital.

Examination on Admission.—He was desperately ill, comatose, flushed, and dehydrated, with temperature 101°F, intense inflammatory œdema of both lids, proptosis apparently beginning, fixed external strabismus, almost inactive pupils, neck rigidity, absent limb and abdominal reflexes, inflamed tonsils, and a blister on the left tympanic membrane. The C.S.F. was purulent and contained gram-negative bacilli; *H. influenzæ* Pittman type B was isolated.

Treatment and Progress.—The standard course of streptomycin was started immediately and continued for ten days (total 275 mg. intrathecally and 4560 mg. intramuscularly). After fifteen hours the œdema of the lids began to regress, and two hours later he was apparently able to see. Next day he could hear, and that afternoon he sat up and started playing. When streptomycin therapy stopped on the tenth day, the temperature had been normal for four days. He was kept under observation a further fourteen days before discharge.

Six months later his doctor reported him completely normal for his age.

Extract from Laboratory Findings.—On admission: C.S.F., 23,000 cells per c.mm.; C.S.F. protein 90 mg. per 100 ml.; C.S.F. culture, blood-culture, and nose and throat swabs, *H. influenzæ*. Second day: C.S.F. culture sterile. Third day: C.S.F. culture *H. influenzæ*; blood-culture and nose and throat swabs negative. Fourth day: C.S.F. culture sterile. Fifth day: C.S.F. cells 230, protein 70, culture sterile. Tenth day: C.S.F. cells 35, protein 50, culture sterile. (Streptomycin treatment stopped.) On discharge: C.S.F. cells 35; protein 30; culture sterile.

Case 2.—A boy, aged 3 years 3 months. On Oct. 23, 1947, he vomited, and he continued vomiting all night. Next day he seemed better, and was apyrexial, and no abnormal signs were found. On Oct. 25 he would not play or talk and seemed only semiconscious. His temperature was 99°F and he had neck stiffness. At the local hospital lumbar puncture revealed a turbid C.S.F. under pressure. Penicillin 100,000 units followed by 50,000 units intramuscularly, and sulphapyridine 1·5 g., 1·0 g., then 0·25 g. were given three-hourly for forty-five hours. On Oct. 27 the growth of *H. influenzæ* was reported from the original C.S.F., and he was transferred to Addenbrooke's Hospital.

Examination and Initial Treatment.—The child did not seem very ill. Though he had slight neck rigidity and the right ankle and abdominal reflexes were absent, he was fully conscious and afebrile. No organisms were seen in the stained films from the C.S.F., and the subsequent culture was sterile. As he had apparently responded so well already, he was not considered suitable for the clinical trial of streptomycin; therefore the original treatment was continued, but the penicillin was given in doses of 25,000 units four-hourly, and sulphadiazine 1·5 g. followed by 0·75 g. four-hourly was substituted for sulphapyridine for six and a half days. The neck rigidity had almost disappeared by Oct. 29. The temperature remained normal and the patient played happily. On Nov. 7, while playing in his cot, he fell out on to his head. No abnormal physical signs were detected and radiography of his skull showed no fracture. Next day he complained of headache and was found to have a temperature of 100°F, absent lower limb reflexes, and neck rigidity. A turbid C.S.F. contained gram-negative bacilli, and *H. influenzæ* Pittman type B was isolated.

Streptomycin Treatment and Progress.—The standard course of streptomycin was started at once and continued for eight days. The total given was 225 mg. intrathecally and 4700 mg. intramuscularly. Clinical improvement was obvious after nineteen hours; the temperature settled within twenty-four hours, and the child made an uninterrupted recovery. He was kept under observation for thirteen days after streptomycin had been stopped. A full examination three months later confirmed his complete recovery.

Extract from Laboratory Findings.—On admission: C.S.F. cells 230 per c.mm.; C.S.F. protein 30 mg. per 100 ml.; C.S.F. culture, blood-culture, and nose swab, negative; throat swab *H. influenzæ* (negative five days later). Relapse: C.S.F. cells 725, protein 40, culture *H. influenzæ*. Second day: C.S.F. cells 3000; culture sterile. Third day: C.S.F. cells 185, culture sterile. Fifth day: C.S.F. cells 20, protein 30, culture sterile. Eighth day: C.S.F. cells 12, protein 25, culture sterile. (Streptomycin treatment stopped.) On discharge: C.S.F. cells 7, protein 25, culture sterile.

Case 3.—A boy, aged 1 year 11 months, had been poorly since Nov. 11, 1947, when he vomited twice and had a temperature of 103°F. During the next six days his temperature remained raised. At times he seemed dazed and he gradually developed head retraction. On Nov. 17 he was admitted to the local hospital with tonsillitis. Next day he had definite neck rigidity, the C.S.F. was cloudy and under pressure, and *H. influenzæ* was subsequently isolated. Penicillin 800 units intrathecally and sulphadiazine 0·5 g. four hourly to a total of 3 g. were given. On Nov. 19 he was transferred to Addenbrooke's Hospital.

Examination.—The child was obviously ill and apathetic, with temperature 103°F, well-marked neck rigidity, absent abdominal reflexes, and much inflamed tonsils. A turbid C.S.F. contained gram-negative bacilli; *H. influenzæ* Pittman type B was isolated.

Treatment and Progress.—The standard course of streptomycin was started at once and continued for ten days, 275 mg. being given intrathecally and 6200 mg. intramuscularly. Within forty-eight hours he was sitting up and playing, and recovery was uneventful. He was kept under observation for eleven days after treatment ceased. Three months later he was reported by his doctor to be normal in every way.

Extract from Laboratory Findings.—On admission: C.S.F. cells 300 per c.mm.; C.S.F. protein 50 mg. per 100 ml.; C.S.F. culture *H. influenzæ*; blood-culture and nose and throat swabs negative. Second day: C.S.F. cells 320, protein 40, culture sterile. Fifth day: C.S.F. cells 55, protein 40, culture sterile. Tenth day: C.S.F. cells 20, protein 40, culture sterile. (Streptomycin treatment stopped.) On discharge: C.S.F. cells 9, protein 30, culture sterile.

Case 4.—A boy aged 7 months had been fully breast-fed, and weaning had just been started. His parents described him as perfectly well until Nov. 23, 1947, when he had vomited several times, stared vacantly at the light, and begun jerking movements of the limbs. These continued for seven days and "his head gradually arched further and further backwards." In the evening of Nov. 29 he was admitted to Addenbrooke's Hospital with a provisional diagnosis of tuberculous meningitis.

Examination.—He was comatose and in well-marked opisthotonos, with spastic limbs and increased briskness of tendon reflexes. His temperature was 104°F. A turbid C.S.F. contained gram-negative bacilli; *H. influenzæ* Pittman type B was isolated.

Treatment and Progress.—The standard course of streptomycin was started at once: 395 mg. was given intrathecally in fourteen days and 6675 mg. intramuscularly in fifteen days. Clinical response was definite but somewhat slow. By the eighth day of treatment the temperature had settled. On the tenth day he was smiling responsively and showed minimal stiffness of the neck. However, that evening he vomited and continued to do so once or twice daily. On the thirteenth day his temperature started to rise, the neck rigidity returned, he was fretful, and the vomiting continued. During this time the C.S.F., though sterile, never contained less than 150 cells per c.mm. and the amount of protein remained

TABLE I—SUMMARY OF CASES

Case no.	Sex	Age	Days ill before start of streptomycin	Intramuscular streptomycin (mg. daily × no. of days)	Intrathecal streptomycin (mg. daily × no. of days)	Average range of C.S.F. streptomycin level (μg. per ml.)	Days from admission on which C.S.F. culture positive	Sensitivity of organism to streptomycin (μg. per ml.)	Clinical severity	Result
1	M	1 yr. 9 mos.	2	480 × 10	50 × 1 25 × 9	1–8	1 3	4 2	Fulminating	Complete recovery
2	M	3 yr. 3 mos.	17	600 × 8	50 × 1 25 × 7	1–2	13*	2	Mild	Complete recovery
3	M	1 yr. 11 mos.	9	600 × 10	50 × 1 25 × 9	1–2	1	2	Moderate–severe	Complete recovery
4	M	7 mos.	7	450 × 15	50 × 1 25 × 13	1–37	1 2 3 14 25 32 43 (p.m.)	2 4 4 1000 1000 1000 1000	Severe	Died

* On admission C.S.F. sterile; no streptomycin given until relapse 13 days later.

TABLE II—SENSITIVITY OF *H. influenzæ* TO STREPTOMYCIN, PENICILLIN, AND SULPHATHIAZOLE

Case	Source	Relation to specific therapy	Minimal inhibiting dose		
			Streptomycin (μg. per ml.)	Penicillin (i.u. per ml.)	Sulphathiazole (mg. per ml.)
1	C.S.F.	On admission	4	1	4
		Streptomycin 2nd day	2	1	4
2	Nasopharynx	On admission	2	4	2
	C.S.F.	Relapse after penicillin and sulphadiazine	2	4	4
3	C.S.F.	On admission	2	1	4
4	C.S.F.	On admission	2	1	4
	,,	Streptomycin 1st day	4	..	..
	,,	Streptomycin 2nd day	4	..	..
	,,	Streptomycin 14th day (streptomycin stopped)	1000	..	..
	Ventricular fluid	Penicillin and sulphamezathine 11th day	1000	1	4
	,, ,,	,, ,, 18th day	1000	1	4
	,, ,,	Necropsy on 43rd day (no specific therapy for 10 days)	1000	..	..

increased. However, though the streptomycin level had risen as high as 37 μg per ml. by the twelfth day, there was still no evidence of spinal block.

On the fourteenth day *H. influenzæ* was again grown from the C.S.F., and this strain was shown to be highly resistant to streptomycin. Streptomycin therapy was accordingly abandoned, and penicillin (to a total of 5,990,000 units in twenty days and 'Sulphamezathine' to a total of 31 g. in fourteen days) were given instead. Next day lumbar puncture which had been becoming increasingly difficult, could not be done. By the nineteenth day opisthotonos was again so severe that daily ventricular taps were performed for three days. These specimens of ventricular fluid were sterile. There was no clinical improvement, and vomiting continued. On the twenty-fifth and thirty-second days *H. influenzæ* was isolated from the ventricular fluid. The child eventually died on Jan. 11, forty-three days after admission.

Extract from Laboratory Findings.—On admission: C.S.F. cells 4500 per c.mm.; C.S.F. protein 180 mg. per 100 ml., C.S.F. culture *H. influenzæ*; blood-culture not done; nose and throat swabs negative. Second day: C.S.F. cells 11,500, protein 160, culture *H. influenzæ*. Third day: C.S.F. cells clotted, culture *H. influenzæ*; blood-culture sterile. Fourth day: C.S.F. cells 835, protein 100, sugar 18 mg. per 100 ml., culture sterile. Eighth day: C.S.F. cells 245, protein 100, sugar 32, culture sterile. Thirteenth day: C.S.F. cells 145, protein 70, sugar 47, culture sterile. Fourteenth day: C.S.F. cells 800, protein 70, sugar 1, culture *H. influenzæ*. (Penicillin and sulphamezathine substituted for streptomycin.) Nineteenth day: C.S.F. (right ventricle) cells 2000, culture sterile; blood-culture sterile. Twentieth day: C.S.F. (left ventricle) cells 360, protein 140, culture sterile. Twenty-fifth day: C.S.F. (left ventricle) cells 430, protein 200, sugar 1, culture *H. influenzæ*. (Sulphamezathine stopped.) Thirty-second day: C.S.F. (right ventricle) cells 2400, protein 300, sugar 20, culture *H. influenzæ*. (Penicillin stopped.) Forty-third day (post mortem): C.S.F. (right ventricle) cells 970, culture *H. influenzæ*.

Necropsy Findings.—There was a purulent leptomeningitis with pyocephalus and a thrombosis of the left lateral sinus. The ventricular system was enormously dilated, with reduction in thickness of the brain substance everywhere. The cisterna magna was bounded by greatly thickened meninges, and it was obvious that the foramina had been occluded; they could no longer be identified. The subarachnoid space throughout the length of the spinal canal was filled with inflammatory exudate, which in the cervical region had become organised. Histological changes in the nervous tissue were relatively slight considering the severity of the meningitis. There were no other significant abnormalities and no additional foci of infection, such as pneumonia, sinusitis, or mastoiditis. A pure culture of a strain of *H. influenzæ* resistant to streptomycin was obtained from the purulent ventricular fluid.

BACTERIOLOGY

All strains of *H. influenzæ* isolated from these cases grew readily on 10% (horse blood) chocolate agar, were indole-positive, and required X and V factors for growth on 1% peptone agar. They were all Pittman type-B strains.

Bacterial Sensitivity.—The in-vitro minimum inhibitory dose of an antibiotic varies not only with the species of organism under test but also with the size of the inoculum and the constitution of the substrate used. Therefore, to ensure comparable results, a constant technique * using a standard inoculum and the same batch of culture medium was used for all tests of sensitivity to streptomycin, penicillin, and sulphathiazole. The results obtained with 12 strains of *H. influenzæ* isolated from these cases at various stages of treatment are summarised in table II.

STREPTOMYCIN LEVELS

Daily estimations of the streptomycin level in the C.S.F. twenty-four hours after the intrathecal injection of streptomycin, and single observations on the serum-streptomycin level one and four hours after an intramuscular injection were carried out in each of these cases. The technique suggested by the Medical Research Council (M.R.C. 47/241, May 8, 1947) was used in cases 1, 2, and 3, and Mitchison's method (M.R.C. 47/503. Revised 10/47) in case 4. The streptomycin levels in the C.S.F. are summarised in table I. The serum-streptomycin levels in cases 1, 2, 3, and 4, estimated at one and four hours after an intramuscular injection of streptomycin, were 16 and 8, 4 and 2, 8 and 4, and 4 and 2 μg per ml. respectively.

DISCUSSION

The cases described provide a good illustration of both the success and failure of streptomycin in the treatment of *H. influenzæ* meningitis.

The most impressive response to streptomycin was seen in case 1. In fact, the child's condition on admission to Addenbrooke's Hospital was such that without chemotherapy he would probably have died within a few hours, whereas two days later he was sitting up and playing, and his recovery was uneventful and complete.

Case 2 provided a good example of a relapse following an apparently successful course of penicillin and sulphadiazine. This was rapidly controlled by immediate treatment with streptomycin.

In case 3 the minimum course of streptomycin recommended by the Medical Research Council was extended by two days, because the temperature had remained normal for only forty-eight hours before the seventh daily consecutive sterile specimen of C.S.F. was obtained. Apart from this slight prolongation of pyrexia the clinical response in this case was also entirely satisfactory.

The initial response to streptomycin in case 4 was again satisfactory, though not so impressive as in the other three cases. Though the C.S.F. was sterile by the third day of treatment and remained so for the next

* *Sensitivity tests.* 0·25 ml. of an 18-hour culture, in 2·5% Fildes's (horse blood) digest broth, of the organism to be tested was inoculated into 10 ml. of the same medium and 0·5 ml. of this added, immediately, to each tube of a twofold serial dilution of streptomycin, penicillin, or sodium sulphathiazole in similar amounts of 0·85% NaCl. The minimum inhibitory dose was taken to be the least amount of the drug in which there was no visible growth after 48 hours' incubation at 37°C.

nine days, clinical improvement was rather slow. Next day there was a relapse, coinciding with the isolation of a highly resistant strain of *H. influenzæ* from the C.S.F. Despite immediate substitution of full dosage of penicillin and sulphamezathine for streptomycin, and the periodic relief of intraventricular pressure by tapping, the child went steadily downhill and died on the forty-third day. All strains isolated after this relapse also showed the same high degree of resistance to streptomycin. On the other hand, the subsequent failure of a combined course of penicillin and sulphamezathine was not reflected by any decrease in sensitivity to these drugs. The strain isolated from case 2 after the apparently successful course of penicillin and sulphadiazine also showed no appreciable increase in resistance to these drugs.

In the past the response of *H. influenzæ* meningitis to treatment with specific antiserum, sulphonamides, or penicillin, either singly or in combination, has usually been somewhat protracted (Alexander 1944, Zinnemann 1946, Gottlieb and Forsyth 1947, Gerrard 1947, Thomson et al. 1947). The outstanding feature of successful streptomycin therapy is the immediate clinical response and rapid control of the infection.

Failure of streptomycin therapy is almost always associated with the development of resistance to streptomycin. Alexander and Leidy (1947a) have presented convincing evidence that in any large population of *H. influenzæ* studied in vitro there is a constant proportion of organisms naturally resistant to streptomycin, and though these resistant variants are only a minute fraction of the total population they constitute a constant potential source of relapses in every case of *H. influenzæ* meningitis treated with streptomycin alone. They are, however, just as sensitive as the parent strains to penicillin and sulphonamides. In cases 1 and 3 penicillin and sulphonamides were given before transfer to Addenbrooke's Hospital, and though this preliminary treatment was insufficient to cause obvious clinical improvement it may have reduced the total number of organisms present, including the naturally resistant variants, before treatment with streptomycin was begun, and thus lessened the risk of relapse later.

Since neither clinical assessment nor the bacteriological examination of the C.S.F. is an accurate guide to the total number of organisms present, there is no reliable way of estimating the chances that resistance to streptomycin will develop during treatment. Further, by the time such a relapse takes place the organisation of the inflammatory exudate may have rendered the residual foci of infection inaccessible to alternative methods of treatment. The failure of penicillin and sulphamezathine to control the relapse in case 4 on the fourteenth day of streptomycin therapy was probably due to this.

Therefore, in spite of some outstanding successes with streptomycin alone, there is already a strong case for the treatment of *H. influenzæ* meningitis with both streptomycin and a sulphonamide from the outset; the possible addition of penicillin and even specific antiserum in the more severe examples of this condition might also be considered.

SUMMARY

Of four children with *H. influenzæ* meningitis treated with streptomycin three showed a rapid response with complete recovery and the fourth died after developing resistance to streptomycin. In view of the tendency to resistance to streptomycin the use of a sulphonamide in combination with streptomycin should be considered.

We wish to thank Professor Sir Lionel Whitby and Dr. F. B. Parsons for access to their cases; Dr. R. Mayon White for assistance with case 4; Dr. A. M. Barrett for the necropsy findings; Dr. A. B. Rosher for the Pittman typing; and the Medical Research Council for supplies of streptomycin.

References at foot of next column

FOLIC ACID IN THE TREATMENT OF AGRANULOCYTOSIS

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Black and Stanbury (1947) have suggested that folic acid is of value in the treatment of granulocytopenia and agranulocytosis due to drugs. The basis of its use in this condition is the treatment of leucopenia in nutritional deficiency states as observed in animal experiments (Spicer et al. 1942, Welch et al. 1942, Wilson et al. 1942, Ransone and Elvehjem 1943, Cooperman et al. 1946, Doan 1946).

Apart from industrial chemicals, many drugs now in use may produce agranulocytosis, and it is important to record all available data relating to its treatment. The use of penicillin enables us to control infection during the period of agranulocytosis, and if this is done there is a tendency to spontaneous recovery in many cases (provided the offending drug is discontinued); hence it is difficult to assess the effectiveness of other forms of treatment. In recording cases subjected to special forms of treatment it is essential to keep in mind the possibility of spontaneous remission and to be able to recognise when this is impending. Of the 5 cases of drug-induced agranulocytosis reported here 2 were treated with folic acid.

Case 1.—A woman, aged 47, was admitted to hospital on Feb. 24, 1947, with a tentative diagnosis of diphtheria. From Jan. 15 to Feb. 17, she was treated for syphilis, receiving nine injections of neoarsphenamine (total 4·65 g.) and eleven injections of bismuth (total 0·88 g.). During this period she had two febrile attacks accompanied by a scarlatiniform rash. On Feb. 18 (five days after the last injection of neoarsphenamine and a day after the last bismuth dose) she became acutely ill with headache, high fever, and rigor. she was given 'Pyramidon' 0·3 g. t.i.d. and sulphathiazole 0·5 g. t.i.d. On Feb. 21 she complained of sore throat.

On admission she had membranous stomatitis and tonsillitis, with ulceration and fœtor oris, and auricular fibrillation. A blood-count showed leucopenia, with white cells 1800 per c.mm. (granulocytes 15%). Serological reactions for syphilis were strongly positive. Throat-swabs gave on culture Vincent's organisms and hæmolytic streptococci, but no *C. diphtheriæ* were found.

Treatment.—The patient was given anti-diphtheria serum 20,000 units, anti-gas-gangrene serum 15 ml., 'Campolon' 5 ml., and sulphanilamide 1·5 g. on Feb. 24; penicillin 900,000 units from Feb. 26 to March 1; 'Pentnucleotide' 40 ml. on Feb. 28 and March 1, and 20 ml. on March 3. Blood-transfusions of 160 ml. on Feb. 26 and 120 ml. on Feb. 27 were given.

Progress.—The patient's temperature, which had been 101·2°F on admission, became normal in two days. A blood-count on March 4 showed red cells 4,790,000 per c.mm., Hb 101%, white cells 1900 per c.mm., granulocytes 4%, (segmented 2%, "stab" 2%), platelets normal, and reticulocytes less than 0·5%. From March 4 to 14 the patient received pentnucleotide 10 ml. and ascorbic acid 250 mg. daily; on March 7 she was given pyridoxine 50 mg. intravenously. From March 10 to 17 she received penicillin three-hourly to a total of 1,300,000 units. Swinging fever recurred on March 7, reaching 103·5°F on the 11th and 102·2°F on the 13th. The stomatitis improved, but one ulcer persisted on the cheek. The white-cell count rose slightly, reaching 2700 per c.mm. on March 7 and remaining at this figure,

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granulocytes varying from 0 to 13%. On March 14, when the white-cell count was 2700 per c.mm. (segmented 7%, stab 6%) treatment with folic acid was begun, 5 mg. t.i.d. being given for three days. On March 15 the white cells numbered 2800 per c.mm., and on the 16th 3500 per c.mm. (segmented 10%, stab 4%, metamyelocytes 6%, which now appeared for the first time in the blood films). The temperature became normal on March 17, and the stomal ulcer began to heal two days later. The white-cell count remained at 3500 per c.mm., with a temporary drop to 2500 per c.mm. (segmented 16%, stab 8%) on March 24. On March 25 the white cells numbered 2700 per c.mm. (segmented 7%, stab 1%, basophils 1%). On March 27 they numbered 3400 per c.mm. (segmented 12%, stab 3%).

Sternal puncture on March 27 revealed a few nucleated cells with 12% granulocytes. A further course of folic acid 5 mg. t.i.d. was given from March 28 to 30. On March 29 the white cells numbered 3900 per c.mm. (segmented 28%, stab 10%); on the 31st 5000 per c.mm. (segmented 50%, stab 8%, metamyelocytes 1%).

The patient was discharged on April 10 and received further antisyphilitic treatment (penicillin 4,000,000 units and bismuth 0·98 g. in June, and penicillin 4,000,000 units and bismuth 1·35 g. in September) without any effect on the white-cell count, which remained above 5000 per c.mm. (granulocytes over 50%) up to December, 1947.

Case 2.—A woman, aged 49, under treatment from Feb. 3 to 12, 1947, for cystopyelitis, received sulphathiazole 18 g. in four days. On Feb. 4 her white cells numbered 4200 per c.mm. (segmented 83%, stab 2%, lymphocytes 15%). On Feb. 17 she became acutely ill with fever, headache, vomiting, cough, and dysuria. On Feb. 20 she was readmitted to hospital with a diagnosis of central pneumonia and periostitis of left femur.

The patient was given sulphathiazole to a total dosage of 29 g. from Feb. 21 to March 1. She had a swinging temperature up to 102·2°F for two days. The temperature then became normal but rose again to 99·7°F on March 2. Since her leg did not improve, a course of penicillin 20,000 units three-hourly was started. On March 3 a blood-count showed severe granulocytopenia: red cells 3,400,000 per c.mm., Hb 70%, and white cells 1500 per c.mm. (segmented 16%, basophils 1%). Platelets increased in number. During the next ten days the patient received, in addition to the penicillin (which was continued throughout), ascorbic acid 250 mg. daily, pentnucleotide 20 ml. daily for three days, pyridoxine 50 mg. intravenously on one day, and four blood-transfusions totalling 540 ml. Daily blood-counts showed white cells 1300–1800 per c.mm. with only occasional granulocytes (stab 0–2% and an occasional basophil). Throughout the illness the mouth and throat remained healthy. On March 13, after a transfusion of 160 ml., the white-cell count had risen to 2700 per c.mm. (segmented 0%, stab 2%, eosinophils 2%, basophils 2%, plasma cells 3%, monocytes 2%, lymphocytes 89%).

A sternal-marrow film on March 13 showed only 10,300 nucleated cells, with 5% cells of the myeloid series (segmented 0·5%, promyelocytes 1·5%, myeloblasts 1%, basophils 1%). Hardly any cells were more mature than promyelocytes. Apart from a large number of cells of the erythroblastic series (34%) and an increased number of lymphocytes (41%) there were also an increased number of plasma cells (7·5%). Megakaryocytes were numerous.

From March 13 to 15 the patient was given folic acid 5 mg. t.i.d. The white-cell count dropped to 2100 per c.mm. on March 14 and 1800 per c.mm. on the 15th, but on the 17th there was a sudden rise to 2700 per c.mm. (segmented 16%, stab 8%). On this day the temperature became normal. On March 19 the white cells numbered 5500 per c.mm. (segmented 44%, stab 14%, metamyelocytes 1%, myelocytes 3%). On March 21 they numbered 10,500 per c.mm., with a similar differential count. Subsequently the blood-counts remained normal, except for a temporary slight leucocytosis while the patient had a septic tonsillitis and a gluteal abscess.

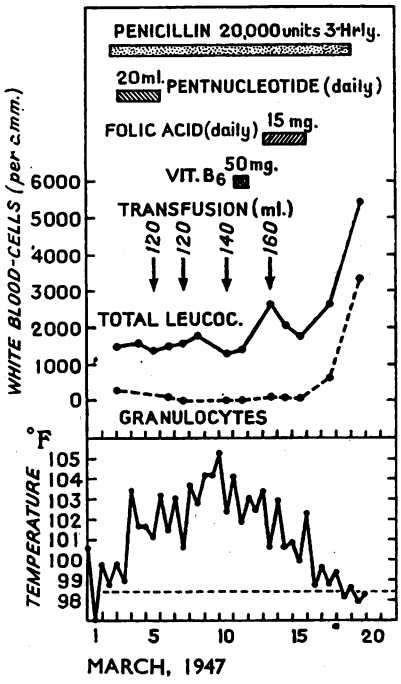

Fig. 2—Treatment, temperature, and white-cell counts in case 2 (treated with folic acid).

These 2 cases improved shortly after the administration of folic acid, suggesting that folic acid is of value in treatment of agranulocytosis. However, cases 3, 4, and 5 improved equally rapidly without folic acid.

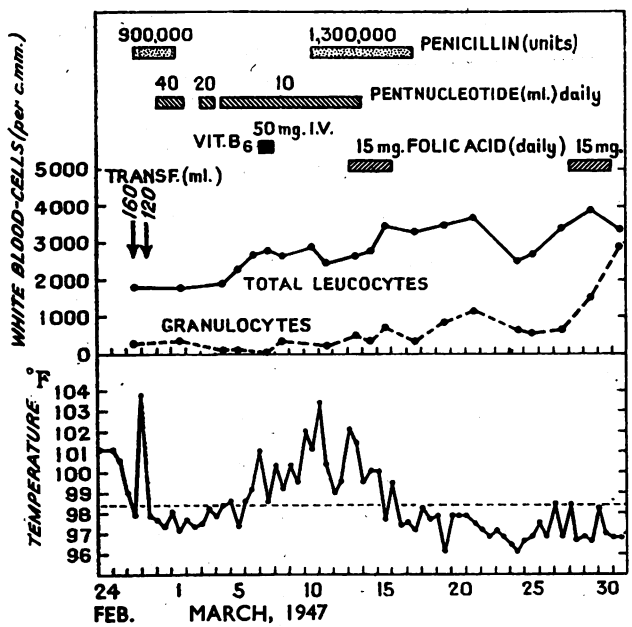

Fig. 1—Treatment, temperature, and white-cell counts in case 1 (treated with folic acid).

Case 3.—A man, aged 34, developed agranulocytosis after twelve weeks' treatment of toxic goitre with methyl thiouracil (total 21·8 g.). His lowest white-cell count was 600 per c.mm. (granulocytes 0%). A blood-count and a sternal-marrow count made only two days after the discovery of the agranulocytosis already showed recovery of the bone-marrow. The blood-count showed red cells 4,320,000 per c.mm., Hb 95%, white cells 9100 per c.mm., granulocytes 47% (segmented 21%, stab 10%, metamyelocytes 6%, myelocytes 7%, disintegrating granulocytes 3%), platelets normal. The sternal puncture showed nucleated cells 34,800 per c.mm., the ratio of myeloid cells to erythroblasts being 13·5 : 1, and 81% granulocytes with increase of young forms and mitosis.

Case 4.—A woman, aged 56, developed agranulocytosis after taking tablets containing acetylsalicylic acid, amidopyrine, 'Novatophan,' 0·3 g. of each, and codeine phosphate 0·1 g. thrice daily for about three weeks. Blood-counts and sternal-marrow counts showed recovery in three days. On July 11, 1947, a blood-count showed red cells 5,110,000 per c.mm., Hb 90%, white cells 2100 per c.mm. (granulocytes 2%), platelets normal, and a sternal-marrow count showed nucleated cells 9500 per c.mm. (promyelocytes 27%, myeloblasts 11%, no mature granulocytes). Next day there was already a slight improvement, the white cells numbering 3700 per c.mm. (granulocytes 11%, stab 4%, metamyelocytes 2%, promyelocytes 2%, myeloblasts 3%). On the 14th white cells numbered 15,200 per c.mm. and granulocytes 77% (segmented 20%, stab 22%, metamyelocytes 22%,

myelocytes 5%, promyelocytes 4%, myeloblasts 2%, abnormal myeloblasts 2%). A sternal puncture on July 15 showed nucleated cells 52,100 per c.mm., the ratio of cells of the myeloid series to nucleated red cells being 6 : 1—a shift to the left but no abnormal number of promyelocytes or myeloblasts. A blood-count showed white cells 26,900 per c.mm., granulocytes 74%, with a well-marked shift to the left.

Cases 3 and 4 had severe agranulocytic membranous angina.

Case 5.—A woman, aged 55, had developed agranulocytosis after three weeks' treatment with sulphathiazole 3 g. daily. Her lowest white-cell count had been 1200 per c.mm., with only 4% degenerated stab cells. Three days later recovery was evident, with 6500 white cells per c.mm., granulocytes 80% (segmented 25%, stab 42%, metamyelocytes 6%, myelocytes 6%, promyelocytes 1%, myeloblasts 1%). Sternal puncture on the same day showed nucleated cells 47,400 per c.mm. the ratio of cells of the myeloid series to nucleated red cells being 10 : 1, with a pronounced shift to the left.

The temperature curves, treatment, and variations in total white-cell and granulocyte counts in these cases are shown in figs. 1–3.

DISCUSSION

The impression first gained, that in cases 1 and 2 folic acid had probably been a factor in recovery, was corrected by observation of cases 3, 4, and 5, who received

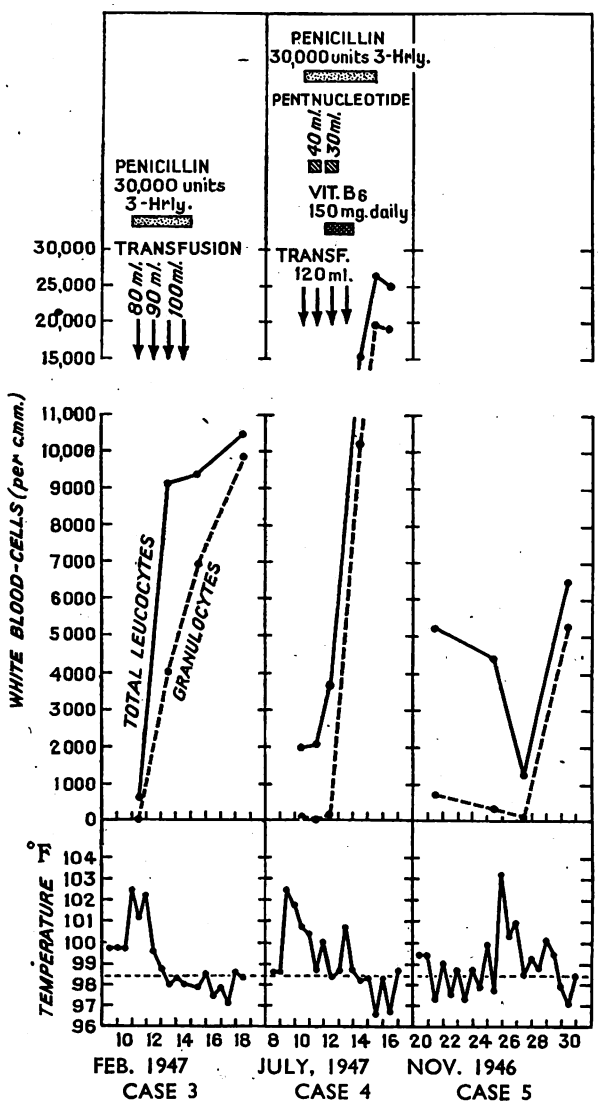

Fig. 3—Treatment, temperature, and white-cell counts in cases 3-5 (not treated with folic acid).

no folic acid. On comparing the courses of the 5 cases, with particular attention to the temperature charts, it seems probable that in cases 1 and 2 the improvement manifested shortly after the administration of folic acid was in fact a spontaneous remission. The diagrams published by Black and Stanbury (1947) suggest a similar conclusion. In all these cases, whether treated with folic acid or not, it appears that the earliest sign of recovery, preceding the reappearance of the granulocytes, is a fall in temperature, though this may be obscured if secondary infection is very severe. If some new treatment happens to be started during this phase, it is easy to gain the impression that the treatment is the cause of the improvement. In general, however, it is only in retrospect that the cause of the improvement can be assessed.

In case 5 the agranulocytosis, due to sulphathiazole, was only transient, was not accompanied by any secondary infection, and cleared without any treatment after discontinuance of the drug; this case and case 2 were both notable for the absence of stomal ulcers and angina during the period of agranulocytosis. Cases 1–4 were all treated with penicillin and received several small blood-transfusions; in all of them the effect of the penicillin on the secondary infection is evident. Cases 1, 2, and 4 all received pentnucleotide and pyridoxine in various amounts without any apparent effect on the disease.

Cases 1 and 2 also received folic acid, and in both of them an improvement in the white-cell count was noted after two days' treatment. It is tempting to attribute the improvement to the folic acid, especially in case 1, where improvement took place on two occasions, both of them after forty-eight hours' treatment with folic acid. None the less, for the reasons stated above, this view does not appear to be justified. During the second course of folic acid in case 1 the number of segmented forms increased less than twenty-four hours after the start of treatment. The leucocyte and granulocyte curves also show an upward tendency coincident with the decline in the temperature before treatment with folic acid was started. In case 2 the temperature had tended to decline three days before folic acid was given, though the sternal-marrow count and the blood-count did not yet show any sign of recovery. With the increase in numbers of leucocytes and granulocytes the temperature became and remained normal.

Cases 3 and 4 are notable for their very rapid recovery, high granulocyte-counts in peripheral blood and bone-marrow being noted two or three days after almost complete agranulocytosis. Both of these cases are remarkable for the fall of the temperature to normal as the granulocytes reappeared, despite the presence of severe ulcerative angina with membrane. In cases 2 and 4 the sternal marrow at the height of the agranulocytosis showed low figures of nucleated cells, but there was a contrast in the proportion of cells of the myeloid series, which was low in case 2 and high in case 4.

Davidson and Girdwood (1947) emphasise that the number of leucocytes and thrombocytes will be increased as a result of treatment with folic acid only when the leucopenia and thrombocytopenia are part of a nutritional syndrome resulting from a deficiency of folic acid. Later they reported (Davidson and Girdwood 1948) a case of pernicious anæmia which developed severe leucopenia (800 white cells per c.mm.) while actually under treatment with folic acid. The folic acid was discontinued, and treatment with liver extract and penicillin instituted, and recovery followed, the white-cell count reaching 9000 per c.mm. in fifteen days.

SUMMARY

Of 5 cases of agranulocytosis due to drugs 2 were treated with folic acid, which appeared to cause improve-

ment, but closer study suggested that this improvement was a spontaneous remission.

My thanks are due to Miss Miluše Doležalová, S.R.N., for her valuable technical assistance.

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PARACENTESIS IN PYOPERICARDIUM

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INTERESTING reports have been published of the conservative treatment of pyopericardium by paracentesis. In one of the most recent cases (Wingfield 1948) penicillin was injected into the pericardial sac.

Price (1946) states that in rheumatic fever a massive serous pericardial effusion is nowadays uncommon and that in rheumatic fever paracentesis is rarely necessary; and Gee (1908) wrote:

> "We dare not puncture upon the bare suspicion that a pericardial effusion may be present; we require that its presence should first of all be rendered most highly probable by other means of physical examination."

But if the case is thought to be one of pyopericardium, early paracentesis must be considered to enable specific treatment, if possible, to be given without delay. Whereas in serous pericarditis the especial dangers of paracentesis are damage to the heart and great vessels or the internal mammary artery, in purulent pericarditis there is also a risk of spreading the infection to one or other pleural cavity.

Ballance (1920) stated the extreme view when he considered that paracentesis of the pericardium should be banished from surgical practice because pericardiotomy was safer.

Sites of Paracentesis.—King (1941) records the many sites for paracentesis which have been advocated: immediately to the left of the sternum through the third, fourth, fifth, or sixth space; through the fifth space immediately to the right of the sternum; external to the internal mammary artery in the fourth and fifth left spaces; external to the apex-beat but inside the area of cardiac dullness; through the posterior chest wall; and by the costoxiphoid approach. Often the lines of reflexion of the pleuræ are behind the sternum to the level of the sixth costal cartilage on the left and of the seventh costal cartilage on the right. Normally the bare area of the pericardium often does not extend beyond the left margin of the sternum, and therefore pericardial paracentesis to the left of the sternum is likely to puncture the pleura. At least one case has been reported in which a serous pericardial exudate so needled has emptied itself into the left pleural cavity, from which it was aspirated.

Risk of Empyema.—During the course of a pericarditis with effusion there may be a concomitant pleurisy; and it has been suggested that it is caused by pressure on one or other lung root. But, if an empyema develops on that side of the chest through which a pyopericardium has shortly before been needled, direct infection is a likely explanation. The following fatal case of pyopericardium is reported because at the time it was considered to be an illustration of this danger; but the eventual outcome was undoubtedly due to dissemination of the infection to the opposite side of the chest.

In June, 1943, an officer of the R.C.A.F., aged 33, became ill in Malta with bouts of fever and loss of weight. After three months his blood was found to agglutinate suspensions of *Brucella melitensis* in low titre, cysts of *Entamœba histolytica minuta* were isolated from the stools, and on sigmoidoscopy the mucosa appeared marbled. The patient was treated with emetine injections, but his general condition remained unchanged and he was invalided to the U.K. with a diagnosis of undulant fever.

In December, 1943, he still felt ill, with headaches and palpitations; one day he fainted while at stool. No fever or abnormal signs were reported on admission to hospital or during the subsequent two weeks, but then his temperature rose to 102°F, and from then onwards he was febrile and had a persistent cough. Radiography of the chest, blood-counts, and agglutination tests at this time showed no abnormality.

On Dec. 28 a few moist sounds had been heard at the right lung base and there was deep tenderness in the right hypochondrium. A day later he was reported to have been very ill and complaining of pain in the left lower chest on breathing. Fever had increased to 104°F, and there were traces of blood-stained sputum, cyanosis, and pleural and pleuropericardial friction to the left of the sternum. The leucocyte-count was 22,000 per c.mm. The liver was enlarged to one finger-breadth below the costal margin, and screening of the chest showed some diminished movement of the right half of the diaphragm. The possibility of hepatic abscess had been considered and the liver needled, but no pus was found, and a further course of emetine had been started, together with sulphapyridine.

On Jan. 2 the patient was very ill, with temperature 101°F, pulse-rate 104, respirations 24 per min., a thready pulse, poor peripheral circulation, and a diminished renal output. The cardiac impulse was not felt, the cardiac dullness extended beyond the left nipple line, and pericardial friction was present. There were a few basal crepitations, liver enlargement as before, and meteorism, but no œdema. The presence of a large pericardial effusion was confirmed by radiography, but its cause remained obscure.

Paracentesis.—On Jan. 4 pericardial paracentesis was performed through the fourth left interspace 1 in. from the sternal border. The pericardium was felt to be thickened, and $3^1/_2$ oz. of turbid fluid containing thick fibrin flakes was obtained; its leucocyte content was 50% neutrophilic but it was sterile on culture. Within the next three days the condition had deteriorated and cardiac tamponade was well marked; the blood-pressure was 102/90, and the leucocyte-count had risen to 48,000 per c.mm. A further $1^1/_2$ pints of stinking pericardial pus was aspirated through the fourth left interspace, and this was reported as containing short-chain anaerobic penicillin-sensitive streptococci.

Operation.—The patient was then seen by the late Mr. Tudor Edwards, who performed an open drainage of the pericardium under local anæsthesia, the fourth, fifth, and sixth costal cartilages on the left side being resected. More than 2 pints of thickened pus was sucked from the pericardium. At this time 20 ml. of clear fluid was withdrawn from the pleural cavity. Pericardial washouts with penicillin followed, and the pericardial sac became perfectly clear and glistening, but within two days the left pleural effusion had increased considerably, a specimen of the fluid now growing anaerobic streptococci.

During the next two weeks, at repeated needlings of the left pleura, $3^1/_2$ pints of exudate was withdrawn and penicillin 60,000 units was inserted; penicillin was also given parenterally. With this treatment the pleural exudate had become much clearer, but there was evidence that it was loculating, and it was decided to drain the pleura through an intercostal catheter. Nevertheless the temperature began to rise again, and there were now signs of fluid at the right base, which was sampled and found to grow streptococci. Four days after the insertion of the intercostal drainage on the left side the right pleural cavity was drained similarly. After this the right lung collapsed, there was an ever increasing toxæmia, with respiratory embarrassment, and the patient died eight days later. Necropsy was not performed.

The costoxiphoid approach for pericardial paracentesis was first suggested by Larrey (1829) and has since been used repeatedly, but the references to this method appear most frequently in the continental reports, English workers having emphasised a transthoracic approach. But Rowlands (Rowlands and

Turner 1937) considered that the safest approach for needling was a subcostal one, and Horsley and Bigger (1937) have favoured it in suppurative pericarditis.

Briefly, a needle or a fine trocar and cannula passed from the left costoxiphoid notch upwards, backwards, and slightly outwards immediately behind the costal margin avoids the peritoneal cavity and, on piercing the diaphragm, immediately enters the pericardial sac. Therefore, when pus is being aspirated, soiling of the pleural cavity is avoided.

I wish to thank Dr. Geoffrey Bourne for his comments on this case.

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Reviews of Books

The National Health Service Act, 1946, Annotated

Together with various Orders and Regulations made thereunder. S. R. SPELLER, LL.B., secretary and director of education, Institute of Hospital Administrators. London: H. K. Lewis. 1948. Pp. 498. 42*s*.

Mr. Speller provides an annotated text of the National Health Service Act, and the texts of 29 orders and regulations made thereunder. Despite his industry, and the celerity of his publisher, he has been unable to keep up with the spate of statutory instruments; but he has ingeniously met the difficulty by including a supplementary index which itemises the contents of a further 18 orders and regulations.

The foreword expresses a modest hope that the book "may provide a useful guide to the Act and to delegated legislation thereunder, alike for members of the legal profession and for those engaged in the administration and provision of the health service." It will; in fact it seems destined to become the standard work on the subject. The main index, of some 60 pages, stands up well to hard sample testing, and the annotations are clear and concise. On p. 8 Mr. Speller even attempts to define a specialist—a task which the Royal Colleges in their wisdom have by-passed.

Most of those whose duty it is to make the Act work have found little time to familiarise themselves with even a part of the relevant legislation. Here in convenient form are provided the orders and regulations on regional hospital boards, executive councils, general dental services, general medical and pharmaceutical services, superannuation, and many other matters. A second edition will unfortunately but usefully contain many more. (Room for these could be partially derived from omitting some of the more technical orders of local application only, such as the Monmouthshire and Rutland Executive Council Order.) Possibly Mr. Speller will consider including also at least a digest of the more important circulars and memoranda issued by the Ministry of Health, which so far, perhaps inevitably, have had a limited circulation.

Clinical Laboratory Methods and Diagnosis

(4th ed.) R. B. H. GRADWOHL, M.D., D.SC., pathologist, Christian Hospital, St. Louis, Missouri. St. Louis: C. V. Mosby Co. London: H. Kimpton. 1948. Vols. I and II, pp. 2284; vol. III, pp. 864. £10 10*s*.

THE latest edition of this well-known compendium appears in three volumes instead of two. The section on tropical medicine, parasitology, helminthology, and allied subjects has been bound in a separate volume, and the name of Dr. Pedro Kourí, of Havana, is very properly placed on it. This section remains one of the best accounts of the subject, and the lavish standard of illustration has been maintained.

Dr. Gradwohl states that every section has been brought up to date, and we may thus avoid a catalogue. Any section into which the reader dips is likely to offer evidence of this detailed revision, and the man who uses the index will hardly find any topic left out. The section on the Rh factors is very good, and a gallant attempt is made to explain "blocking" antibodies. The hæmatological colour plates are still disappointing; they picture results obtained almost exclusively with Giemsa stain, now rarely used by itself; indeed, the text recommends its combination with Wright's stain. The techniques given are those popular in America, and current British methods are often omitted: for example, the Haldane hæmoglobinometer is not mentioned though other less reliable instruments are fully described. And, as in so many comprehensive books, there is nothing to indicate which of several alternative methods is the best.

The fourth edition does not differ from the third so much that replacement is essential; but every laboratory should have one or other on its reference shelf.

Hæmostatic Agents

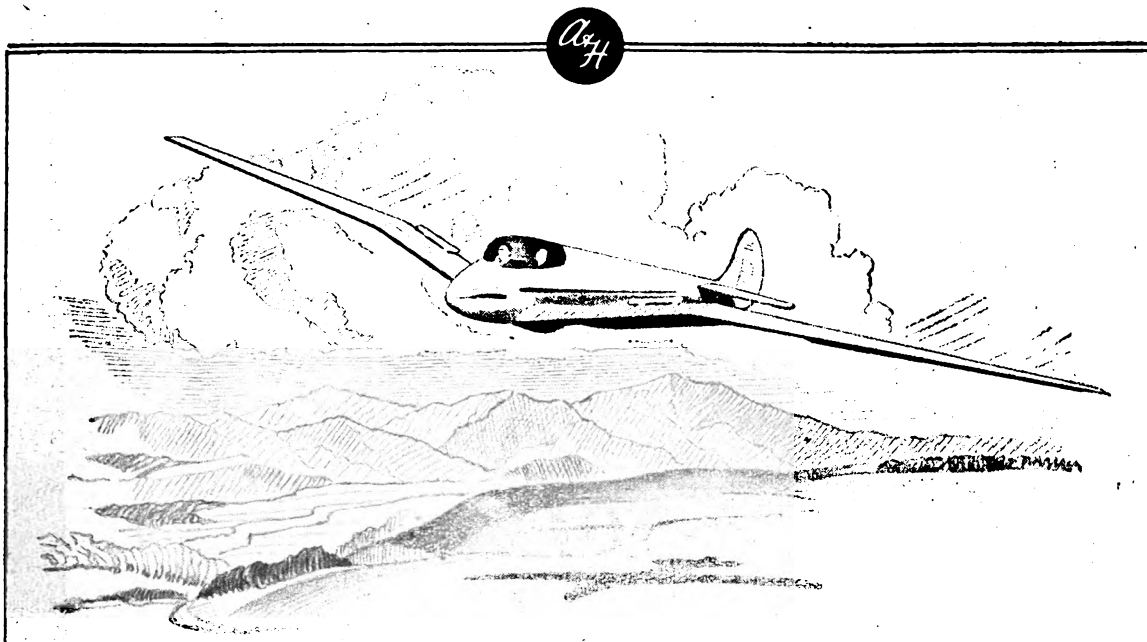
WALTER H. SEEGERS, M.S., PH.D., professor of physiology, Wayne University College of Medicine, Detroit; ELWOOD A. SHARP, M.D., SC.D., director, department of clinical investigation. Springfield, Ill.: C. C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 131. 25*s*.

THIS monograph deals competently with the preparation, properties, and use of the absorbable hæmostatics fibrin foam, oxidised cellulose, and gelatin sponge, with and without the addition of thrombin. There is a not very clear introductory section on the mechanism and biochemistry of blood clotting, and then a reasonably full account of the preparation and use of thrombin. Bovine thrombin and fibrinogen can be used as hæmostatics provided they are used only topically, and experiment has shown that sensitivity does not develop in patients when these materials are applied. The departments of surgery in which these absorbable hæmostatics can be employed are detailed, and clear instructions about the techniques for getting the best results are given. Finally comes a list of no less than 370 references, many of them not very relevant to the matter discussed.

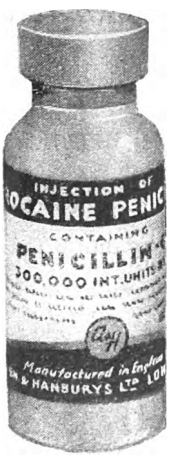
The book is well produced and contains some fine colour photographs. It is a disadvantage, however, that the review of this rapidly developing subject stops short in 1946; and the question of hæmostasis in the hæmorrhagic diseases is ignored.

Treatment and Disposal of Industrial Waste Waters (H.M. Stationery Office. 12*s*. 6*d*.).—A publication of the Department of Scientific and Industrial Research, is the first new British book on this subject in 35 years. It describes much of the work of the water pollution research laboratory set up by the department in 1927; but it also sets out the chief results reported elsewhere.

Identification of Tumours (Philadelphia and London: J. B. Lippincott. 1948. Pp. 397. 36*s*.).—The author, Prof. N. Chandler Foot, of New York, says that his "ready reference book" for use in the diagnosis of tumours is intended for use "by student, pathologist, surgeon or practitioner." A chapter is given to each tissue, organ, or system, and the commoner tumours are listed with brief notes on their source, site, relationships to age and sex, gross and microscopical appearances, metastasising propensity, and prognosis. At the end of the book these tumours are arranged in tabular form under the headings of type cell, stroma or matrix, differentiation, mitotic figures, other features, chemical admixture, and diagnosis; and the whole is illustrated by 241 photomicrographs of very varying quality. The objection to this labour-saving attempt is that morbid histology cannot be learned or honestly practised by any penny-in-the-slot method. There is only one road, which is long and arduous, though very satisfying to the few who are willing to travel it. The trained morbid histologist will find the "ready reference book" quite insufficient; the laboratory technician in training may for a time be pleased with it, but will discover that its help is specious; and the medical student will learn more surely from his own teachers.



Prolonged action



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THE LANCET

LONDON: SATURDAY, DEC. 4, 1948

Underpaid

WHAT came out most clearly from the Conference of Local Medical Committees last week was the conviction of general practitioners up and down the country that in the new service they are being underpaid. Delegate after delegate testified to the hardships that falling incomes were causing in their constituencies; and these consistent reports made it clearer than ever that many practitioners—especially those with practices in rural, semirural, or suburban areas, or in resorts where the proportion of the elderly or invalid is high—are getting an inadequate return for a heavy day's work. It may be (as Dr. GUY DAIN believes) that many will find at the end of their first year in the service that their total receipts amount to much more than four times their first quarter's cheque. But in general it seems unlikely that any adjustments that can be made within the sums now allotted for capitation, mileage, and inducement funds will suffice to overcome the present discontent.

The progress reports given to the conference also showed once more that work—particularly work in the consulting-room—has increased everywhere. Dr. DAIN pointed out one aspect of, and one reason for, this increased work when he said that "we no longer are called to see a patient, we are called to see a family." This is more and more true. Whether the doctor is called in or is visited, no financial barrier remains to prevent his being asked to advise on each and every ailment afflicting each and every member of the family. Perhaps for the first time, he fully realises the scope of the task he undertook when he set out to be the family doctor. It is this extra work per patient (or per family) that has made most doctors already busier than they have ever been in these two summer and autumn quarters—quarters which are usually regarded as the healthier part of the working year. And because they are so busy now, many look uneasily to the winter months ahead, and wonder what extra load these months will bring. The conference deserves credit because it showed no unwillingness to undertake extra tasks which under suitable conditions should provide more opportunity for early detection of illness and for preaching and practising positive health. But the members were certain that the present terms do not allow for, or encourage, the fullest and most careful service, and that they do not even offer sufficient payment for work done—except perhaps to the men with the largest practices, who are seriously overworked.

Ways of alleviating hardships have been sought, and it is hoped that early payment of subsidies from the inducement fund to doctors in the hardest-hit practices may give some help. It is also being pointed out to the Treasury that the total sum set aside for the capitation pool, calculated with the expectation of employing some 17,900 practitioners, will hardly suffice to remunerate the 19,400 who are now known to have joined the service. Certainly, with this increased number, unless there is a proportionate increase in the pool, it will be very difficult to give effect to the recommendations of the Spens Committee and see to it that the various incomes which that committee suggested for different portions of the profession are really attained. It was announced that a careful survey of actual practice incomes from State sources is being made in one of the major counties, and that the result of this survey will be placed with little delay before the Whitley Council, when the case will be argued for a capitation fee much higher than at present—large enough, it is hoped, to translate the Spens promises into fact.

Some discussion took place on the desirability of a further limitation of doctors' lists, but no general agreement was reached for the time being. Though it was agreed that, with the bigger demands on practitioners, it is becoming difficult, if not impossible, for those with the really large practices to satisfy the demands and needs of their patients, it was felt that the redistribution of patients in industrial areas which would take place if practice ceilings were lowered would in itself do little to relieve the situation. Many of the doctors with lists which are not inflated, and which would still be permissible even after any likely reduction was made, are reporting themselves already fully extended; and it would be no comfort to them to offer them further patients whom they could not contentedly accept. The chief help that such a limitation would give would be that, combined with an increased capitation fee, it would allow the industrial practitioner to give more care to each patient and would provide many more openings in such areas for new entrants to practice. The principal need is for an increase in the capitation fee. Next after this was placed the separation, and generous subvention, of the mileage fund. Basic salaries, unless paid from a separate fund, resolve fewer difficulties than they cause.

That some solution must be found is clear. Delegates were deeply concerned about what most of them regard as a deterioration in the mode of practice. They rightly showed that they have no wish or intention to perpetuate conditions which do not allow a doctor to give an unhurried and reasonably efficient service except at grave financial cost to himself.

Surgery in Portal Hypertension

SURGICAL relief of obstruction of the portal circulation in man is a newcomer among feasible operations. In animals the Eck fistula has long been a recognised aid to physiological research; but it carries a fatality-rate which has encouraged the belief that portacaval anastomosis is fatal in human beings. The work of BLAKEMORE and LORD and of WHIPPLE [1] has dispelled all doubt that portal blood can be shunted into the systemic circulation, before it has passed through the liver, without serious consequences to the metabolic economy of the human body; it has brought general recognition that most of the symptoms of Banti's syndrome, and some of the symptoms of hepatic cirrhosis, are due to a rise of pressure in the portal system; it has indicated that "Banti's disease" is not a disease but a syndrome; and it

1. See *Lancet*, 1946, 1, 743.

has explained why splenectomy has only occasionally relieved those suffering from this syndrome.

Operation for portal hypertension is indicated chiefly for relief of the hæmatemeses which are the most usual cause of death in those afflicted. It depends for its success, at least in the first instance, on discovering the site of the causal obstruction to the portal blood. (The importance of this can be understood from a study of fig. 5 in LEARMONTH and MACPHERSON'S paper, which appears in this issue.) The essence of the operation is to anastomose the obstructed section of the portal bed to any large vein of the systemic circulation which is anatomically convenient. There are therefore a number of alternative sites for the anastomosis, none of which is applicable to all cases. Thus obstruction due to cirrhosis of the liver can be overcome by a portal-systemic shunt at any point of suitable size in the portal tree, whereas obstruction of the splenic vein would not be relieved by joining the portal vein to the inferior vena cava. LEARMONTH and MACPHERSON record their experience in 16 cases of portal hypertension, the largest series so far published in this country. In 9 cases they performed a lienorenal vein anastomosis (after splenectomy and left nephrectomy) with 6 excellent results, 2 deaths, and 1 case too recent for evaluation; in 3 cases of splenic vein obstruction they removed the spleen with good effect; and in 4 cases they were unable for technical reasons to achieve what was required. They find that cases of portal hypertension fall into three clinical groups—the acute, the episodic, and the chronic—and that it is the last group that benefits most by operation. They emphasise the need to make sure that hæmatemesis is due to portal hypertension and not to lowered prothrombin levels in the blood caused by liver damage, and also to make sure that any patient operated on possesses two normal kidneys. To praise their work would be almost impertinence.

For accounts of alternative methods of producing portacaval shunts, and for further details of the selection of cases, the techniques available, and the postoperative treatment, one must turn to American sources. BLAKEMORE [2] in 1947 had done 23 portacaval shunts, 15 being accomplished by the same technique as LEARMONTH and MACPHERSON used. In 1 case the splenic vein was anastomosed to the vena cava, and in 7 an end-to-side junction of the portal vein to the vena cava was done. In this series there were 4 deaths. The junction of the portal vein to the vena cava has the obvious advantage of providing the most complete possible shunt of portal blood, and its size and the speed of blood flowing through it give the best guarantees that the hypertension will be relieved and that thrombosis will not occlude the shunt. Morbid changes in and around the portal vein, or a block in the portal system distal to the point where the splenic and superior mesenteric veins join, may make this procedure impossible or useless. It also suffers from the disadvantage that work on the upper part of the inferior vena cava must be rapid if the kidneys are to survive, since they will tolerate venous obstruction for only 15–20 minutes. WELCH [3] has described an ingenious method of overcoming this difficulty, but the technical problems, especially when the liver is enlarged, must be great. LINTON [4] has described 4 cases where splenectomy and injection of œsophageal varices had been performed without relief, in which anastomoses of the superior mesenteric vein to the vena cava, of the inferior mesenteric to the ovarian vein, of the splenic vein to the renal vein, and of the inferior mesenteric to the left adrenal vein have been carried out. Only the last case was unsatisfactory, probably because extreme technical difficulties prevented veins of suitable size being anastomosed. LINTON believes that an end-to-side lienorenal vein anastomosis is the most satisfactory type of portacaval shunt, and that it should be done at the same operation at which the spleen is removed if the surgeon is not "to miss the bus." BLAKEMORE [5] has now brought his series up to 40 cases, with an operative mortality of 12%. He also favours the end-to-side lienorenal anastomosis (which makes sacrifice of the left kidney unnecessary) and he prefers direct suture of the vessels to the 'Vitallium'-tube technique (of which he was a pioneer). It is naturally essential to the success of the operation that the shunt should remain patent, and to achieve this the anastomosed veins must not be twisted or lie kinked or angled. Postoperative abdominal distension and early ambulation may cause pressure on, or tension of, the anastomoses, and it is well to prolong the clotting-time with heparin while the patient is in bed.

An operation in which selection of suitable cases, choice of the most suitable site for shunt, and execution of the anastomosis are all matters of considerable difficulty, is for experts only. The portacaval shunt is, however, no longer an experiment. It can save life in cases where hæmatemesis from œsophageal varices makes death the early and sole alternative. Its more remote effects have still to be assessed.

2. Blakemore, A. A. *Surg. Gynec. Obstet.* 1947, 84, 645.
3. Welch, C. S. *Ibid*, 1947. 85, 492.

Changing Ends of Social Medicine

IN some mythologies, giants peopled the world before men. Dr. J. A. CHARLES, in his Bradshaw lecture last week,[6] presented just such a pensive notion of the public-health service; and indeed, the great names in which he dealt—Chadwick, Simon, Bristowe, Barclay, and others—belonged to personalities which in the main were a good deal more than life size; or appear so through the dust they raised. We owe much to them: to Chadwick's description of the squalor in which the poor lived; to Simon's classical reports when he was medical officer of London; to Bristowe's investigation of phosphorus hazards; to Anstie, Carr, and Hart, THE LANCET'S commissioners, for their accounts of workhouse infirmaries; to Lankester, who succeeded Thomas Wakley as coroner of Middlesex and maintained his tradition; to Tom Taylor, Simon's secretary on the General Board of Health, who wrote *The Ticket of Leave Man* and later gave up public health to edit *Punch*. They were all-round men, widely educated, the doctors among them distinguished in their profession, with minds that ranged deep into

4. Linton, R. R. *New Engl. J. Med.* 1948, 238, 723.
5. Blakemore, A. H. *Surg. Clin. N. Amer.* 1948, 28, 279.
6. Victorian Medical Administrators. Delivered at the Royal College of Physicians on Nov. 23.

and round their subject. Dr. CHARLES regretted that by 1890 the pattern of the whole-time medical officer of health was already set, and becoming fixed among sanitary details; though later, he admitted, it was enriched by the addition of maternity and child welfare. The M.O.H. of today, he thinks, specialises too early, lacks the breadth of outlook of the pioneers, and seldom, once he has settled into his job, has time to acquire the ripeness of judgment that social medicine demands. Routine work hampers him. Dr. CHARLES believes that the M.O.H. should have, like M'Gonigle, a pastoral mission among his community; but those who do their work in such a spirit are few.

But if the men have changed, so has their destiny. The pattern of sanitary detail is melting before our eyes, as Dr. J. N. MORRIS pointed out not long ago in a broadcast talk.[7] Social medicine is nowadays hard to define; it strikes into so many aspects of contemporary life. Perhaps the regeneration of man must always begin with a good drainage system: certainly the Victorian administrators and philanthropists found that people who are forced to live like beasts can behave like them. Lambert, working for the Rockefeller Foundation in the South Seas, proved that for a people ravaged by hookworm the first civilising procedure is to build latrines. The same principle doubtless holds for the sick native races of Africa; and an echo of the message is to be found in the French film, *Monsieur Vincent*, now running in London: "You cannot save people's souls until you have given them a life worth living."

Social medicine began in squalor, and squalor is not yet defeated. Of the six needs of man—air, water, food, housing, clothing, and fuel—set out in 1848 by Dr. Hector Gavin in his book, *Sanitary Ramblings*, several are still defective: our air is polluted, a pure water-supply is not universal, houses are too few, and fuel costly. There is still much sickness, though relatively little from defective sanitation. Much of it is hard to define except as sickness of the mind or spirit—nervous and psychosomatic illness, and what Dr. MORRIS called "unfitness, incapacity for work, and mere absence of wellbeing." Here is a wide and difficult country opening before the M.O.H. His specialty is rapidly spreading into a social service, and as well as preventing disease by physical measures he must now take part in promoting health by social action. That is how Dr. MORRIS sees it; and he illustrated his point from the case of the man with the chronic duodenal ulcer—a physical disorder associated with some emotional disturbance such as money trouble, a desire to achieve more than he is really capable of achieving, disharmony in his personal relationships; a disorder, in short of the man in his social setting. Duodenal ulceration is only one expression of this disorder. Social medicine, because it deals with man as a social being, a member of his group, must take account of the disease in all its manifestations, and if, as some think, nervous and psychosomatic disorders are increasing, it means that more and more people are finding it hard to adjust themselves to their surroundings. Dr. MORRIS would have us look for the social forces which have encouraged such disorders. The question can be approached in two ways: we may ask why so many people have personalities that are liable to break down; or why society, as it is, causes the breakdown of so many people. Neither question can be answered alone, for society shapes personality and people make society. The growth of personality and character, and, up to a point, of intelligence, are related to the stimuli provided by the environment. The individual has to adjust himself to his own potentialities—to learn to live with his own nature—and to do it within the cultural pattern of his group. If this is narrow or warping, many of his potentialities will die of inanition, just as his muscles would waste if he spent his life in a cage. As Dr. MORRIS put it, "personality is not finished off, complete, in early childhood." The culture in which the child grows up is first transmitted and interpreted by the family unit; and parents whose opportunities have been narrow will transmit a thin and imperfect version of their nation's culture to their child—a version which he may never get the chance to expand or outgrow. A society composed mainly of dwarfed or limited personalities will have a narrow culture. Thus a nation which breeds many skilled craftsmen, though it may be turbulent at times, will be mentally alert and growing, whereas a nation of factory hands might well be very different. Dr. MORRIS suggested that "our urban industrial culture is restlessly changing, complicated and contradictory, impersonal and anonymous; work is often reduced to the lowest common denominator of the many meanings that work can have." Yet the same sorts of people who may suffer mentally and physically under this kind of stress—of which boredom is perhaps the leading characteristic—may respond to another kind of stress by growing beyond recognition: Dr. MORRIS cited a convoy of Wingate's Chindits who arrived at a hospital in India in 1944. "It was hard to believe," he said, "that these remarkable personalities had started as just ordinary youngsters from the mean streets of our industrial towns."

Here then is the new enterprise to which social medicine must address itself—the task of finding out how men living in society can grow to their full mental and moral stature, and how the State can provide them with the opportunities for such growth without forcing them into a statutory pattern. This is no less than the problem of government which has confounded rulers since men first began to live in groups. We have seen many attempts to solve it: in some, the State overrides the individual, in others the individual can coerce the State—but only at the expense of other members of the community. Neither will serve. Men have yet to learn to live together; and perhaps one of the reasons they have failed to do so successfully is that there has never so far been a community whose adults were fully grown. Physical well-being is important, but social medicine must also study the frustrating and stultifying forces in our culture which cause ill health of the mind; and ultimately it must be in a position to suggest remedies. Here is a giant's undertaking for medical officers of health; and if we agree with Dr. MORRIS that men grow in response to the demands and opportunities of their calling, then Dr. CHARLES's fears can be allayed: another race of giants is on the way.

7. Social Science of Medicine. Broadcast in the Third Programme on Sept. 24.

Annotations

THE NEGLECTED FAMILY

IN the Lloyd Roberts lecture published in these columns on Nov. 20, Mr. R. M. Titmuss pointed out that, though we respect the family as a social unit, we behave in a way that makes the propagation of children a common source of poverty. This behaviour is not deliberate: it is merely the result of our finding it simpler to ignore the problem. The question is whether we can afford to go on doing so.

In Sweden public concern about the position of the family has been awakened by the work of two population commissions.[1] These have put forward many practicable schemes of assistance, since adopted by the Swedish parliament. The new family allowances, which are tax-free and given for first as well as subsequent children, amount to 260 kroner per child per year (about £18). They are given irrespective of income, and for those earning up to 20,000 kroner they give more relief than did the former tax rebates, which have been discontinued. The object of this change was to benefit the large families, most of which got no benefit from the rebates because their income was not large enough to attract tax; but it works to the disadvantage of those with more than about £1380 a year. In Sweden it is thought more important to raise the general standard of living than to enable the middle classes to obtain for their children special advantages in education. But in this country, until the public system of education has considerably improved, a great many people of the professional and managerial classes will continue to restrict their families to the number to which they can give what they think a good education. For most of them this number is already small, and with the rise of school and other fees it is getting smaller. Family allowances would have to be on a very different scale in order to have any significant effect on a far from negligible section of the community. For this section there would be more incentive to childbearing, as well as to individual effort, if income-tax rebates for children, so far from being abolished, were to rise proportionately with income, as proposed by Mr. Richard Hughes.[2]

The problems of the family cannot, of course, be solved by rebates or allowances alone. Children not only cause poverty but also severely restrict the activities of their parents. In the report on maternity in Britain, reviewed in a leading article a fortnight ago,[3] it is shown, for example, how mothers with large families are unable to make full use of the maternity services. Family ties prevent them from getting early and regular ante-natal supervision and from taking their children to welfare centres. They live in the most overcrowded homes, yet are unable to leave their families for a hospital confinement. Often they have to get up a few days after delivery to supervise and take an active part in the housework. In addition, their impoverishment is shown by economies, progressing with each new birth, on maternity clothes and layette. In planning satisfactory health services, clearly we must think in terms of the family unit rather than of individuals, and in this respect Sweden has much to teach us.

The fact is that in many directions our policies will be unsound unless they are based on a detailed knowledge of the social, economic, and medical needs of the family in this country, and it is important that research should be stimulated along broad lines. New family budget studies, and inquiries into the burden of domestic work in the home, and into the lack of spare time which of necessity arises from having many children, are all important and have a medical as well as a social significance. Dr. Stella Instone's report on the housewife, appearing in our present issue, is an independent study with no little relevance to the birth-rate, and we are glad to hear that others are in progress. The results of all these investigations must not remain buried in the pages of specialised journals, but must be used to arouse and sustain the public interest which is a necessary preliminary to any adequate legislation by the Government. Meanwhile, without legislation, there is a great deal that the Government could do if they were to put encouragement of the young family high among their purposes. The change of policy about Service allowances made in 1945 was socially retrograde: as Titmuss says, "childlessness was rewarded, and disapproval was shown to those with more than two children." Yet last week, when Service pay was again revised, this basic error was perpetuated.

1. Gille, H. *Population Studies*, 1948, **2**, 3, 129.
2. *Times*, Nov. 23, p. 5.
3. Maternity in Britain: report by a joint committee of the Royal College of Obstetricians and Gynæcologists and the Population Investigation Committee. London: Oxford University Press. 1948.

ENTEROGASTRONE

SOME years ago Kosaka and Lim[1] obtained from the mucosa of the small and large intestine of dogs an extract which was found to inhibit gastric secretion; the active principle they called enterogastrone. Later Ivy and his co-workers[2] prepared a more potent extract from the duodenal mucosa of swine, and further work on animals has suggested that this substance is a safeguard against the development of peptic ulcer. Ivy, and Greengard and others[3] have, indeed, evidence that in man the administration of enterogastrone by mouth helps to prevent the development or recurrence of ulcers.

Hopes born of these experimental and clinical studies are shaken by a report from Sandweiss and his colleagues,[4] who treated 48 ambulatory patients, suffering from proved duodenal ulcer, with enterogastrone parenterally and by mouth. After injection most of the patients had pain, and the first two to be injected developed urticaria. The results were wholly disappointing. Only 55% became symptom-free, while 70% relapsed within one year after treatment. (The comparable figures for an ambulant diet-alkali régime were 79% and 57%, and for treatment with parenteral injections of distilled water 59% and 92%.) This does not detract from the interest of previous experimental findings in Mann-Williamson dogs—animals subjected to a gastrojejunostomy plus surgical duodenal drainage—where enterogastrone treatment appears to protect against jejunal ulcer.

DANGEROUS DRUGS

LAST year's official figure for the number of addicts to dangerous drugs in Great Britain and Northern Ireland is 383.[5] Of these, unhappily, no fewer than 82 were doctors, of whom 10 were convicted of violating the Narcotic Laws. Morphine and diacetylmorphine are, it seems, the principal drugs of addiction, and in about 95% of cases only one drug is used. Cocaine is an increasingly rare cause of addiction; indeed pethidine is said now to take precedence over it. The only real illegal traffic is reported to be among alien seamen who bring in opium and indian hemp for use by themselves and their fellow-countrymen in the seaport towns, including London. Opium remains almost exclusively the drug of the Chinese smuggler and smoker, while the

1. Kosaka, T., Lim, R. K. S. *Proc. Soc. exp. Biol. Med.* 1930 **27**, 890.
2. Gray, J. S., Bradley, W. B., Ivy, A. C. *Amer. J. Physiol.* 1937, **118**, 463.
3. Greengard, H., Atkinson, A. J., Grossman, M. I., Ivy, A. C. *Gastroenterology*, 1946, **7**, 625.
4. Sandweiss, D. J., Sugarman, M. H., Lockwood, B. C. *J. Amer. med. Ass.* 1948, **138**, 552.
5. Traffic in Opium and Other Dangerous Drugs: Report to the United Nations by His Majesty's Government in the United Kingdom of Great Britain and Northern Ireland for 1947.

traffic in indian hemp originates with the Indian, Arab, or negro seaman and extends by way of the dock areas of London to the West End, where it is smoked and peddled on a small scale by a few coloured men.

During the year there were only 20 instances of prescriptions forged with a view to obtaining narcotics illegally. The smallness of this number probably reflects less the true demand for illegal narcotics than the known efficiency of preventive legislation. (The duties of doctor and dentist in this respect have lately been described in the new edition of a Home Office memorandum.[6]) Drug addiction is, of course, much less rare than these figures indicate; for some of the commoner drugs of addiction do not come within the province of the report.

RUSSIA, EUROPE, AND W.H.O.

THE second session of the executive board of the World Health Organisation opened at Geneva on Oct. 25 with a setback. Telegrams were read from the U.S.S.R. and Byelorussian members, the former stating that he would not come because the late receipt of the agenda did not allow him to contribute usefully to the discussion, and the latter that he was "prevented" from attending. Although the board replied that it deeply regretted their absence, and still hoped they would be able to come later in the three weeks' session, nothing further was heard. This Russian action certainly did not stem from the delegates themselves, or the health authorities, and must have been political in origin. We trust that the Soviet leaders will speedily return to their former view that world collaboration for health is possible and that one of the few remaining bridges between the East and West should not be permanently destroyed.

The remaining 16 members, including those from Poland and Yugoslavia, did valuable work. The most important item was perhaps the 1950 budget, which —incredible as it may seem—must be ready this month. Discussion of the principles involved led back to the basic question whether a serious effort can be made to raise the level of health of the peoples of the world or whether W.H.O. must content itself broadly with the old-style inexpensive activities of its predecessors.[7] From a body of individuals "technically qualified in the field of health" there could be but one answer, and, after brilliantly dispelling certain hesitations, the director-general, Dr. Brock Chisholm, received the board's mandate to prepare for the next assembly a New Look budget for 1950. Meanwhile the board learned with satisfaction of the establishment of the first of the W.H.O.'s regional organisations, that for South-East Asia, with headquarters at New Delhi, and approved the appointment of Colonel C. Mani, at present the member of the board nominated by India, as regional director. It also decided to leave to the director-general the complicated and thorny subject of allocations to countries for programmes of assistance by means of demonstration teams, experts, fellowships, and medical literature, for which a total of about $1\frac{1}{2}$ million can be used in 1949. A pleasant interlude from administrative matters was afforded by the account of the vast B.C.G. vaccination programmes being undertaken by the Scandinavian Red Cross Societies and the International Children's Emergency Fund and of the proposed epidemiological and statistical research arising out of them.[8] Discussion of a proposal by the member from France, Prof. J. Parisot, to reduce the number, length, and cost of organisational meetings of the governing bodies was deferred to the third session. Now that the end of the organisational stage of W.H.O. is in sight, it should clearly be possible to reduce the budget allocations for meetings of the executive board and the assembly, and also the undue demands on the time both of the members of these bodies and of the secretariat. W.H.O. has not, as yet, followed UNESCO in overloading the administrative side of the staff,[9] but it must constantly guard against the similar danger of spending too much time and money on meetings of its governing bodies.

On Nov. 15, immediately after the meeting of the executive board, there was a two-day conference of representatives of European countries. Of 23 invited, 16 sent representatives, including Bulgaria, Czechoslovakia, Hungary, Poland, and Yugoslavia—but not the Russians. The assembly had decided that, as the headquarters of W.H.O. are to be in Geneva, a regional organisation in the full sense of the constitution will not be necessary for Europe, and that a special temporary administrative office for the health reconstruction of war-damaged countries should be set up instead. The object of the conference was to advise the director-general on the tasks of such an office—i.e., the health needs of Europe which might be met by W.H.O. in 1949 and 1950—and on its location and staffing. Dr. C. van den Berg (Netherlands), who was elected chairman, had a somewhat difficult task because the Czechoslovak delegation, supported by their colleagues from eastern Europe, persisted in trying to reverse the assembly's decision and set up a complete regional organisation, to be located in Czechoslovakia. In view of the very limited funds available, agreement might well have been reached on the compromise proposal of the vice-chairman, Dr. B. Kozusznik (Poland), that a special office should be established provisionally at Geneva, but for the unexpected and stubborn intervention of the delegate of Denmark in favour of Copenhagen. Despite this failure to achieve unanimity, useful information was provided for the secretariat in drawing up plans for 1949 and 1950.

RAPID DIGITALISATION

RAPID digitalisation is required by the patient in distress from congestive heart-failure due to a rapid ventricular rate from auricular fibrillation or other causes. Over thirty years ago Eggleston introduced a method by which dosage was calculated from body-weight. By this method dosage was unnecessarily large; but today, on the other hand, the tendency is to give far too little digitalis and needlessly postpone the relief it gives.

In an inquiry by William Evans and his colleagues[10] twenty patients with auricular fibrillation, heart-failure, and high ventricular rate were each given a series of digitalis drugs, with an interval of 3 to 14 days between each drug to allow the rate of ventricular contraction to rise again. The criterion adopted was the extent of ventricular slowing within 4 hours—a standard which is fully justified because there is reason to think that ventricular slowing is as much the result as the cause of improved myocardial function.[11] Results are usually believed to be better with redigitalisation after a short interval than when the patient is digitalised for the first time; but this difficulty was overcome by administering the preparations in a different order in the various patients. Three drugs—'Digoxin,' lanatosid C, and digitaline (Nativelle)—were found to be the best. Digoxin by mouth was effective within 4 hours, usually with a dose of 2 mg. and always with a dose of 3 mg. Intravenous digoxin 1·5 mg. produced still quicker results, but such rapidity is rarely essential and may be attended with some slight risk. Intravenous strophanthin

6. Dangerous Drugs Acts, 1920 to 1932: Memorandum as to Duties of Doctors and Dentists. D.D.101, 5th ed. H.M. Stationery Office. Pp. 12. 3*d*.
7. See *Lancet*, July 3, p. 17.
8. *Ibid*, Nov. 27, p. 855.
9. See *New Statesman and Nation*, Nov. 20, p. 431.
10. Evans, W., Dick, P., Evans, B. *Brit. Heart J.* 1948, **10**, 103.
11. Luten, D. Clinical Use of Digitalis. London, 1936. Gold, H. *Science*, 1943, **97**, 125.

was not nearly so effective, especially when the dose was no more than gr. $^1/_{100}$, which is generally regarded as the maximum to be given with safety. This seems to refute the Continental view that strophanthin has a special virtue not present in digitalis. However, the purer strophanthin-G (ouabain) was not tested often enough to justify comparison. The older preparations —digitalis leaf (gr. 6) and the tincture (2 drachms)— proved comparatively ineffective, but these doses are small in proportion to those of the other preparations tested. In all the 76 tests toxicity was noted only once. In another study, De Graff and his colleagues [12] report poor results from digitoxin with an initial dose of 1·2 mg. orally in patients with auricular fibrillation and a rapid ventricular rate. This rate was reduced only slightly 24 hours after the drug was given; but the degree of heart-failure was usually severe, many of the patients were elderly, the doses were smaller, and the timing of the observations was different.

It is over 170 years since the historic work of Withering on digitalis. Even now each increase in knowledge brings a fresh problem, and shows once again that in the last resort the correct use of digitalis must be determined for each case individually.

OUR FALLING STANDARDS

MEN do not behave honestly without the help of stringent training. Honesty and truthfulness are no more inherent in them than cleanliness and punctuality. We are born uncivilised, grasping, and self-important, and only learn to live like reasonable citizens after many years' schooling by precept and example. In regretting the increase of crime, and especially of juvenile crime, since 1938, the Archbishop of York, speaking in the House of Lords on Nov. 23, ascribed our national decline in honesty and truthfulness to the many factors which have interrupted this training—the war, the breakdown of home life, and a growing disrespect for law, bred, he thinks, by the multiplication of trifling and unnecessary restrictions. Again, goods are scarce, and the temptation to appropriate them is therefore greater, while police are fewer than they should be. Some recovery from the moral decline that commonly goes with war should now be apparent, but we still lag behind the 1938 level. Thus in 1947, indictable offences showed a 47% increase over the 1938 figure of 78,000, while larceny had increased by 37%, breaking and stealing by 88%, receiving of stolen goods by 141%, sexual offences by 46%, and violence by 58%. More than a quarter of those found guilty of larceny were under the age of seventeen, and a further 12% were between seventeen and twenty-one. More than half those convicted for breaking and stealing were under seventeen, and a further 16% were between seventeen and twenty-one. The increase of offences among those under twenty-one was nearly 70% of the 1938 figure. Actually, there were slight signs of a change for the better in recent years, as Viscount Maugham noted in the same debate. He was borne out in this by the Lord Chancellor, who mentioned that the number of children found guilty of indictable offences declined, erratically, from a peak of 43,000 in 1941 to 36,000 in 1946. Unfortunately the figure for the first half of 1948 is 22,000; so the number for the whole year may be expected to exceed even that for 1941.

The remedies are hard to decide. In the debate all agreed that a bigger police force would help; and all were anxious to see our country recover its former moral standards. It is no use, the Archbishop felt, to expect the Churches to accomplish unaided this moral regeneration: they have been preaching the value of truthfulness and honesty for nearly 2000 years, but "the vast majority of the people of the country no longer pay attention to what is said by the Churches." He made the refreshing suggestion that the State should have a drive for honesty and truthfulness, calling in the help of the press, the cinema, and the wireless. The appeal should be made, he thinks, largely on social grounds, and should call attention to the harm done to the nation by dishonesty and untruthfulness; and in such a movement to train and build up conscience in every department of life the Churches would of course have a part to play. This idea is surely sound and modern. The B.B.C. has already made a beginning, on negative lines, with that excellent series, "Crime Doesn't Pay," which was running last year. The State, by encouraging us to work harder, to save, to travel between the rush hours, to stagger our holidays, sneeze into our handkerchiefs, economise fuel, and keep death off the roads, has already done much to build us better consciences, and it might well expand the good work on the lines contemplated by the Archbishop.

12. De Graff, A. C., Batterman, R. C., Rose, C. A. *J. Amer. med. Ass.* 1948, 138, 475.

U.G.C.

THE University Grants Committee, which was set up in 1919, used to issue quinquennial reports; but these were interrupted by the war, and the one published this week covers twelve years.[1] They were momentous years that have brought big changes. "Any conception that may have existed of the universities as places of cultural luxury catering for a small and privileged class has passed away and will not return. The heightened sense of social justice generated by the war has opened their doors more widely than ever before . . . The phase of their development on which the universities are now entering is beset for the moment with obstacles and difficulties which are the immediate heritage of the war, but it is rich, beyond all precedent, in opportunities." The committee record their view that the principles of central planning and academic autonomy are not irreconcilable opposites, and they believe that the relation between the universities and the State can be regarded as a form of partnership, in which full recognition is given to "the overriding duty of those who follow the academic path to ascertain the truth and to proclaim it without respect to the convenience of Governments." The proportion of university income derived from the State, which was 34·3% in 1935–36, may well be over 60% in 1951–52; and this takes no account of grants for building, sites, and equipment, for which the Chancellor of the Exchequer is prepared to provide £20 million for 1947–52. The committee, whose 16 members include two medical men (Prof. G. W. Pickering and Prof. J. C. Spence), describe the principles on which they act as intermediaries. In this work they have set new precedents of great value to the nation.

1. University Development from 1935 to 1947. H.M. Stationery Office. Pp. 106. 2*s*.

THE KING'S HEALTH

THE following bulletin was issued on Nov. 29:

As a result of relief from walking, standing, and fatigue, improvement in the general health of the King is apparent. This is an important factor in re-establishing arterial circulation to the feet, which is also being encouraged by the appropriate medicinal and physical measures.

In this condition restoration of circulation is a slow process, extending over a period of months. Some improvement has already taken place and there is less cause for immediate anxiety regarding the right foot.

MAURICE CASSIDY
THOMAS DUNHILL
J. R. LEARMONTH
MORTON SMART
JOHN WEIR.

Since Nov. 11 the King has not left his apartments in Buckingham Palace. This more reassuring bulletin was therefore issued after he had had 18 days of rest.

Special Articles

THE WELFARE OF THE HOUSEWIFE

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"Strength and dignity are her clothing; and she laugheth at the time to come."—*Proverbs*, xxxi, 25.

THE housewife and her problems have lately received some attention in the press and elsewhere. But though there have been expressions of sympathy for her difficulties and respect for her courage, no detailed study has been made of the housewife or her daily life. It therefore seemed of interest to assess the welfare of housewives, with special reference to their health, any disorders peculiar to or prevalent among them, and the important causes and results of fatigue in them. The scope and implications of such questions are obviously wide enough to justify a large-scale sociomedical survey. Nevertheless, a small hospital has afforded opportunities for a limited investigation which might serve as a pilot survey for future work.

This report is based on a study of 61 housewives seen with the help of the almoner at the New Sussex Hospital for Women, Brighton. The hospital has 74 beds for medical, surgical, and gynæcological cases, and out-patient clinics are held each day. So far as possible we chose women with young children at home, preferably with large families. Unmarried women, whatever their home responsibilities, were excluded. Our aim was to study the whole-time housewife doing no remunerative work outside her home. So far as possible we selected "healthy" women under hospital care for some purely local complaint, so that the findings could be attributed only to their occupation and environment.

The 61 housewives all came voluntarily for interview. One difficulty, early apparent, was the reluctance, and more often the inability, of many women to spare the time for an appointment. In most cases where an interview was refused this seemed to be due to genuine pressure of work, but in an appreciable minority it was due to bad management of the day's commitments.

The housewives in the survey are all drawn from the income-group of £5 a week or less (husband's wages). Their ages range from 26 to 64. No attempt has been made to concentrate on a particular age-group, though most of the women were under 50; they could all be described as working women. They all lived in, or within 15 miles of, Brighton and Hove. It was decided to take in each case the fullest possible history, even at the risk of obtaining many irrelevant facts. Often it was not until she had been talking for some time, gradually gaining interest and confidence, that a woman made any remark of special importance. Each housewife was asked the same questions.

Not one of these women resented the interview. Their complete lack of reticence was surprising, as was the eagerness with which they answered questions about their life and work. This suggests that lack of recognition by her family may contribute to the disgruntled first impression which the working housewife often gives.

Each woman was first questioned on the subjects given below. This conversation was made as informal as possible, and no housewife needed any encouragement to talk. On the contrary, they seemed to welcome an opportunity of airing their problems, and many expressed surprise that these were thought to be worth discussing. Each woman was then given a careful physical examination. Any noteworthy findings were recorded, together with an impression gained of her intelligence and general appearance, especially as regards fatigue. This was followed by an interview with the almoner, which served to amplify, and often to augment, the facts already obtained about the background of each woman. Where it seemed necessary, the woman was visited in her home. Ideally a visit should have been made in every case, but this was impracticable.

Whenever domestic difficulties were found to dominate the picture, the housewife in question was followed up, and in many cases of this type the almoner gave practical help and advice. Often—and especially where the veracity of the housewife was in doubt—the husband or other members of the family were questioned.

In this account no attempt has been made to present accurate statistical records, for many aspects of the welfare of the housewife cannot be statistically assessed. It might almost be said that none of her problems is absolute, but that each one arises from the effect of circumstance on the individual.

The main points in the history and examination of each case were as follows:

HISTORY

Age. Marriage: duration and nature. Husband's work. Own work; home commitments; amount of help available. Children: ages, number at home.

Past health. Housing conditions. Sleep: duration and effects.

Appetite: fair share of rations; meals for a day. Leisure: recreations.

Obstetrical history; menstrual history. Anxiety. Smoking. Holidays.

EXAMINATION

General appearance, facies, intelligence. Posture. Hands. Feet. Back. Legs.

Cardiovascular, respiratory, digestive, and nervous systems. Skin. Joints. Endocrines. Emotional state.

Summary of incidental findings.

The almoner inquired briefly into the social, economic, and domestic background.

HISTORY

Circumstances of Marriage.—Most of the housewives said that their marriage had been happy. On further questioning many of them qualified this statement with such remarks as: "Apart from arguments . . .," "On the whole . . .," or "I mustn't grumble, considering. . . ." Serious unhappiness, sufficient to cause constant preoccupation, was admitted in 10 cases.

Housing.—In 13 cases the housing conditions were seriously inadequate as regards the number of rooms or the physical environment. In many more cases there were constant difficulties owing to sharing accommodation with other members of the family.

Work.—Nearly all these housewives were fully occupied with their own cooking, shopping, housework, and laundry. One had help with her housework for two hours on two days a week, 17 were given limited but regular and willing help by other members of the family; in 2 cases the shopping was done by a child or by a neighbour, who asked for 2*s.* 6*d.* an hour for this service; and 4 housewives were doing regular part-time daily work in addition to their home duties.

Children.—The number of children at home ranged from one to thirteen. Children of 12–15 years were the most helpful to their mothers; those who had left school and were going out to work were generally reluctant to help, even at the weekends.

Sleep.—Sleep lasted between 6½ and 11 hours a night; the most usual duration was 8–9½ hours. Nevertheless 53 of the 61 housewives said they woke tired every morning. Several of them dreamed regularly of cooking, shopping, and standing in a queue. A few admitted to waking up at intervals during the night and planning the next day's meals. The majority became most tired in the early afternoon when they were liable to fall asleep at their work or on sitting down.

Diet.—In only 14 housewives was the diet for the day judged adequate, even by present standards. This improper feeding was never attributable to lack of money. The housewife's family always fared much better than she did. Very few housewives took a proper breakfast and supper, and in most the day's food consisted of a cooked meal at midday or in the evening when the family was at home, and snacks at other times. Many women gave up their own rations to the family, but some of those who did not eat properly seemed to lack the inclination for food or the energy to cook for themselves alone. Some women were definitely lazy and only prepared to eat a meal cooked by one of the family at weekends. Throughout the series the consumption of starchy foods was far too high, and most families were disinclined for fish unless it was fried. Very few of the housewives used dried eggs. Mostly their attitude to the planning of meals was one of defeatism and of habit, without the exercise of any imagination. The younger women were more adaptable than the older ones, who had known better days.

Worries.—Only 12 housewives said they had no worries. Each of the remaining 49 had some significant anxiety about marital problems, the family, housing, money, or rationing; and 4 said they were "anxious about everything." The large number of strained tired worried-looking women seen at interviews confirmed the significance of these preoccupations.

Smoking.—There were 27 non-smokers. Of the remainder, only 3 smoked more than twenty cigarettes a day; many were trying to cut down smoking to save money.

Holidays.—There were 17 housewives who had had no holiday since their marriage, and many more had never had longer than a week at a time.

Leisure.—There were 21 women who said they had "no leisure at all." Of the remainder, most were free for an hour or two in the afternoon or evening, but even then they were often occupied with sewing, mending, or knitting.

Recreations.—All but 7 of these housewives went to the cinema, usually once a week but sometimes twice. They all seemed to enjoy this visit, which was the one item that they would not give up to save money. Their reason for enjoying the cinema was usually that it took their minds off their home affairs, but a few women said what they most enjoyed was the chance of sitting down. A few said that even at the pictures they continued to worry about home affairs. They seemed to have no other recreation except 4 women who enjoyed gardening, playing whist, dancing, and listening to music.

CLINICAL FINDINGS

In every case physical examination revealed some noteworthy condition. The most common findings were:

Tired appearance	54
Varicose veins	16
Postural defects	15
Dental and oral sepsis	14
Hallux valgus	10
Hypertension	10
Obesity	9

A significant degree of anæmia was noted in 4 cases, in each of which the cause was menorrhagia. Nutritional anæmia was not found. Granulopenia was noted in 1 case. Signs of nutritional deficiency, such as angular stomatitis, marginal glossitis, and indentation of the edge of the tongue, were fairly common, but no case of frank vitamin deficiency was observed.

The high incidence of postural defects, foot troubles, varicose veins, and arthritis is not likely to be diminished by standing in queues or by carrying heavy baskets. The question also arises of the possible ætiological importance of continued anxiety in the production of hypertension; it is generally accepted that established hypertension may be increased by fatigue and mental strain.

Though only 9 cases of gross obesity were seen, many more of these women said they had been putting on weight in recent years; since most of them continue to take a high-starch diet this is not surprising. Unduly thin women were not often seen.

The outstanding impression made by these housewives was their look of fatigue. This was reflected not only in the face and manner, but often also in slow laboured movements and lack of muscle tone. In trying to answer questions many women seemed incapable of thinking or speaking clearly, and would make such remarks as: "I can't seem to remember anything these days . . . ," or "I don't know what is happening to my brain . . . ," by way of excuse. Many of them had a look of defeat. Others looked harassed and ill at ease, and admitted that they were thinking of work waiting to be done at home. One woman fell asleep while she was waiting for five minutes to be examined. Most of the housewives were tidily dressed and fairly clean, though usually the condition of their hands gave away their occupation. Despite their preoccupied and sometimes bewildered looks, many of these women were not without a certain dignity of their own.

When seen for the first time, these housewives were all following their usual daily routine. In view of the variety of the clinical findings, this fact is remarkable. One feels that in other occupations some of these complaints might have been made the excuse for absenteeism.

From time to time in the course of this work one saw a serene and cheerful woman radiating contentment and good health; one welcomed her as a rare and pleasant surprise, and invariably found that her home background was a happy one.

ALMONER'S REPORT

Mrs. K. M. Kershaw reported on interviews with these 61 housewives as follows:

"I have found most of them only too willing to discuss their individual difficulties. In my opinion these are divisible into marital problems arising mainly through war conditions, and problems arising from economic conditions—e.g., housing shortage, rationing, and queueing. The marital problems in many cases had arisen through infidelity of the husband—less often of the wife—during the war. In other cases the husband, on demobilisation, was unwilling to take his share of responsibility in the home. Economic conditions complained of were inadequate food, especially where there were growing children in the family. Many women admitted that they regularly gave up their butter, egg, and bacon rations to the children. They all complained of having to queue for food, sometimes for as long as an hour.

"The very serious problem of housing is causing considerable anxiety to many housewives, especially in cases where the family have to live with in-laws. One family I visited was living in a damp basement flat, father, mother, and four children sleeping in one room. For two years they had been trying without success to find other accommodation. They said that the housing authorities considered their present flat to be adequate. All these children were unhealthy, the mother was a nervous wreck, and her husband was habitually unfaithful.

"I consider that the most important preoccupation in these housewives has been with problems of marital friction. I place housing problems second. The least preoccupation is caused by rationing and 'austerity'; but the women in this low-income group have in most cases been accustomed to hardship all their lives."

HOUSEWIVES IN HIGHER INCOME-GROUPS

Though no detailed work has yet been done on the welfare of housewives in the income-groups of £500 p.a.

or more, yet from conversations with a fair number of such women one gains the impression that their problems are of a different order. Partly owing to their higher standards of education and of upbringing, they are less often troubled by marital and domestic problems, but when these do occur they cause much emotional preoccupation. On the whole these housewives have higher standards, both personal and objective, in their attitude to life and to work; they also feel the need for interests outside their homes. At present many of them are conscious of a sense of frustration, which may be produced in various ways:

They lack the time and energy to keep their homes as they would like. They are much more affected by the lack of domestic help than are their counterparts in the working-class; being often untrained to their task they tend to expend much unnecessary energy of body and mind on trivial routine in the house. In some cases they may become obsessed with the importance and urgency of their household commitments, and almost cut off from their former social contacts and recreations. They are thus unable to provide for their families that companionship which is their due. Many of these housewives come to resent their household obligations, and they may develop a sense of conflict between their duties to the house and to the family, doing justice to neither.

Further, there seems to be a definite tendency in the younger members of this group to shirk responsibility for their own lives and families, preferring to impose their problems upon their parents.

Housewives in this group tend to show less defeatism and more common sense and ingenuity in their management of the food problems, though it is often their practice to deprive themselves for the benefit of the family. Again, the younger housewives are more adaptable, more capable, and less inclined to complain than are those over 45. These women are able to have more meals out than are those in the lower income-group, who for reasons of economy or from force of habit have most of their meals at home.

DISCUSSION

The state of health of housewives at present is not good enough for the lives which they have to lead. It cannot be concluded from this short series that there are any specific occupational diseases of housewives, but it is clear that many of the conditions to which they are liable may be considerably aggravated by the circumstances of present-day life.

The chief factors which produce fatigue in the housewife seem to be mental preoccupation of any kind, and inadequate diet. Lack of sleep cannot be incriminated.

The effects of fatigue in the housewife exceed those of fatigue in any other type of worker. They are reflected not only in the woman and her work but also throughout her home and family. It is obvious that the housewife largely determines the atmosphere in her home. Once she is tired, discontented, or frustrated she ceases to enjoy her vocation, and in one way or another she becomes inefficient. As a result it may happen that the husband no longer spends much time at home, and the children often become unmanageable, suffering from the lack of a secure background when it is most needed.

CONCLUSION

It is recognised that no-one can do well if he is not happy in his work, and equally that contentment and efficiency at work can be spoilt by mental preoccupation. This was well seen during the late war, when efficiency was impaired by boredom and anxiety rather than by danger or physical hardship. The vocation of housewife calls for the most natural, as well as for the greatest, of human qualities. A woman can find contentment in her work only if she can approach it with an unpreoccupied mind. Even at this time a good housewive can take her work in her stride if she is trained to her task and happy in its performance. This also implies that she is happy in her marriage, and that all her preoccupations are pleasant ones. The ideal housewife described in the last chapter of *Proverbs* can still be found today.

The need for amelioration in the conditions of the work and environment of the housewife is widely recognised. Of equal importance is the need for every woman—and man—to be equipped by early training and education for the assumption of responsibility in every shape and form as a natural privilege without question or resentment.

My thanks are due to Mrs. Kershaw, almoner of the New Sussex Hospital, and to the hospital staff for their coöperation.

BRITISH ORTHOPÆDIC ASSOCIATION

ANNUAL MEETING

THE annual meeting of the British Orthopædic Association was held in Belfast from Oct. 21 to 23 under the presidency of Mr. S. A. S. MALKIN, who referred in his address to the firm establishment of the specialty during the 1914–18 war, the great advances between the wars and during the late war, and the present flourishing condition which attracted many to this branch of surgery. He thought, however, that the art had been cultivated to the neglect of the science, and that much more attention should be given to clinical and other research in close liaison with the physiologist. The most fertile ideas and research work had come from young men, and it was they particularly who should be encouraged in the research tradition.

THE PAINFUL SHOULDER

Prof. GEORGE PERKINS, opening a discussion on intrinsic pain of the shoulder, referred to invariable complete recovery in capsulitis—a generalisation disputed by subsequent speakers.

Mr. V. H. ELLIS found it difficult to fit such conditions as the stiff shoulder complicating coronary disease into a simple classification of extrinsic and intrinsic causes. He described the production of supraspinatus injuries, and pointed out that loss of power in this muscle might be reflex and recover quickly, or it might result from a complete tear demonstrable by arthrography. Removal of the acromion would facilitate suture of the supraspinatus and hasten recovery.

Mr. J. TULLOCH BROWN (Killearn) had found that, in severe cases of the supraspinatus syndrome, procaine infiltration was useful in distinguishing patients with loss of movement from spasm, requiring conservative treatment in the first instance, from those in whom structural changes demanded operation.

Mr. R. J. W. WITHERS (Belfast) had found 61 cases of capsulitis among 100 patients with intrinsic pain of the shoulder. Two stages might be distinguished: (1) "irritative" capsulitis in which the stiffness was due to spasm and disappeared under anæsthesia; and (2) "adhesive" capsulitis in which stiffness persisted under anæsthesia. Irritative capsulitis was treated by rest in a sling, followed by active exercises at the end of about 6 weeks. Adhesive capsulitis demanded primary manipulation followed by exercises.

Mr. W. C. SOMERVILLE-LARGE (Dublin) spoke of the value of anæsthesia in distinguishing between muscle spasm and structural change as the cause of limitation of movement, tenderness as an aid to diagnosis, and the importance of radiography in various projections.

Mr. STEWART H. HARRISON (Birmingham) had found radiological changes in 30% of patients with pain and stiffness of the shoulder following injury, and had observed that such cases did not completely recover.

Mr. F. A. SIMMONDS (Pyrford) had found in a three-year follow-up that some patients still had slight pain, weakness, and stiffness. Biopsy in the active stage

had revealed degenerative changes in the tendinous cuff with a chronic inflammatory reaction but no intra-articular change. The use of a sling and the performance of exercises within the painless range was useful, but he agreed with others that heat was of doubtful value.

Mr. J. R. ARMSTRONG advised excision of the acromion in patients with the supraspinatus syndrome who did not recover spontaneously. He had found a variety of lesions with similar symptoms: supraspinatus tendinitis, partial and complete supraspinatus tears, calcification in the tendon, and subdeltoid bursitis. The whole acromion should be excised.

Mr. G. BLUNDELL JONES (Exeter) referred to acute supraspinatus calcification with sudden pyrexial onset, short course, and early dispersal of the calcium deposit.

Mr. W. E. TUCKER mentioned focal sepsis and gout as causes of shoulder pain and agreed upon the importance of rest in the acute stage.

POSTERIOR DISLOCATION OF THE SHOULDER

Mr. C. K. WARRICK (Newcastle-upon-Tyne) suggested that with posterior dislocation of the shoulder, unless stereoscopic views could be taken and inspected, the ordinary anteroposterior view should be supplemented by a vertical view with the tube in the axilla, or a vertical view with a curved cassette in the axilla or a profile scapular view.

HIP ANKYLOSIS AND OPERATIONS ON FEMUR

Mr. J. S. BATCHELOR described removal of the femoral head and neck from 50 hips of 44 patients, with the object of promoting mobility. In 32 a subtrochanteric osteotomy also was performed for the promotion of stability; this might be done at the primary operation with plating of the fragments, or 3–5 weeks later through a separate approach, a tongue being cut in the distal fragment to ensure its engaging with the proximal. After a period of light skeletal traction walking was resumed at 8–10 weeks. Operation had been undertaken for osteoarthritis, ankylosing spondylitis, fracture-dislocation, ununited fracture of the femoral neck, and ankylosis from old acute arthritis and chronic suppurative arthritis. The results were: satisfactory 39; unsatisfactory 10; death 1. Unsatisfactory results included instability (3), pain (3), lack of coöperation (2), restriction of movement (1), and non-union of osteotomy (1).

Mr. H. A. BRITTAIN (Norwich) showed a film of his operation of ischiofemoral arthrodesis. Mr. H. H. LANGSTON (Alton) had performed 30 of these operations, without sciatic nerve injury but with failed union in 5, perforation of the obturator foramen with the graft in 2, and sequestration of the graft in 1.

Mr. W. B. FOLEY (Oxford) advocated open operation through a posterior incision reflecting gluteus maximus upwards and inwards. Fusion had occurred in 16 out of 17 cases.

Mr. G. K. MCKEE (Norwich) gave a preliminary communication on the use of a lag screw in combination with cancellous grafting in iliofemoral arthrodesis.

Mr. JOHN CHARNLEY (Manchester) gave an account of preliminary and unsuccessful attempts at arthrodesis by impaction of the tapered femoral head into a hole in the acetabular floor.

Mr. E. MERVYN EVANS (Birmingham) had used the Capener nail plate in trochanteric fractures of the femur. Of such fractures 28% were unstable because of fracture of the cortex in the neighbourhood of the calcar. The advantages of operation seemed to be: greater comfort and mobility, perhaps a lower mortality, and shorter residence in hospital.

Mr. E. N. WARDLE (Liverpool) had found aseptic necrosis of the femoral head in 14 out of 46 cases of fracture of the femoral neck, and he advocated that Smith-Petersen nailing be accompanied by grafting.

Mr. A. CHANCE (Dublin) spoke of intramedullary nailing of the femoral shaft for fracture, the most suitable type being a transverse interlocking fracture of the middle third without any loose fragment. The preservation of knee mobility was excellent.

THE HAND

Mr. W. H. GERVIS (Tunbridge Wells) reported on 18 cases of arthritis of the first carpometacarpal joint treated by excision of the trapezium with good results in all cases of osteoarthritis but with poor results in 2 cases of rheumatoid arthritis.

Mr. A. DORNAN (Sheffield) had found that in Kienböck's disease conservative treatment usually gave good results; so did excision of the lunate (semilunar) bone, even after failure of conservative treatment.

Mr. GORONWY E. THOMAS (Liverpool) had investigated the results of treatment for non-union of the carpal scaphoid bone carried out three years before. The 28 patients treated conservatively had done very much better on the whole than 52 treated operatively, of whom only 7 were able to return to heavy work. Backward subluxation of the lunate bone indicated a bad prognosis.

OTHER PAPERS

Mr. J. ROWLAND HUGHES (Preston) described spontaneous necrosis of the anterior tibial group of muscles, especially the tibialis anterior, occurring as a fatigue condition in young adults or complicating systemic disease. At first, cellulitis was usually diagnosed, but later the group of muscles became contracted, hard, and sometimes even calcified. In the acute stage sections showed massive muscle necrosis like that of Volkmann's disease. The fatigue cases might be caused by arterial spasm possibly promoted by muscle metabolites.

Mr. W. SAYLE CREER (Manchester) had successfully treated 14 fractures of the shaft of long bones with boiled cadaveric bone-grafts.

GENERAL MEDICAL COUNCIL

SESSION NOV. 23 AND 24

As recorded last week, Prof. Sydney Smith, chairman of business, presided over the 174th session of the council. Dr. J. J. O'Donnell took his seat as representative of the Apothecaries' Hall of Ireland.

Penal Cases

Mrs. *Ethel Grundy Toward*, registered as of Brookside, Durham Road, Birtley, Co. Durham, M.B. Durh. (1925), was charged with having been convicted on July 19, 1948, of driving a motor-car when under the influence of drink or drugs. She was represented by Mr. L. Mulcahy, Gateshead. The council found the charge proved, but postponed judgment for two years.

Frederic Syson, registered as of 60, Tower Gardens Road, London, N.17, M.B. Glasg. (1925), was charged with having been convicted of various offences in 1945. The council found the charge proved; but on medical evidence that he was unfit to attend, judgment was postponed until next May.

Reuben Denny, registered as of 64, Twyford Avenue, London, W.3, L.R.C.P.E. (1929), was charged with having been convicted last August of being in charge of a motor vehicle when under the influence of drink. The council found the conviction proved, but postponed judgment for one year.

Arthur Mervyn Rhydderch, registered as of Coppelia, Clements Road, Chorley Wood, Herts, M.R.C.S. (1926), was charged with having been convicted on three charges of driving and being in charge of a motor vehicle while under the influence of drink. He was represented by Mr. W. E. D. Churcher, of Messrs. Virtue, Son, and Churcher. The charges were found proved, but judgment was postponed for two years.

William Melrose, M.M., registered as of 15, St. Paul's Square, Liverpool, L.R.C.P.E. (1924), was charged with having been convicted, at Liverpool, in 1946, and again last July, of driving a motor-car while under the influence of drink. Dr. Melrose was represented by Mr. Joseph Norton, of Liverpool, instructed by Mr. A. Shaw. The council found the charge proved, but postponed judgment for one year.

Archibald Thomas Macmaster Glen, registered as of 16, Telford Avenue, London, S.W.2, L.R.C.P.E. (1935), was charged

with having been convicted in 1947, and again last July, of driving a car while under the influence of drink. Dr. Glen was represented by Mr. Norman Richards (on behalf of the Medical Protection Society). The council found the charge proved, but postponed judgment for one year.

Francis Murray, registered as of 417, Evelyn Street, London, S.E.8, M.R.C.S. (1930), was charged with having been bound over last June for an assault on his housekeeper occasioning bodily harm. He was represented by Mr. Norman Richards (on behalf of the Medical Protection Society). At the time of the offence Dr. Murray was not practising, and he stated that he would not return to practice until he had completed treatment and had been pronounced fit. The charge was found proved, but judgment was postponed for six months.

William Francis Hirsch Coulthard, registered as of Balwinnam, Aspatria, Carlisle, M.B. Edin. (1927), had had judgment postponed from November, 1946. The council did not erase his name.

William Allan, registered as of 31, Hill Crest, Burnley Road, Sowerby Bridge, Yorkshire, M.B. Glasg. (1926) had had judgment postponed from November, 1947. Judgment was postponed until next May.

In November, 1947, the council postponed judgment on *Hugh Boyd Gillespie*, M.B. Glasg. (1935), registered as of 16, Blairhall Avenue, Langside, Glasgow, S.1, until November, 1949, directing him meanwhile to appear and produce testimonials. This he did.

Restorations

The acting president announced the restoration to the Medical Register of the names of *Alfred Edward Bartley*, *David Davidson*, *Zaky Risk*, *Graham George Robertson*, and *Paravasthu Gopaula Sawmy*.

Council Affairs

Prof. David Campbell, giving the report of the Pharmacopœia committee, stated that 31,215 copies of the 1948 edition had been sold so far. The report of the British Pharmacopœia Commission showed that work had already started on the addenda, which would be issued between 1948 and 1953, and on the next *British Pharmacopœia*, which the council had decided should be issued in 1953.

Dr. Frank Kane was elected to the Pharmacopœia committee by the Irish Branch Council. Dr. Campbell was reappointed to the Poisons Board for a further term of three years.

The Act in Action

3. PHARMACEUTICAL SERVICES

Britain has some 15,000 chemists' shops, served by about 17,000 pharmacists. These pharmacists are now dispensing nearly 100% more prescriptions than a year ago, the increase being accounted for partly by the Act's provision for medicines without charge, and partly by the enforced cessation of dispensing at doctors' surgeries except in some rural areas and for private patients.

At the present rate National Health Service prescriptions would total some 160 million per annum—about $2^1/_2$ times the 66 million dealt with under National Health Insurance. In England and Wales £1,905,447 was paid out for pharmaceutical benefits up to Sept. 30,[1] but this gives little clue to the charges incurred up to that time. Middlesex Pharmaceutical Committee[2] reports that in its area during July 553,541 prescriptions were dispensed, with a total value of £75,117 (of which £40,036 represented the cost of ingredients, £29,316 dispensing fees, and £5765 containers); the average cost per prescription was 2*s*. 8½*d*. At this average price the annual cost of 160 million prescriptions would be about £22 million.

It has been correctly pointed out that the cost of each prescription is now some 50% higher than under N.H.I.,[3] but a large proportion of the increase is accounted for by improvement in dispensing fees, which have been brought more into line with private dispensing charges. Nevertheless, pharmacists have noted that prescriptions now follow a more liberal trend. Quantities ordered are commonly larger than hitherto—no doubt because the busy doctor wishes to postpone the day when he must see the patient again to give him a repeat prescription. These larger orders have taxed, but never broken, the pharmacist's resources in large bottles. Furthermore, whereas under N.H.I. proprietary medicines amounted to some 5% af all items ordered, they now number about 7–10%; and in a few areas the proportion is said to be much larger. There is also greater readiness to prescribe proprietary preparations in their original packs, the doctor writing simply "1 original bottle of . . ." without further instructions.

As pharmacists see it, practitioners are on the whole using the service judiciously. Exceptionally the amounts prescribed are excessive—for example, a 6-oz. bottle of a vitamin preparation of which the dose is 2–3 drops. Less seldom the prescription is for a proprietary medicine of which there is an efficient non-proprietary equivalent; and sometimes the substance prescribed might perhaps be deemed a food rather than a medicine. Guidance on these borderline prescriptions will probably be given, as the *Pharmaceutical Journal*[4] has indicated, by the joint subcommittee to be set up by the medical and pharmaceutical standing advisory committees of the Central Health Services Council.

Any initial difficulties over supplies have now been overcome; makers and retailers anticipate no serious delays in the future. According to some manufacturers the demand is particularly great for the galenicals; syrups, malt and cod-liver oil, and other medicaments for children; and, to some extent, phenobarbitone. Though often hard-pressed, pharmacists have mostly been able to deal with the new demand without loss of speed. In some ways their work is simplified: proprietaries, of which more are now prescribed, are easier to dispense than individual prescriptions, and whereas private prescriptions have to be copied into a book, N.H.S. prescriptions are simply filed. Nevertheless, the growth in dispensing has made heavy calls on time, and non-professional work now has to be left to unqualified assistants. Pharmacists point out, however, that they cannot altogether neglect the counter: doctors who look in expect to talk to the pharmacist in person; he must supervise the sale of all drugs; and he must see customers seeking remedies for minor disorders and decide whether they should be urged to consult a doctor. One of the present difficulties is over the operation of the rota system. By agreement minimum hours of business are fixed at 9 A.M. to 6 P.M., with one extra hour—between 6 and 7 P.M.—for premises open under the rota system. Since many surgeries do not end until 8 P.M., these premises should, it seems, remain open for anyhow two extra hours.

As secretary of the National Pharmaceutical Union, Mr. G. A. Mallinson points out that the public and pharmacists would be helped if surgeries were begun as early as possible in the evening. At a number of other points integration between doctor and pharmacist is not yet complete. Quite often schedule-4 poisons are prescribed without mention of dosage; and time is then lost to patient and pharmacist while the doctor's instructions are being obtained. A small but important detail is that practitioners very often misuse, or do not use at all, the space left on the N.H.S. prescription form for the patient's age; the pharmacist is then left

1. *Lancet*, Nov. 6, p. 752.
2. *Pharm. J.* Nov. 27, p. 361.
3. *Ibid*, Sept. 25, p. 209.
4. *Ibid*, Oct. 30, p. 293.

in doubt whether the preparation is for child or adult. Then again the prescription form is still used for all manner of articles not included in the schedule of appliances. This gives rise, as Mr. Mallinson points out, to time-consuming telephone calls between pharmacist and doctor. Doctors who have hitherto done their own dispensing have commonly used concentrated proprietary medicines which they diluted before handing out to the patient; now the pharmacist finds that he is required to stock a number of these mixtures to satisfy the habit of each practitioner in his neighbourhood. More serious perhaps is the situation over new proprietary medicines. Representatives of drug firms call on doctors, arouse their interest in a new preparation, and then warn the local pharmacist that some should be ordered. This the pharmacist does; the doctor prescribes the medicine once or twice only; and at the pharmacist's half-dozens of proprietaries pile up, unused, and forgotten by all except the pharmacist himself, who has paid for them.

The pharmacist's principal trouble just now is over delay in payment of his accounts under the N.H.S. This delay, which is very much worse in some areas than in others, will doubtless be reduced; but in the meantime it is making heavy inroads into capital. Pharmacists recognise that the terms offered under the Act are an improvement on N.H.I. conditions, but there are various anomalies which they hope to see rectified. For example, they would welcome a greater share of dispensing in rural areas, where, they hold, they should also receive a delivery allowance so that the patient in urgent need who has no messenger can be assured of getting his medicine. It will be a year or more before the effect of the Act on the pharmacist's earnings can be gauged. Against the gain represented by a greater total of prescriptions dispensed has to be set the reduction by 50% or more in private prescriptions, which are more profitable to him than those dispensed under the Act. According to some central bodies over-the-counter business is now reduced, but this is denied by individual pharmacists interviewed; they say that possibly the increase perceptible up to July 5 is slightly slowed, but there is no actual reduction. For the more expensive drugs patients are certainly now referring more often to their doctors for a prescription, but for the "homely" remedies the demand is unabated, patients continuing as before to purchase these privately.

Will pharmacists be able to meet every call this winter? A little hesitantly they answer Yes. One large firm has created a pool of volunteers who will go to any area where the need is particularly great; but though this precaution is an effective cushion against local stresses, it will of course be ineffective in an over-all epidemic. Some pharmacists are trying to improve speed and efficiency by enlarging their dispensaries and—in the larger premises—by getting patients to bring their prescriptions to a single desk where a pharmacist can rapidly decide how soon these can be made up. At least one firm has established a bonus system for the dispensing pharmacist. This firm has always been extremely considerate to its employees; but the addition of the bonus is thought to have had an appreciably good effect. Nothing can disguise the need for more dispensers. Mr. Hugh Linstead,[5] secretary of the Pharmaceutical Society, has lately returned to the suggestion of "more regulation of unqualified labour," arguing from the analogy of laboratory technicians. Here the example of Messrs. Boots might perhaps be copied. This firm trains—allowing time for study—not only indentured pupils but also (provided they are of good education) unindentured pupils, who take exactly the same course of study and are encouraged to continue and qualify as pharmacists. For the indentured pupil there are scholarships, and there is a fund to help all worthy candidates.

Most pharmacists in retail business in England and Wales have high hopes that their work will be made easier by the introduction of the promised *National Formulary*; looking further ahead, they regard with unconcealed dismay the prospect of dispensaries in health centres.

5. *Chemist and Druggist*, Nov. 13, p. 642.

Disabilities

18. EFFECTS OF ENCEPHALITIS LETHARGICA

SLEEPY sickness is perhaps one of the cruellest afflictions to be endured by man. Though myself a doctor, I know little about the pathology of the disease; and indeed I have no knowledge of its clinical course or ultimate end, beyond the sequence of events that have already befallen me. I make no inquiries, nor do I dip into periodicals and books dealing with the complaint; for it is foolish, in my estimation, to anticipate what may never happen.

"Creeping paralysis"—the title already given to another disease—would be an excellent name for this disability, which drags unrelentingly along its laborious course. It is quite impossible to say "I'm worse than I was a week or a month ago." It is necessary to look back much further to recall little things that could once be managed but are now impossible or very difficult.

I am supposed to have contracted the disease in 1924, when I was 29. I ran a temperature for a few days and saw double for a week. This diplopia rather alarmed me at the time, but a brother houseman reassured me by saying that this phenomenon indicated only fatigue of the eye muscles, which was to be expected in any febrile condition. Previously the Navy had claimed me for eight years, but now I went into general practice at a seaside town, where I joined the local sailing club.

It was while sailing that I got the first inkling that all was not well with my make-up. Several boats had reached a mark-buoy round which it was necessary to gybe—a tricky moment, which would have disturbed the most hardened seaman, for a general smash-up seemed inevitable. Suddenly my hand started to vibrate on the tiller; it was a most curious sensation though only momentary. I mastered myself, regained my grip, both mental and physical, and steered round the buoy without incident.

Another warning came a few days later at a public luncheon. I was on my feet, proposing a vote of thanks to the speaker, when my right hand started to vibrate again. I havered a bit, rammed my hand into my trouser-pocket, and continued. I don't think anyone else noticed the contretemps. Some time after this I noticed that it was becoming difficult to write, quite a short letter taking a considerable time; and my handwriting, which always had been a bit of a puzzle, became completely illegible. Soon I lost my nerve for the excitement of sailing. There is always a spice of danger in navigating, even in local waters; and competing in the single-handed race—which I myself had instituted—became for me a most alarming affair.

At this stage I consulted my brother, a general practitioner, who arranged for me to see a London neurologist. The three of us rendezvoused at the great man's country house; and without my knowing, he diagnosed my ailment over the teacups. Afterwards he took me for a stroll in the garden. I remember he asked me if my mouth seemed wetter than usual. I answered No. Little did I realise that as the years

went by excessive salivation was to become the greatest tribulation of my life. In the kindest and most gentle way he told me what I was suffering from. In a way it was a relief to know something definite.

Things went from bad to worse, and I had difficulty in memorising my patient's faces and what I had prescribed for them. Deciding to give up my practice and go back to the Navy—my first love—I went to the Admiralty for medical examination, and felt guilty enough at putting my signature to a written statement that I was free from physical disability. In this early stage I could easily have fooled the whole Royal College of Physicians. But life on a submarine depot-ship, spending hour after hour with nothing to do but just sit and think or perhaps listen to Service jargon—proved an impossibility for me. I lasted just a couple of months, then collapsed and was invalided out of the Service.

This just about finished me, and I found it beyond my powers even to think of a job of work. In the backwater of a village, with my wife and child, life became happy; and in the winter months I enjoyed rough-shooting, though slow on the trigger. My age was now 34. Then tremor and salivation began to trouble me. The embarrassment of excessive salivation is comprehensible only by those who have suffered it; it is very trying to have one's mouth perpetually full of fluid, waiting to spill over at the slightest relaxation of the facial muscles. My brother put me on a proprietary preparation of scopolamine, which for years acted like a charm, drying up the mouth, reducing tremor, and making me feel fairly well. But as time wore on it lost its almost magical effect, which has never returned. I was now treated with a preparation of stramonium, which still has a remarkably consistent action. Unfortunately it takes an hour to act, and in that time there is an almost overpowering temptation to hurry things up by taking a little more. The result of an overdose is devastating: a bone-dry mouth, a feeble heart-beat, a feeling of distress, and hysteria producing an exaggerated sense of humour, though in the background all the time is a sober awareness. If, on the other hand, I take too little, salivation deluges me. It is remarkably hard to strike a happy mean, for the path between the two extremes is very narrow. Owing to the atropine in stramonium, the pupils dilate, and strong glasses are needed. Before a fire the heat is sufficient to dry up the conjunctivæ and the upper lid tends to stick to the eyeball. This is sometimes quite painful. The trouble is alleviated by a kettle steaming on the hob, or a dish of water placed before the fire.

Gradually difficulty in swallowing has manifested itself; it is impossible to get down any food without copious draughts of water, and even this does not always work. I never take a meal with any but my own family, for eating demands my whole attention. Though right-handed, I use a fork in the left hand (the less affected) for almost all varieties of food; a fork is much easier to manipulate than a spoon. Crisp dry food is the most readily masticated; anything that cloys is anathema. 'Ryvita,' recrisped in the oven, is ideal. Of a different texture, sponge-cake is also excellent, seeming to dissolve in the mouth. A satisfying meal entails an hour's hard work. One of the greatest irritations is the inability, through being unable to swallow quickly, to join in the conversation, however trite my unspoken comment. By the time I have swallowed the talk has swung on to some fresh subject.

My speech has become indistinct. Until I got used to it, this caused me great annoyance. How maddening it is to receive a grotesquely irrelevant answer to some simple remark, from someone trying his best to understand. How much better it would be if he said that he did not comprehend. My latest affliction is an ability to walk well—the "festinating gait." This is much worse indoors, when my way is beset with many corners. Once on an open road I can get along with a certain ease; but there are ominous signs that this will not last. Curiously enough it is easier to walk backwards than forwards.

For the last twenty years I have been writing, punching the typewriter with my left forefinger—the only digit of the ten that will perform this duty. Free-lancing is surely the most disappointing of all occupations. I must have had some two hundred articles rejected; but slowly my name is getting known, for I seem just now to be selling two articles a month, and two plays have been accepted by the B.B.C.

This tremendous interest keeps me going; but a snag—inevitably, I suppose—has recently developed. I can no longer type with any ease or dexterity, my one good finger refusing to function. This is really distressing but, as nearly always happens, there is a way out. In America they are manufacturing an electric typewriter, which at the softest touch does everything, even rolling on the paper and shifting the keyboard; but naturally it is expensive.

I have to fight my own peculiar demon—the devil of frustration. Everything is difficult to accomplish; little details which come like second nature to the normal person are a series of puzzles to me; and sometimes there is no solution. Putting on clothes, doing up shoelaces, fastening shirt buttons, holding a cup of tea without its slopping over—all these are obstacles in the routine of life. Some of these things have to be done for me.

So here I am, at the age of 55, with difficulty in walking, talking, eating, writing, and typing, with a whole host of minor ailments; yet a happy man with dozens of compensations. How has this disease affected my character and temperament? All for the better, I think. I can bear the keenest disappointment with almost complete equanimity; this happens two or three times a week when those big buff envelopes, addressed by myself, pass through the letter-box, and also when some new disability asserts itself. I am now much more sympathetic and can better understand other peoples' foibles, peculiarities, bothers, and ailments.

My belief that man possesses a separate entity apart from his husk of a body has been greatly strengthened by my experiences. I sit, as it were, inside my carapace watching my person behaving in its vile fashion, while my being is a thing apart, held a prisoner for a time. This rather queer sensation of being outside oneself has been exaggerated by my complaint: it is most comforting, and strengthens my faith that there is not complete extinction ahead, but a better deal in a new life.

"We may observe that Governments are not infallible, yet must be obeyed. This reflection should make us more than ever alert to preserve intact the prized freedom of science in our own domain. Actually no direct attack is likely here, and should the unexpected happen it will certainly not be along the lines of compelling us to espouse some particular scientific theory or doctrine. Conceivably it could take the more subtle form of control of the character and direction of our scientific work. There is immediate danger in the current deprecation of fundamental research, not of course absolutely, but relatively, in comparison with technological applications. . . . It is certainly not sufficiently realised that the body scientific can only flourish when all its organs are in a healthy condition. As in a biological equilibrium there is a natural interdependence between pure and applied research. Pure science is fertilised by the advance of technology and vice versa. It would be quite consistent, though lamentable, to take up the position that we will have no more research at all and devote our energies to the exploitation of present knowledge. But it is impossible to dissect the elements of real progress. If we isolate one of the limbs of the organism it will not grow and will soon die."—Sir ROBERT ROBINSON, P.R.S., in his anniversary address to the Royal Society, Nov. 30.

In England Now

A Running Commentary by Peripatetic Correspondents

"CORSE," said No. 20, as he passed my bed on his way to the bathroom, "the doctors can't know everything. You've got to be a gastric yourself to know what's going on inside. As I see it (and I've read about it in them medical books), the gas forms in the ulcers in this 'ere duodenal cap, and every now and then it lifts the top off 'em and that's when you get the pain. You can 'ear the gas rumbling round, and if you bring it up you feels better. But that's the trouble—to get it up. I've tried everything, but when one of these attacks is on nothing will shift it. Then again, in a week or two, it begins to move and after that it comes up lovely."

"One thing," he went on, when I had expressed agreement, "they've confirmed that I 'aven't got the T.B. I'll show my daughter the report when she comes and then perhaps she'll believe it." His skinny old face wrinkled up, showing an assorted collection of blackened false teeth. "I first went round to the clinic on account of getting so thin. I 'ad a bit of a cough, too, but I didn't tell the doctor there about my gastric—he only asked me whether I'd coughed up blood and that kind of thing. I 'ad the X ray and when I come up later to 'ear the result 'e took another. 'E looks at the pictures a long time and then 'e says 'I'm sorry, but you've got the T.B.' Corse, when I told the missus she was in a proper flap—made me keep to my own cup and plate and I've kept to 'em ever since. What with children and grandchildren there's about 40 in our family, so you 'ave to be careful. I went back to work, but next week the Care Committee sent me to Fergushill 'Orspital, the T.B. place. It was full of Service chaps then. Four months I was in there, and never 'ad no treatment. A nice old doctor come round every morning and asks 'How're you?' and when we says 'All right' 'e passes on to the next bed; 'e never looked at none of us. We 'ad grand grub—cream, and cod-liver oil and malt, and what else—and I got quite fat. Then one day a new doctor comes round, a young chap what 'ad been at one of these sanatoriums and knew all about T.B. 'E examined every one of us, thorough, stomach and all. When 'e'd finished with me 'e says to the sister: 'What's this man in here for? There's no T.B. there. He can go home.' Another chap what 'ad been in the ward longer than me 'e found 'ad a growth on the lung. When I got 'ome I used to go to the clinic every six months as they'd told me, but I didn't tell them what the 'orspital doctor 'd said—I didn't like to some'ow, seeing as 'ow they'd given me an allowance all the time I was in there. The sister would say, 'You're doing very well, dad,' and I would think so I ought to be, since I'd nothing the matter with me chest. It just shows, don't it, that they can make mistakes with them shadders on the lungs?" He wrinkled again and trundled his chair down the ward.

* * *

After your leader on Hospital Manners, I feel it is fair to send you the reason—given in a letter to our almoner—why the doctors and nurses "don't tell you anything." They just can't get at the facts, and nor can the mothers-in-law.

DEAR MADAM,—I do hope you will not mind me writing to you again, but my little grandson was in the Radcliffe, I was informed while in oxford and I ask the person what was the matter she said she did not know for certain but the Rumor had gone round that he had stoppage through constipation but she did not know how true that was, and of course it upset me and I felt quite ill while at the baby great-grandmothers, I did not know what to do for a time, then my daughter-in-law wrote and told me, that the baby was taken ill with pains in the stomach and was sick and had hemarage in the back passage, he was sent to Radcliffe and she informed me if they could find the lump they would oprate, which they did, now they have wrote and said he is out of hospital and said it was his pipe where the food went Down was to narrow in one place he was alwright when he drank anything but when he had Solids it use to block his feed pipe up, but as you know my daughter-in-law told me several Different Storys about herself that you cannot rely on her for the truth, she as told me one story about baby and Relations another and to be on the safe side, I would like to know the truth, for she as blamed it on to several different things at Different times in her letters so I hope you dont mind me asking you.

* * *

Dear Mr. Attlee,—Perhaps you are not really responsible for the practice of putting the clock back, but I have to blame someone. The farmers, I believe, have always opposed this jiggery-pokery, and as a father perhaps I may add my humble plea.

Ever since the clocks were fiddled, my two small boys have been awake at 5.30, and that means no more sleep for Father. They play for a bit and then the elder one gets fed up and takes to tormenting the younger. On the second day, after many threats, Father eventually leapt from bed, beat them somewhat unsatisfactorily as there was no bare skin to get at, and flung them into their respective beds. Breathing fire, he hissed through clenched teeth that if they continued to cry they would be beaten again. They pursed their lips, but continued awhile in muted fashion.

This Victorian approach certainly bore fruit, and though Father is still woken at 5.30 they are a little more circumspect in their behaviour. Heaven knows what complexes have been formed to mar their future happiness. Father's nerves are getting decidedly frayed, for, not being a Napoleon, he needs more than six hours sleep.

What makes this particularly hard to bear is the knowledge that the situation will repeat itself throughout the years. As soon as the boys begin to settle down the clocks will be fiddled with again, and whichever way they are changed the result, strangely enough, is the same.

Multiply all this misery a million times, Mr. Attlee, and you will have some idea of the magnitude of this orgy of human suffering. All I ask is that, when at last we reach the age of plenty, we should dispense with this man-made burden. But I don't know; by then the little devils will have children of their own, and why should they not suffer as they make us suffer now?—Yours &c., P. Familias.

* * *

But surely it is better than (Churmann and AcMahon 1933, Rieberg and Oss 1934, Allory 1936, Anny 1940, Aln 1941, Oschcowitz 1945) this, don't you (Yatt, Icks, and Hompon 1936, Olbrook and Ill 1936, Rtiak and Aug 1936, Teck, Eutsch, Eed, and Truck 1937, Brams and Auer 1938, Teinberg 1938, Locumb 1932, Reyberg 1942, Anavski, Inkler, and Eters 1945, Reeman, Hoads, and Eager 1946, Ovey and Hitlock 1946, Aul, 1946, Evans and Aylor 1941, Aufmann, Eck, and Iseman 1947, Agnuson, Elvenny, and Ogan 1947) think? Not exaggerated.

* * *

Do the anatomists know what the war has done to women's hands? I do not refer to roughened skin, stains, cuts, broken nails, but to size. Work develops the muscles and broadens the hands, but I maintain that the bones in mature adults are hardly likely to lengthen. The manufacturers of gloves and the shopkeepers who sell them seem to think otherwise; the leading drapers in my district assert that unaccustomed rough work in house and garden has enlarged hands to such an extent that no gloves smaller than size 6½ need now be made. Only ocular demonstration would convince them that a hand that took size 6 before 1939, and that works as hard as any other, still takes 6, and looks ridiculous in 6½, with flapping finger-tips like a stage comedian. After several enjoyable chats between the saleswomen and myself it was finally announced that some day three pairs of gloves size 6 will be included in "the quota."

The fact must be that the hands and feet of the younger generation of women and girls, like their bodies in general, are larger than those of their mothers and grandmothers. Sir Grafton Elliot Smith used to teach that increased use of the hand led to increased differentiation of the small muscles and stimulated cortical development; though I have heard it suggested that it was the other way round. It would be interesting to hear from the psychologists whether increased size is correlated with greater intelligence.

Letters to the Editor

DIETARY FAT

SIR,—In his comments on my letter of Sept. 18, Dr. Leitner (Oct. 2) questions the accuracy of some of the information given; he then stresses the importance of the non-caloric functions of fat.

Regarding the first point, he avers that the fat intake of the Swiss was 40–50 g. daily for just over a year during the war period. It is clear, however, from Fleisch's [1] graph that the *average* intake for the normal consumer was less than 50 g. daily for approaching three years. While supplementary rations were granted to certain groups of workers, I presume Fleisch is referring to the bulk of the population when he states in his summary, "We have lived for years with 40–50 g. fat."

Dr. Leitner then states that in a properly balanced diet the absorption of the fat-soluble vitamins and of calcium and phosphorus depend on adequate fat intake. It is true that fat promotes the absorption of such vitamins, but is the improvement of quantitative significance? Drummond [2] considers that there is no indication from war-time records that subsistence on diets poor in fat accelerated the appearance of signs of a deficiency or aggravated them. Since the calcium metabolism of the human body reaches a steady state slowly with changes in diet, only long-term balance observations are of value in absorption studies [3]; the effect of high and low fat intakes on calcium absorption under these experimental conditions has not yet been investigated, so far as I am aware. But surely of greater moment are observations such as those made by Wilson and Widdowson [4] in India; they found that although the people in the Central Provinces and Orissa consume only 0·2 g. calcium and about 12 g. fat daily, little or no rickets or osteomalacia are found. It may also be of interest to add that at this laboratory balance observations on a small number of healthy young Bantu when living on their customary diet (about 0·3 g. calcium and 30 g. fat) showed them to be in equilibrium in regard to calcium: further, X-ray studies revealed their bones to have normal calcific density. Evidently at such places a very low fat intake does not prevent a proportionately meagre calcium intake from being effectively assimilated. Since it is unusual for diets to be deficient in phosphorus, in contrast to calcium, the effect of different levels of fat intake on phosphorus absorption need not be considered here.

The next advantage that Dr. Leitner attaches to an adequate fat intake is its sparing action on many of the B vitamins. From the recent review of Elvehjem and Krehl [5] it appears that while a high fat intake may have a sparing action on the requirements of certain members of the B group, it may actually *increase* the requirement of other members.

Dr. Leitner then alludes to recent experiments which indicate that a mixed diet containing an adequate amount of fat confers great efficiency on the utilisation of food energy, and secures extra calories for work, growth, and storage. But how many extra calories? In the study of Forbes and his associates [6] cited by Dr. Leitner, altering the fat content of the diet of the growing albino rats from 10 to 30% resulted in an "energy retained" change from 456 to 460 calories daily—a gain of less than 1%. Supposing such findings are applicable to man, then at the 3000-calories level the gain would be less than 30 calories. More recent experiments,[7] however, show that the gain is appreciably larger when the diet includes extremely high vitamin supplements. That sufficient recognition is not always accorded to these non-caloric functions of fat is regretted by Dr. Leitner: but in practical nutrition it would seem that the benefits to be derived are very limited.

Finally, Dr. Leitner quotes the conclusion of Burr and Barnes [8] that there are ample reasons for recommending that the fat intake be not reduced below the normal established by habit. But among these reasons there was no mention of the fate of groups of persons or of communities who had suffered from having had their fat intake reduced. In the present state of our knowledge there does not seem to be any conclusive evidence that diets low in fat are injurious to man: it is hardly necessary to add, however, that such diets are neither approved nor advocated.

A. R. P. WALKER.

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2. Drummond, J. C. *J.R. Soc. Arts*, 1948, **96**, 569.
3. Steggerda, F. R., Mitchell, H. H. *J. Nutrit.* 1941, **21**, 577. Kraut, H., Wecker, H. *Biochem. Z.* 1943, **315**, 329.
4. Wilson, D. C., Widdowson, E. M. *Indian med. Res. Mem.* 1942, no. 34.
5. Elvehjem, C. A., Krehl, W. H. *J. Amer. med. Ass.* 1947, **135**, 279.
6. Forbes, E. B., Swift, R. W., Elliott, R. F., James, W. H. *J. Nutrit.* 1946, **31**, 203.
7. Forbes, E. B., Swift, R. W., James, W. H., Bratzler, J. W., Black, A. *Ibid*, 1946, **32**, 387.

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SIR,—Dr. Wyburn-Mason's appetite for contentious argument is a healthy one; not content with the solitary bone, he now desires to pick an entire skeleton—vasodilator nerves, causalgia, ophthalmic zoster, and "belligerency" are some of the new bones. He complains that I have "misconstrued" what he said. I wish that I had the temperament of that old surgeon, John Murphy, and could be content to let it stand, and "let the record show." But in the language of Oscar Wilde, I can resist everything except temptation. I shall deal with only a few points.

(*a*) "Acetylcholine *has* been shown to accelerate blood-clotting." Thus runs the statement in his first letter. Weary, and glutted like a leech, I rose from the *Index Medicus*, but still without a taste of such evidence. Now we are given to understand that this is a personal observation and *will be* published later.

(*b*) To my great surprise I am informed that I do not believe that proctocaine block is capable of producing vasodilatation. Every surgeon knows this, and accepts it as natural. What I did say was that massive limb œdema, blisters, punctured sloughing sores, following such injection, would indeed be news.

(*c*) I now pass on to Dr. Wyburn-Mason's request for me to reconcile my views with the vasodilator effects of stimulation of the peripheral ends of the posterior roots, and the axon reflexes of Lewis. This phenomenon of "antidromic" vasodilatation is generally accepted,[9] and physiologists are agreed that a large percentage of posterior root fibres are capable of transporting centrifugally-directed impulses.[10]

But I hope that it is not being suggested that the thiopentone injection was into the posterior nerve-root, or that the œdema twinkles up and down the nerve-sheath. Such vasodilatation only follows posterior nerve-root stimulation; the effects are entirely different on stimulation of the peripheral nerve pathways with which we are here concerned. At this stage the nerve has received its vasoconstrictor component, and with stimulation the vasoconstrictor effects predominate. Moreover, neither in man nor in animal has it been possible to produce œdema following such stimulation; the erythralgic skin of herpes and causalgia is an affair of days or of weeks, and does not come on in a matter of minutes or hours. These two statements come with the full authority of Lewis.[9]

Causalgia is not a very apposite lesion to draw into any discussion, for our knowledge of its disordered physiology is as yet incomplete. I must, therefore, merely correct the statement that there is "sensory loss" in tissues supplied by nerves, not directly damaged. Shumacker et al.,[11] on the evidence of a particularly large series of cases, emphasise "that examinations carried out before the pain had been eliminated are notoriously misleading, the extent of nerve dysfunction often appearing greater than is actually the case."

I am beholden to Dr. Wyburn-Mason for his suggestion that I read A. D. Speransky *Basis for the Theory of Medicine* (1935), for information as to the identical effects of injection of irritants in animals. But, having studied

8. Burr, G. O., Barnes, R. H. *Phys. Rev.* 1943, **23**, 256.
9. Lewis, T. Pain. New York, 1942.
10. Richards, R. L. Peripheral Circulation in Health and Disease. Edinburgh, 1946.
11. Shumacker, H. B., Speigel, I. J., Upjohn, R. H. *Surg. Gynec. Obstet.* 1948, **86**, 452.

the records of some of the experiments performed, I came away with the conviction that one can gather everlasting converts to every crude suggestion. May I quote three extracts.:

"Trauma of the sciatic nerve sometimes produces trophic ulcers of the hind extremities and sometimes papillomatosis of the mucous membrane of the mouth."

"As a matter of fact who would have believed, even recently, that it is possible to blind a dog by acting upon the sciatic nerve, or to kill an animal through the pulp cavity of the tooth, producing intestinal hæmorrhage by means of one drop of formalin, two or three months after, not only the formalin, but the tooth itself had been removed."

Two dogs are pictured with gangrenous ulcers on the hind extremities, "after section of the sciatic nerve and injection of a drop of pus in the centrifugal end (with subsequent extraction of the cerebrospinal fluid)."

Sir, when truth jostles fiction, those who try to part them oft buffet one another, be it with tongue or pen. There was a worthy biblical injunction in your last issue: "A soft answer turneth away wrath."

London, W.1. SOL. M. COHEN.

HOSPITAL BIOCHEMISTS

SIR,—May I be permitted to comment on a recent advertisement in your columns? The post advertised was that of a hospital biochemist, and the salary offered was (*a*) for a medical graduate with *experience* in biochemistry £1500 per annum subject to possible increase under the new scales, or (*b*) for a science graduate £750–1000 according to age and experience.

If the larger salary were being paid to a fully trained chemist (at least to M.SC. standard) who also possessed a medical degree, this letter would not have been written. However, according to the advertisement this need not be the case. I may be wrong, but I consider that to carry out his duties a hospital biochemist should be first and foremost an efficient and fully qualified chemist. If he is also medically qualified, so much the better; but I am at a loss to understand why a medical graduate with a limited knowledge of chemistry is worth at least £500 per annum more than a chemist with a limited knowledge of medicine. PH.D.

TESTING ANALGESICS

SIR,—The work on quantitative evaluation of analgesics both in this country and in the United States has revealed great variations in pain-threshold values, even in the same individual under identical experimental conditions. Two factors are worth noting as having a limiting value upon the interpretation of the action of analgesics: one is neurophysiological and the other pharmacological.

Relief of pain may mean a reduction of (*a*) peripheral reception (nerve-endings), (*b*) neural transmission (including the spinothalamic tracts), (*c*) central pain perception. Analgesic action is fairly clear-cut when it results from the elimination of pain reception and from interference with neural transmission, but when it comes to central pain perception we are dealing with a composite cerebral entity. Its component parts—the thalamus, the hypothalamus, and the cortical somæsthetic area—play their various rôles in the formation of psychic, somatic, and autonomic reactions. The interrelationship of these cerebral components makes for interdependence of the reactions.

There is no evidence that analgesics of the phenanthrene derivatives, the barbiturates, the anæsthetic gases, the antihistaminics, procaine, and so on, have all got a central, global, uniform, and therefore comparable action. On the contrary there is some evidence that these widely differing drugs have to a degree a preponderantly selective action—viz., cortical or diencephalic. Apart from pain-threshold-raising influence, there are the degree of involvement of the autonomic system, different degrees of respiratory depression, different ways of losing consciousness or producing lethargy and sleep. Thus the site of action of these numerous drugs is unlikely to be either identical or total within the brain.

With these reservations the term "analgesic" is useful clinically, but less so for the purpose of precise estimation of their action.

London Hospital. BERNARD KENTON.

CONTRACEPTION IN GERMANY

SIR,—I regret that my letter of Sept. 11 contained an error of dictation, when I said that contraception was forbidden in the British and American "zones." I should have said British and American "sectors" of Berlin.

I am also informed by the public-health division of the Military Government that "there are no restrictions whatsoever." The position, however, is still obscure because the Himmler police ordinance forbidding contraception has never been officially repealed, although the Hitler laws in general have been annulled. Confusion arises, therefore, as to the exact legal position. I understand from various sources that in actual practice, since the reduction of the censorship, the Himmler laws have been disregarded, although not repealed. Nevertheless the fact remains that, for whatever reason, contraceptives, certainly up till September, were almost unobtainable under Allied rule in Berlin.

According to my information, contraceptives sent through the post (unless in considerable bulk) are now unlikely to be stopped.

Urmston, Lancs. BERNARD SANDLER.

A REGISTRARS' GROUP

SIR,—A Registrars' Group has been formed in the Liverpool region to discuss conditions of service under the National Health scheme. We would be interested to hear if such groups have been formed in other regions as we consider that interchange of ideas on this subject would be of great value.

Ingleside, Hightown, near Liverpool. W. H. R. COOK.
Ashley, Reservoir Road, Prenton, Birkenhead. C. S. MCKENDRICK.

HOME NURSING OF PREMATURE BABIES

SIR,—I was interested in Dr. Miller's article of Oct. 30 on home nursing of premature babies in Newcastle-on-Tyne. He expresses the hope that the experience of others will be recorded. The accompanying table gives the figures of premature babies born and nursed at home, in comparison with those born and nursed in a hospital, maternity home, or nursing-home in the West Riding (1945–47) and in Warwickshire (1943–44),[1] in comparison with the figures for Newcastle.

C. FRASER BROCKINGTON
County Medical Officer, West Riding of Yorkshire.

Wakefield.

1. Brockington, C. F. *Arch. Dis. Childh.* 1944, **19**, 93; *Publ. Hlth, Lond.* 1945, **58**, 101.

Weight (lb.)	Newcastle-on-Tyne 1945–47				West Riding 1945–47				Warwickshire 1943–44			
	Home group		Hospital group		Home group		Hospital group		Home group		Hospital group	
	Births	Deaths	Births	Deaths	Births	Deaths	Births	Deaths	Births	Deaths	Births	Deaths
→ 2½	36	35 (97%)	33	33 (100%)	85	80 (94·1%)	38	37 (97·4%)	16	14 (87·5%)	25	21 (84%)
→ 3½ ..	52	32 (61·5%)	53	35 (66%)	198	144 (72·7%)	72	42 (58·3%)	24	14 (58·3%)	55	44 (80%)
→ 4½ ..	124	22 (17·8%)	117	23 (19·6%)	369	138 (37·4%)	231	66 (28·6%)	54	14 (25·9%)	125	21 (16·8%)
→ 5½ ..	167	14 (8·4%)	334	14 (4·2%)	1032	99 (9·6%)	828	52 (6·3%)	67	10 (14·9%)	297	19 (6·4%)
All weights	379	103 (27·2%)	537	105 (19·5%)	1684	461 (27·4%)	1169	197 (16·9%)	161	52 (32·3%)	502	105 (20·9%)

THE VOCATION OF MEDICINE

SIR,—In reply to the letter from Drs. Brockington and Lambert in your last issue, I was not aware that the term public health was a synonym for "social medicine." Had I known that it was used in this sense I should have said "You can engage in those branches of medicine in which the doctor does not make direct contact with the patient."

HORDER.

THE UNIVERSITIES AND THE HEALTH SERVICE

SIR,—Professor Dible in your last issue makes an important protest against the volume of routine and administrative work which medical professors are expected to perform to the serious detriment of some of their more important duties. He rightly says that this state of affairs has been aggravated by the advent of the National Health Service, but it is important to realise that most of it existed long before—at any rate for the clinical professors. It is part of my conditions of service with the university that I take charge of a medical unit at the hospital, for if I am to conduct clinical teaching and research I must surely take clinical responsibility. The inpatient and outpatient teaching which goes on all the year round was traditional long before the National Health Service was ever contemplated.

Professor Dible wisely says: "If a choice is to be made between on the one hand the large financial gains offered to hospital specialists . . . and on the other the status and emoluments of a professor *with the traditional freedom and privileges of that office* [italics mine], even at a much lower salary, I should not hesitate to accept the second." Nor would I. But there is not the slightest likelihood that for the clinical professor such a choice will ever exist. I cannot shirk the responsibilities of being a medical specialist by the mere refusal of a salary, because my ultimate responsibility as a clinician is neither to the hospital nor to the university but to my patients. If I could find some way of evading that responsibility I should cease to be a suitable person to teach young men and women to be doctors. Working at a lower rate of pay will not prevent my hospital and university colleagues and doctors and their wives from seeking my professional advice, nor will it relieve me from being a member of senate and faculty and innumerable committees. We already know by experience of both régimes that the work will be precisely the same in nature, hours, and responsibility, whether paid for by the university or by the National Health Service, and in either case the university will expect us to play a part in the government of the teaching hospital to which we are attached. And so, if we should be given the choice of alternative rates of pay, to take the lower would be a gesture of sacrifice which would merely perpetuate our place in the hospital as the poor relatives of our colleagues, while having no other effect but to prevent any further recruitment to clinical chairs.

Manchester. ROBERT PLATT.

THE GENERAL PRACTITIONER

SIR,—I have just read your special article of Nov. 20, and from my own experience as a general practitioner I differ so much on many of the points raised that I would like to set down some facts as I see them. I should say firstly that, though I have never been in favour of the National Health Service, I have not allowed prejudice to lead me into exaggeration.

The article states that "the public has welcomed the new service . . . both doctor and patient are pleased with their new and easier relationship." I find a large proportion of my patients have not welcomed it, and express a feeling of embarrassment at calling me in; many wish to continue paying fees while taking advantage of the "free" medicines. I too think that patients wishing to remain outside the service should obtain drugs without charge.

Though autumn is normally a slack season, I am doing twice the number of visits that I did at this time last year. The article says that the numbers attending surgery have risen by between a quarter and a half; well, I must live in a peculiar district, for my surgery attendances have trebled.

I am afraid I have not become conditioned to filling in certificates, and do not ungrudgingly write them for things such as extra coal, new houses, telephones, corsets, and brassières. The certificate O.S.C.1. is, I agree, a pointless farce; I have thought of placing a number of these, already signed, in my waiting-room under a notice inviting patients to help themselves and so save my time.

The statement "to the doctor's wife the new régime has made little difference" I showed to my housekeeper who deals with the telephone and door work; her remarks were pointed and unprintable, and to put it mildly and colloquially she is thoroughly "browned-off." With regard to the terms of service I can only say that my income will be reduced by a third and my work very considerably increased.

I may be wrong but I cannot believe that my experience is not similar to that of many other doctors and that it is peculiar to the district in which I live, a residential (not rich) suburb on the outskirts of London.

A. G. WESTON.

VEGANIN

SIR,—In the course of his article of Nov. 13, Dr. Asher writes: ". . . tab. codeine co. (N.W.F.), which is perhaps better known as 'Veganin'." We would point out that this is a complete mis-statement. Tab. codeine co. is the N.W.F. equivalent of the original aspirin-phenacetin-codeine compound tablet sold under the registered trade name 'Veganin,' but the formula is not identical and the performance is usually very different. In a later passage, it is made clear that tab. codeine co. is the tablet referred to, yet lower down 'Saridone' is again compared with 'Veganin.'

Unfortunately, too often our trade-mark 'Veganin' is misused, and when the tab. codeine co., which is supplied under this name, fails to give as much relief as might be expected from 'Veganin,' this reacts unfavourably on our goodwill.

William R. Warner & Co. Ltd.
Power Road, London, W.4. ELIOT WARBURTON.

MATERNITY

SIR,—In your leading article of Nov. 20, you state that, in their survey of maternity, the Royal College of Obstetricians and Gynæcologists and the Population Investigation Committee found that ". . . about half of those originally booked for home delivery are finally admitted as unbooked cases to hospital . . . ." This is, of course, incorrect; the figure given on p. 60 of *Maternity in Great Britain* is 5%.

JAMES YOUNG
Chairman.

Joint Committee of R.C.O.G. and Population Investigation Committee,
London School of Economics,
Houghton Street, W.C.2. J. W. B. DOUGLAS
Director.

SIR,—It is indeed distressing to read in your leading article that only 5% of mothers confined in their own homes receive analgesia—this, fifteen years after Minnitt's introduction of his gas-air technique. Even worse, there are hospitals where women are left without any relief at all until just before the actual birth, and are then given the facepiece of the gas machine and told that they are having analgesia. They are not instructed in the technique of administration; machines are more often than not completely out of order; and not infrequently no-one even bothers to turn on the gas. Yet in the official reports of these same hospitals we read that all patients are offered analgesia in labour.

Throughout our land little is done to ensure success from gas-air analgesia. In how many hospitals in the metropolitan area is it the custom for a staff anæsthetist to make regular visits to the labour ward? To ensure satisfactory relief from pain, hospital apparatus must be examined at least twice a week by an experienced practitioner, and it is the plain duty of a staff anæsthetist to visit the labour ward for a short time during the actual administration of analgesia whenever the opportunity offers. Certainly this visit should be made once every 6–8 weeks. Gas-air analgesia, and 'Trilene' analgesia, will give very adequate relief from pain with attention to the details of administration; but the safety of these methods depends on small doses being given, and there is little margin for error.

Fifteen years' close experience of analgesia in labour has shown me how satisfactory the relief from pain

can be; it is infinitely gratifying to an attendant at a confinement to see how much the patient appreciates the small trouble taken to ensure that all goes well.

New Barnet. J. E. ELAM.

HOSPITAL MANNERS

SIR,—I was pleased to see the timely article and editorial in your issue of Nov. 13, commenting on the unimaginative attitude maintained by some hospitals towards the patients. In the course of my work as personnel officer to a London company, I hear frequent complaints, of the type mentioned in your article, from members of the staff who are attending hospital. One girl, delighted to find that she was pregnant, was sent to her local hospital by her doctor. Her husband came to see me the day after the first visit and said that she had arrived home weeping and in a state of nervous exhaustion, and stated that six students had all been instructed by the doctor to examine her. Shortly after this, she had a miscarriage. Other women who have attended hospital for gynæcological complaints have also complained of being obliged to undergo examination by a succession of students. The majority of these women are sensible enough to realise that a thorough examination must be made if they are to be cured, and so long as they feel that the hospital procedure is directed primarily to this end they make no complaint; but when they are made to feel that they cease to matter as a person, and are just so much interesting material, it is not surprising that they experience a sense of outrage. I think their reactions would be different if their wishes were consulted before they were made the object of a lesson.

Another employee was required to attend a certain hospital for an examination. She had been in bed for several weeks and an ambulance was sent for her at 2 P.M., an appointment having been made for 2.30 P.M. She was left sitting in a draughty waiting-room until 8 P.M., during which time no-one paid the slightest attention to her or offered her so much as a hot drink.

Widmore Road, Bromley, Kent. J. M. MASTERS.

Parliament

Tsetse Fly in the African Colonies

IN the House of Commons on Nov. 22 Squadron-Leader ERNEST KINGHORN called attention to the campaign against the tsetse fly in the African colonies. The total area affected was $4^1/_2$ million square miles. In Sierra Leone and Gambia almost 100% of the territory was given over to the ravages of the fly. In Uganda the figure was slightly less than 80%, while in Tanganyika, so important for the groundnut scheme, 75% of the area was covered by its depredations. Under the Colonial Development and Welfare Act of 1945 large grants were made to combat the tsetse fly, and he would like to know what use had been made of this money, and whether the Portuguese, French, and Belgian governments were coöperating with us.

Mr. D. R. REES-WILLIAMS, under-secretary of State for the Colonies, said he believed that the tsetse fly was the African problem no. 1. The trouble was that there were so many species of the fly, some affecting cattle and others human beings. The problem was being tackled by the clearing and resettlement of certain areas, by the use of drugs, both as cures and as prophylactics, in both human beings and cattle. A drug called "7555" had had an extremely good effect and was now undergoing field-tests as a prophylactic. It was not certain whether this drug was the complete answer, but there were good possibilities it might be.

It was too early to form an opinion as to the effectiveness of spraying with insecticides, but two specially fitted aircraft were now in East Africa and a helicopter was on order. The results of the research experiments must be the deciding factor. The control of game had also been dealt with on a large scale in Southern Rhodesia and the results were being examined.

Since 1945 more than £1 million had been made available for research from the Colonial Development and Welfare Fund, and the Colonial governments had spent a great deal of money on this side of the work. The I.C.I. and Shell companies were also joining in the fight against the tsetse fly. International collaboration had been discussed at a conference at Brazzaville this year, and in London soon there was to be the first meeting of the international scientific committee which would coördinate and direct sleeping-sickness research in both Europe and Africa. Efforts were being made to induce veterinary surgeons to enter the Colonial Service by offering them better terms. Mr. Rees-Williams commended to the attention of the House the reports of Professor Buxton, Professor Davey, and Dr. Nash which contained detailed accounts of the work of scientists for many years past.[1]

Milk (Special Designations) Bill

Under this Bill (which was formally introduced in the House of Lords on Nov. 23), the Government propose to take steps to raise during the next five years the standard of all milk sold for liquid consumption to the highest standard of safety. The standard has been progressively raised until 70% of all milk now sold is regarded as safe, and of milk supplied to schoolchildren 98%. But bovine tuberculosis still takes a heavy toll, and of the 1500 to 2000 deaths a year caused by it, most of the victims are children. Further statutory powers are necessary if improvement is to be made. The Minister of Food therefore is taking powers in the new Bill to enable him progressively to require all milk sold to conform to standards of safety. This will be done mainly by an extension of pasteurisation.

QUESTION TIME

Medical Man-power

Mr. A. C. BOSSOM asked the Minister of Health how many more doctors were required to enable the service promised under the new National Health scheme to be given satisfactorily; and what special efforts were being made to train doctors to supply this need.—Mr. ANEURIN BEVAN replied: Distribution is as important as total numbers. The Medical Practices Committee are obtaining reports from all areas in England and Wales as at Dec. 31 and will then be able to assess where the main under-doctored areas are. The medical schools are already filled to capacity. Mr. BOSSOM: Is it not a fact that there is a shortage in the neighbourhood of 20% of the doctors required and, in the circumstances, why is the Minister requiring people to pay for services which he is not able to give?—Mr. BEVAN: The hon. member is quite incorrect. Until the Medical Practices Committee has reported upon the matter, neither he nor I are in a position to say how far areas are under-doctored. Mr. BOSSOM: Will the Minister urge the speeding up of this report, for the medical profession themselves say that approximately 20% are required?—Mr. BEVAN: I have no information at all that the medical profession does say that. It is a fact, however, that the doctors in particular localities are not anxious to say that their areas are under-doctored.

Mrs. LEAH MANNING: In view of the fact that this is an important and urgent question and that recruitment to the profession is likely to be very much increased in view of the security now afforded to young doctors, can the Minister have any consultations with the Chancellor of the Exchequer about widely expanding the medical schools at a very early date?—Mr. BEVAN: The medical schools are already filled to capacity and it is not possible to expand these schools beyond the capacity of teachers available to teach in them. It is not only the size of the medical schools, but the medical teaching staffs, which forms the limitation.

Colonel M. STODDART-SCOTT: Is the Minister, who has spoken of the fullness of medical schools, prepared to carry out the recommendation of the Goodenough Committee to start another medical school?—Mr. BEVAN: A large number of the recommendations of the Goodenough Committee are already in operation; but, as I have said, it is no use operating medical schools if we do not have the medical teaching staff for them.

1. See *Lancet*, Nov. 20, p. 819.

Basic Salary

Dr. S. SEGAL asked the Minister by what authority local executive councils were empowered to ask a doctor applying for payment of basic salary to submit details of his income from all sources; and if he would give an assurance that a doctor who refused to divulge these details would be in no way prejudiced when his claim for a basic salary came up for consideration.—Mr. BEVAN replied: My view is that it is only the doctor's professional income which should be taken into account in such cases. Dr. SEGAL: Would it not also be advisable to investigate incomes at the other end of the scale, where overworked doctors may have lists of patients they are unable to cope with and may be receiving now incomes larger than they ever had before?—Mr. BEVAN: I think that is another question entirely. That matter is being reviewed by the Medical Practices Committee, and not until we have had a survey of the whole country shall we be in a position to identify those parts where the lists are too large and the areas under-doctored.

Mr. JOHN RANKIN: Is the Minister aware that doctors who apply for the basic salary are being told that that basic salary, if paid, is a charge upon their colleagues in the area in which they practise, and does he think that that policy lends itself to a fair interpretation of decision by those colleagues?—Mr. BEVAN: It is a fact that the £300 per year comes out of the general capitation pool—as indeed it ought to—because it forms part of a doctor's remuneration Where, however, the individual doctor is aggrieved he has the right to appeal to me. Many have appealed and decisions have been given.

Sale of Dangerous Drugs

Mr. BARNETT JANNER asked the Home Secretary to what extent the sale of dangerous drugs is increasing in the West End of London; if he would give the reason for the increase; and what action he was proposing to take to deal with this danger.—Mr. CHUTER EDE replied: I am satisfied that there is no organised illicit traffic in drugs to which the Dangerous Drugs Acts apply, either in the West End of London or elsewhere in this country, and that in most of the individual cases of unlawful use of these drugs the offender is brought to justice. My department, in coöperation with the police and H.M. Customs, will continue to exercise the utmost vigilance in order to secure the enforcement of the law relating to dangerous drugs. I am satisfied that, as a result of the measures taken, addiction to dangerous drugs is not a serious problem in this country. Mr. JANNER: May I ask the Minister if he can say whether in the recent case where sufficient drug to kill something like 5000 persons was stolen, any progress has been made in the recovery of that drug?—Mr. EDE: We are doing what we can to get it back, but it does not appear that it has yet been taken by any very large proportion of the 5000 people.

Mr. JOHN LEWIS: Is the Minister satisfied that in the remarkable number of instances recently where publicity has been given to the loss of drugs from doctors' cars, in every case they are genuine?—Mr. EDE: A doctor reports the loss; whether the drugs or the loss are genuine, I am afraid I do not know.

Hearing-aids

Sir WALDRON SMITHERS asked the Minister of Health whether a patient who had purchased a hearing-aid instrument was disqualified from receiving a free one at a later date.—Mr. BEVAN replied: No, Sir.

In answer to a further question Mr. Bevan stated that over 3000 Medresco hearing-aids had already been supplied to patients. He was advised that this aid gave a performance at least as good as that of any commercial aid.

Equal Pay

Mr. D. MCA. ECCLES asked the Minister why there were differences in the scales of pay between men and women administrative officers in the National Health Service.—Mr. BEVAN replied: The differences are being abolished.

Trial Use of B.C.G.

Mr. W. N. WARBEY asked the Minister of Health what arrangements were being made for a trial use of B.C.G. vaccine in this country, with a view to better protection of nurses, doctors, and other contacts particularly exposed to the risks of tubercular infection.—Mr. BEVAN replied: Arrangements are nearing completion, but I am not yet in a position to make any useful public statement on them. I will do so as soon as possible.

Sickness Benefit

Mr. A. H. E. MOLSON asked the Minister of National Insurance on what date contributors since July 5, 1948, to the National Insurance scheme would become eligible for sickness benefit.—Mr. JAMES GRIFFITHS replied: Dec. 28, 1948, is the earliest date on which employed or self-employed persons who were new entrants to National Insurance on July 5 could qualify for sickness benefit.

National Health Service in Scotland

Replying to questions, Mr. ARTHUR WOODBURN stated that some 2400 doctors and some 1200 dentists were in general practice in Scotland. Of these, 2364 doctors and 1124 dentists had joined the service. Approximately 94% of the population had joined.

Radiography Units in Scotland

Mr. WILLIAM ROSS asked the Minister how many mass-radiography units were in operation in Scotland; and where they were.—Mr. WOODBURN replied: Four mass-radiography units are at present in operation in Scotland, two in Glasgow, one in Edinburgh, and one in Motherwell.

Obituary

JAMES HARRY SEQUEIRA

M.D. LOND., F.R.C.P., F.R.C.S.

Dr. Sequeira, who has died in Kenya at the age of 83, was a leading dermatologist, who attracted to his clinic colleagues from all over the world. He was associated with the introduction of the Finsen lamp into this country, and he pioneered the therapeutic use of X rays and radium.

A doctor's son, he was born in London in 1865 and received his early education at King's College School. In 1884 he won a science scholarship to the London Hospital, and in due course he graduated with honours in medicine and obstetrics. His first ambition was to be a surgeon, and he became F.R.C.S. in 1893; but a surgical vacancy on the staff fell to Sir Frederick Treves, and Sequeira embarked on dermatology via medicine. As a young man he was influenced by Sir Stephen Mackenzie, whose house-physician he was. Dermatology was then emerging as a specialty in its own right. Mackenzie used to treat patients with skin disease in his general wards, but on his retirement a separate department was set up and Sequeira was appointed to take charge of it. In those early days the department's patients were scattered round the hospital, each physician having surrendered one bed, but ultimately separate wards were opened.

British Journal of Dermatology

At the turn of the century Sequeira studied for a time under Niels Finsen in Copenhagen. Always quick to take up new ideas, he returned to London convinced of the value of Finsen's work on actinotherapy. In 1900 the first Finsen lamp, a gift from Queen Alexandra, was installed in the London Hospital, and in the following year Finsen's *Phototherapy*, translated by Sequeira, was published in English. His cosmetic results with this treatment have never been bettered.

He had also visited Vienna, where Freund and Schiff were investigating the therapeutic possibilities of X rays. These trials were followed by the introduction of radium in treatment. Here again Sequeira led the way. Before surgeons in this country grasped the potentialities of radiotherapy he had devised holders for radium plates which enabled him to treat malignant disease of the mouth and throat; and under his hand the technique developed so rapidly that in 1905 he was asked to read a paper at the International Congress of Surgery, in Stockholm, on the Use of Radium in the Treatment of

Malignant Disease. Many years later he recalled, in the *British Journal of Dermatology* (which he edited from 1911 to 1915), how he had had to "work on a system of trial and error, which unfortunately had disastrous effects on some of the workers." These troubles led him to devise and install protective cubicles—perhaps the earliest contribution to the safety of X-ray workers. But he himself was a life-long sufferer from the effects of irradiation.

He and his assistants developed to a fine art the X-ray epilation for ringworm; at one time five X-ray tubes were at work for $5^1/_2$ days a week on children with tinea capitis—now a comparative rarity. He was also early in the field as a clinical photographer.

One of the first to point out the importance of dermatology in medical training (and an advocate of its inclusion early in the curriculum), he used to hold every Thursday morning a teaching clinic at which systematic lectures were given. His textbook, which was first published in 1911 and reached its fifth edition last year, proved very popular. It was not as large or as comprehensive as others—for example that of his contemporary, J. M. H. MacLeod—but it was very readable and contained a wealth of personal observation and clinical experience, and was particularly valued for its sections on treatment.

Sequeira served as president of the section of dermatology of the Royal Society of Medicine (1925–27), and councillor of the Royal College of Physicians (1927). Always interested in the social aspects of syphilis, he was at one time chairman of the executive committee of the Society for the Prevention of Venereal Disease; and he was a member of the Trevethin Committee on venereal disease. In fact the establishment of venereal-disease centres probably owes less to political enlightenment or pressure than to a visit paid to his centre by members of the Local Government Board, including Sir Arthur Newsholme, then chief medical officer, who saw a demonstration of children cured of congenital syphilis.

In 1927 Sequeira retired to Kenya, but not to withdraw from active affairs. He added to his interest in dermatology by studying leprosy; and his acute observation of conditions in Kenya was reflected in his Chadwick lecture in 1932 when he criticised some aspects of the unification of the Colonial Services. "It seems a pity," he then said, "that men should be suddenly removed from the mid-Pacific, with its own problems, to East Africa where the conditions are so different." For a time he was chairman of the Kenya branch of the B.M.A., and until lately he edited the *East African Medical Journal*.

"Throughout his life," writes W. J. O'D., "he had a pioneering spirit, testing and using or rejecting any new weapon offered to the practising physician. He wrote classical papers on lupus, on light therapy, and on the rare association of blood and skin changes. In his year of office as president of the dermatological section of the Royal Society of Medicine he presided with urbane distinction. He had a short square figure, a leonine head early covered with thick white hair, wide blue eyes, great dignity, and the greatest kindness.

"Few dermatologists have had the preliminary training in the whole art of medicine that Dr. Sequeira underwent, and throughout his practice of dermatology he approached his cases with the judgment of a physician and the sure touch of a surgeon. He was a great figure for a quarter of a century at the London Hospital, and is remembered in many homes. His kindness to doctors and to their wives was untiring, and his encouragement to young doctors was never failing."

"Sequeira's eminence," adds R. T. B., "was due above all to his clinical instinct and his sympathetic nature. It was characteristic of him, in his wish to help younger men, that he should have asked two of his former house-physicians and first assistants to collaborate with him in preparing the fifth edition of his famous book. His memory will be revered by hundreds of Londoners, who will always remember his dynamic but diminutive person, rather reminiscent of Mr. Punch, with a grand sense of humour, and a twinkle in his eye as he recounted some amusing anecdote about doctors or patients and dermatological adventures."

Dr. Sequeira is survived by his wife and by two adopted children.

LOUISA HAMILTON

M.D. LOND.

Dr. Louisa Hamilton, who died at her home in Buckinghamshire on Nov. 24, was one of the outstanding medical women of her generation. The grand-daughter of Sir William Hamilton, the philosopher, she was born in Edinburgh, where she received her early education. Coming to London she entered the London School of Medicine for Women, and in 1900 qualified as M.B. from the Royal Free Hospital, with honours in medicine and obstetrics. Six years later she took her M.D.

After a few months as assistant to a general practitioner in Essex, she returned to London to take up resident appointments at the New Hospital for Women (now the Elizabeth Garrett Anderson Hospital). In 1901 the resident medical posts at the Royal Free Hospital were opened to women, and in the following year Dr. Hamilton was appointed house-physician there. The holders of these early posts were critically watched, and tact was called for as well as professional competence. Dr. Hamilton was a first-rate pioneer. Her sound knowledge, her common sense, her genial personality, and her sense of humour stood her in good stead, winning not only the warm appreciation of her chiefs and fellow residents but the confidence and respect of the nursing staff, some of whom were watching the new departure with a somewhat doubtful eye.

After this she acted for several years as demonstrator of anatomy at the school, and as pathologist at the Elizabeth Garrett Anderson Hospital; and from 1905 to 1912 she was in general practice in Brunswick Square. Her interest was, however, mainly in medicine, and in 1912 she moved to Nottingham Place in order to specialise. She was appointed to the honorary staff of the Elizabeth Garrett Anderson Hospital, eventually retiring from the post of senior physician in 1936.

For some years she was medical officer to the North London Collegiate School for Girls, to the Church of England Zenana Missionary Society, and later to the Methodist Missionary Society. These activities greatly interested her; and her good judgment, wisdom, and other personal qualities were much valued. Outside her professional work her great interest lay in her country cottage at Loosley Row in Buckinghamshire, where she planned and made a really beautiful garden, and delighted to entertain her friends. She was also a highly skilled needlewoman and an excellent cook.

J. H. T.

Dr. Hamilton had a very able grasp of medicine and particularly of skin diseases. Herself possessing courage, energy, and great integrity, she sought and encouraged these qualities in her students and house-physicians; and her loyalty to, and protection of, her staff was a firm foundation to an efficient unit. She had a great love for young people, with an unsentimental understanding of their problems which made it possible for young men and women to ask for her advice. This was invariably kind, shrewd, and practical.

K. I.

GEORGE JAMES IRVINE LINKLATER

O.B.E., M.D. EDIN.

Dr. G. J. I. Linklater, chief executive school medical officer to the Edinburgh corporation, died in the City Hospital, Edinburgh, on Nov. 23. He had been in the service of the corporation for 26 years.

Dr. Linklater graduated in medicine at Edinburgh University in 1912. After holding resident posts in Edinburgh at the City Fever Hospital and at the Royal Victoria Hospital he became tuberculosis officer for the city, and with Dr. John Guy, a former medical officer of health, he wrote the well-known textbook *Hygiene for Nurses*. In 1920 he took his M.D. and two years later the M.R.C.P.E. He also held diplomas in public health and in tropical medicine and hygiene.

A keen Territorial, Dr. Linklater served with the Royal Army Medical Corps in both wars, and he received the O.B.E. for his services in the first. During the late war he held the rank of colonel, and for his services to the Red Cross he was awarded the Order of St. John. For

many years he had also been a High Constable of Holyroodhouse.

W. G. C. writes: "Dr. Linklater was one of the city's ablest administrators, and the high standard of the school medical service is due to his unceasing work. He was at his best with children, as those who have seen him hold the rapt attention of large audiences at the junior cinema clubs on Saturday mornings will know. An able and lucid lecturer, he also took a leading part teaching hygiene to nurses and health visitors. His many friends will miss a delightful raconteur and a good companion."

NANCY GWENDOLYN SHUBIK

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

Dr. Nancy Shubik, who died on Sept. 20, was the daughter of Mr. and Mrs. F. S. Rogers of Newport, Monmouthshire. She entered the Welsh National School of Medicine in 1935 and qualified in 1939, taking the D.P.H. in 1941. After two years in clinical and public-health work she became demonstrator in pathology at Cardiff. In 1944 she was appointed junior lecturer in pathology at the British Postgraduate Medical School at Hammersmith, where she also undertook research into silicosis under Prof. E. J. King. Throughout her career she was a most enthusiastic worker, with a great determination to seek the exact answers to the problems that she met in her work. In the following year she joined the Indian Medical Service. She did excellent work in India, and as one observer said, "continued dealing with the sick and wounded when others had decided they had done enough work for the day." On returning to England in 1947 she took up neuropathological research in Sir Hugh Cairns's department at Oxford.

Births, Marriages, and Deaths

BIRTHS

BOOG-SCOTT.—On Nov. 19, the wife of Dr. T. M. Boog-Scott—a son.

CHARLES.—On Nov. 26, in London, the wife of Dr. J. A. Charles—a daughter.

KER.—On Nov. 20, in London, the wife of Dr. J. W. Ker—a daughter.

LAWSON.—On Nov. 20, the wife of Dr. H. M. Lawson—a son.

MAYON-WHITE.—On Nov. 20, at Cambridge, the wife of Dr. Richard Mayon-White—a son.

OAKLEY.—On Nov. 19, in London, to Dr. Margaret Dudley-Brown, wife of Lieutenant (S) G. E. Oakley, R.N.—a daughter.

PEYTON.—On Nov. 23, at Ipswich, the wife of Dr. H. N. Peyton—a son.

SHOOTER.—On Nov. 22, in London, the wife of Dr. R. A. Shooter—a son.

VICKERS.—In November, at Singapore, the wife of Dr. W. J. Vickers—a son.

MARRIAGES

ANDERSON—HESKETH.—On Nov. 20, at Digswell, Thomas Barclay Anderson, M.R.C.S., to Margaret Hesketh.

CONNOLLY—CULLIS.—On Nov. 20, in London, R. Campbell Connolly, F.R.C.S., to Elizabeth Fowler Cullis.

PEATFIELD—WILSON HALL.—On Nov. 20, at Eastbourne, Ronald Peatfield, F.R.C.S., to Ruth Beryl Wilson Hall.

WEBB—WOOD.—On Nov. 25, at Swindon, Eric R. Webb, M.R.C.S., to Mary Wood.

DEATHS

BONAVIA.—On Nov. 20, at Hamburg, Victor Joseph Bonavia, M.D. Malta, M.R.C.P., lieut.-colonel, R.A.M.C., aged 54.

HAMILTON.—On Nov. 12, in New York, George Johnson Hamilton, M.D. New York, M.R.C.S.

HAMILTON.—On Nov. 24, at Loosley Row, Princes Risborough, Louisa Hamilton, M.D. Lond.

KITCHIN.—On Nov. 22, Percy Kitchin, M.R.C.S., aged 78.

LILLEY.—On Nov. 22, Ernest Lewis Lilley, M.B. Lond., F.R.C.S., aged 72.

MAPLES.—On Nov. 16, in Jersey, Ernest Edgar Maples, M.D. Lond., F.R.C.S.

MOSELEY.—On Nov. 21, at Ipswich, Charles Kingdon Moseley, M.R.C.S., aged 84.

PALMER.—On Nov. 22, at Prestbury, Cheltenham, Harold Thornbury Palmer, M.R.C.S.

RAWLINGS.—On Nov. 23, at Cambridge, Grahame Rigby Rawlings, M.B. Camb., D.A.

SEQUEIRA.—In November, in Kenya, James Harry Sequeira, M.D. Lond., F.R.C.P., F.R.C.S., aged 83.

STUART.—On Nov. 26, at Harpenden, Emily Gertrude Stuart, M.B. Lond., aged 76.

Notes and News

PRACTITIONERS' LISTS

THE Minister of Health last week withdrew his general consent to practitioners having on their lists more than the prescribed maximum number of patients. Executive councils have been requested to review as soon as possible the numbers on the lists of doctors in their area; and they are urged to collect by Feb. 1 accurate figures as at Jan. 1. It is suggested that as a preliminary step a doctor with an excess list should be asked not to take further patients on to his list (except relatives of persons already on his list living in the same house) unless the list can be brought within the appropriate limit by taking in a partner or employing an assistant. Councils may still apply in individual cases for the Minister's consent to an increased maximum.

PRODUCTIVE WORK FOR THE HOSPITAL PATIENT

IN the past a number of hospitals have arranged for their long-stay patients to do productive work sent in by neighbouring firms; but to avoid liability for insurance contributions, and disturbance of National Insurance benefits, no direct payment has been made to patients. The Ministry of National Insurance has now provided under the National Insurance (Unemployment and Sickness Benefit) Regulations, 1948, that payment for such work may be made direct to patients without affecting the right to sickness benefit provided that: (1) the earnings do not exceed £1 a week; and (2) the work is undertaken under medical supervision as part of the hospital treatment. If the amount earned exceeds £1 a week, benefit will cease and insurance contributions will ordinarily be payable. (This provision does not alter the arrangements already announced for National Insurance benefits to be reduced or suspended where a patient is undergoing inpatient treatment in a National Health Service hospital; here the reduced benefits will not be further reduced unless the earnings exceed £1, when they will cease.) A patient will not be required to pay National Insurance contributions unless his earnings exceed £1 a week, when a class-1 contribution will be required from patient and employer if the employment is under a contract of service. If there is no contract and the earnings are over £1 a week, class-2 contributions will be payable by the patient, but exception can be claimed if the total income from all sources does not exceed £2 a week. Hospital authorities are urged by the Ministry of Health to introduce arrangements for the employment of suitable long-stay patients; and they are advised to apply in the first place to the disablement resettlement officer at the local office of the Ministry of Labour and National Insurance. The hospital authority will decide the method of paying a patient for his work. Outpatients in receipt of sickness benefit may also receive payment for work.

AUSTRALASIAN PRIMARY FELLOWSHIP

THE primary fellowship examination of the Royal Australasian College of Surgeons is to be reciprocal with that of the Royal College of Surgeons of England.[1] A primary examination for the English fellowship is to be held in Australia next February. Thereafter those succeeding in the Australasian college's primary (for which courses will be held) will be able to proceed to the English final examination.

SWISS HOSPITALITY

THE people of Switzerland have shown their appreciation of the British war effort in many ways, and in 1946 the Don Suisse offered to provide, for one year, 100 beds in sanatoria at Leysin, in Switzerland, for the free accommodation and treatment of British ex-Servicemen with pulmonary tuberculosis. The patients were selected by the Ministry of Pensions according to clinical criteria agreed with the Swiss doctors, and the first hundred patients went to Switzerland at the beginning of 1947. In August 76 patients returned after the agreed period of treatment and 79 others went out. The remainder came back in small groups from time to time. The scheme was extended by eight months through the generosity of Don Suisse, and finally ended last August. The patients settled down well, and all spoke highly of the medical care they received and with great appreciation of the friendly welcome and kindness shown to them in Switzerland.

1. *Med. J. Aust.* Nov. 20, p. 620.

The Ministry of Pensions thinks it too early to assess the lasting effects of this treatment, but the future progress of the patients is to be specially noted.

WHOLE FOOD

AT the inaugural meeting of the Producer Consumer Whole Food Society in London on Oct. 27, Mr. F. N. Turner, the chairman, said that the society exists to encourage the production and distribution of whole food. It was announced that a panel of over sixty producers growing and supplying whole foods had been built up. The society has already taken up with the Ministry of Food the question of subsidies on cereals, on the score that subsidised products are invariably denatured, those who use unprocessed cereals having to pay a much higher price. The society, which includes farmers, is opposed to the use of chemicals for fertilising soil.

University of Oxford

On Nov. 20 the degree of D.M. was conferred on J. E. Duffield.

University of Edinburgh

Sir Edward Appleton, F.R.S., secretary of the Department of Scientific and Industrial Research and Nobel laureate, has been appointed principal and vice-chancellor in succession to the late Sir John Fraser.

Scottish Conjoint Board

The following candidates, having passed the final examinations, have been admitted to the licentiateship of the Royal Colleges of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow:

D. S. Anderson, R. A. Atherton, G. J. Bagley, P. M. Brazil, Philip Freeman J. H. Gentles, Harry Gerber, L. H. Geronimus, Susan M. Gillies, T. E. Grant, J. C. O. Iwenofu, Josef Jochnowitz, Alexander Logan, L. C. Luck, K. E. M. Melville, Martin Metz. A. W. P. Millard, A. J. Mone, William McIlwraith, Monica B. Macnamara, Eleanor D. M. Pierce, David Pride, F. R. Reid, Ellen M. Rosenthal, David Simon, P. H. Slade, R. A. Spalding, Helen L. Steven, David Stewart, J. A. Turner, Robert Wilson, James Winning, J. S. Wood, M. J. Zimmerman.

British Psychological Society

The medical section of the society is holding a meeting at 8 P.M., on Wednesday, Dec. 8, at 1, Wimpole Street, London, W.1, when Dr. Elizabeth Rosenberg, Sir Paul Mallinson, and Dr. O. W. S. FitzGerald will speak on the changing Functions of a Psychiatric Outpatient Department. Psychiatrists are invited to attend the meeting.

British Medical Association

The council of the association are shortly offering the following prize and scholarships:

Nathaniel Bishop Harman prize (£100) is offered to promote systematic observation and research among consultant members of the staffs of hospitals who are not attached to recognised medical schools. It will be awarded for the best essay on work which must include observations collected by the candidate in the course of his practice.

Ernest Hart scholarship (£200), *Walter Dixon scholarship* (£200), *and four research scholarships* (£150 each) are offered for research in any subject, including State medicine, relating to the causation and prevention or treatment of disease.

Insole scholarship (£250) is offered for research into the causes and cure of venereal disease.

Further particulars may be had from the secretary of the association, B.M.A. House, Tavistock Square, London, W.C.1.

Supply of Vaccines and Sera

As already announced, stocks of vaccine lymph and diphtheria prophylactic are being held at laboratories of the Public Health Laboratory Service for issue, free of charge, to medical officers of health or to practitioners taking part in local health authorities' arrangements under section 26 of the National Health Service Act. Certain other substances not readily obtainable at present from trade sources will also be available through the laboratory service. These materials include measles serum, typhus vaccine, rabies vaccine, botulinum antitoxin, anthrax serum, and snake-venom serum.

The protein-free extracts of stomach and small intestine, with which O. Hubacher reported favourable results in gastric and duodenal ulcer (*Lancet*, 1946, ii, 272) can now be obtained from Messrs. Ward, Blenkinsop and Co., under the name of 'Robaden.'

Diary of the Week

DEC. 5 TO 11

Monday, 6th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. W. E. Lloyd: Pleurisy and Pleural Effusions. (Part II.)

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. J. M. Yoffey: Nuclei of the Brain Stem.
5 P.M. Dr. W. S. Feldberg, F.R.S.: Autonomic Nervous System.

Tuesday, 7th

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. F. Goldby: Vagus Nerve and its Distribution.
5 P.M. Dr. Feldberg: Chemical Transmission of Nerve Effects.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3 P.M. Sir Lionel Whitby: Physiology of Hæmopoiesis. (First Harben lecture.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. W. J. O'Donovan: Hysteria Cutis.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Dr. J. W. B. Douglas: Maternity in Britain.

EDINBURGH POST-GRADUATE BOARD FOR MEDICINE
5 P.M. (Royal Infirmary.) Prof. O. L. Richmond: A Scholar's View of Immortality.

Wednesday, 8th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Sir John Parkinson: Heart-failure.

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. S. Zuckermann: Female Reproductive Tract.
5 P.M. Mr. George Brownlee, PH.D.: Chemotherapeutic Drugs.

UNIVERSITY COLLEGE, Gower Street, W.C.1.
5.15 P.M. Dr. J. W. Trevan, F.R.S.: Statistics from the Standpoint of a Pharmacologist. (Second of two lectures.)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE
3 P.M. Sir Lionel Whitby: Dyshæmopoiesis from Nutritional and Specific Deficiencies. (Second Harben lecture.)

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow.
5 P.M. Prof. J. C. Spence: Poliomyelitis.

Thursday, 9th

ROYAL COLLEGE OF SURGEONS
5 P.M. Sir Reginald Watson-Jones: Reactions of Bone to Metal. (Robert Jones lecture.)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE
3 P.M. Sir Lionel Whitby: Dyshæmopoiesis from Noxious Agents. (Last Harben lecture.)

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Prof. G. P. Crowden: Physiological Studies of Mental and Physical Work in Hot and Humid Environments.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. J. L. Franklin: Seborrhœic Dermatoses.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
4.15 P.M. Mr. G. Ewart Martin: Acute Otitis Media.

Friday, 10th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Prof. L. J. Witts: Aplastic Anæmia and Agranulocytosis.

ROYAL COLLEGE OF SURGEONS
5 P.M. Dr. Brownlee: Chemotherapeutic Drugs.

MAIDA VALE HOSPITAL MEDICAL SCHOOL, W.9
5 P.M. Mr. Valentine Logue: Case demonstration.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. J. Smart: Mediastinal Tumours.

Appointments

CARTER-LOCKE, H. B. C., M.B. Lond., D.P.H.: deputy M.O.H., Bromley, Chislehurst, Sidcup, and Orpington, Kent.
FREEMAN, PERCIVAL, M.B. Leeds, D.P.H.: deputy M.O.H. and asst. county M.O., Kent.
KAHN, J. H., M.B. Leeds: psychiatrist, child-guidance clinic. Huddersfield.
PRITCHARD, P. M. M., M.A., M.B. Camb., D.C.H.: registrar, paediatric department, University College Hospital, London.
TUCK, IVY, M.B. Lond.: morbid anatomist and hæmatologist, North Middlesex Hospital.

Colonial Service:

AUSTIN, F. C. K., M.D. Edin., D.T.M. & H.: district M.O., Windward Islands.
BROWNE, R. E., M.R.C.S.: supernumerary M.O., Leeward Islands.
CONACHER, D. G., M.B. Edin.: M.O., Tanganyika.
EDDEY, L. G., M.B. Aberd., D.T.M. & H.: director of medical services, British Guiana.
FAIRLEY, DOUGLAS, M.D. Glasg.: senior medical officer, St. Helena.
FOWLER, A. F., M.R.C.S., D.T.M. & H.: M.O., Tanganyika.
HEARD, R. G. P., B.A., M.B. Dubl.: M.O., Tanganyika.
YAP, P. M., M.A., M.B. Camb.: M.O., Hong Kong.
ZWIERZ, MACIEJ, M.D. Beyrouth: M.O., St. Vincent, Windward Islands.

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CONTENTS

THE PATHOGENESIS OF THE ACUTE EXANTHEMS

AN INTERPRETATION BASED ON EXPERIMENTAL INVESTIGATIONS WITH MOUSEPOX (INFECTIOUS ECTROMELIA OF MICE)

FRANK FENNER *
M.B.E., M.D. Adelaide, D.T.M.
FRANCIS HALEY RESEARCH FELLOW, DEPARTMENT OF EXPERIMENTAL MEDICINE, UNIVERSITY OF MELBOURNE
From the Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

ONE of the most intriguing problems of human virus infections is the pathogenesis of the acute exanthems—smallpox, chickenpox, measles, and rubella—which are characterised by a long incubation period and by a rash which develops some days after the onset of symptoms. Experimental investigation of these diseases is hampered by the lack of suitable susceptible laboratory animals. In the absence of direct studies it seems reasonable to investigate the pathogenesis of such natural virus diseases of laboratory animals as are characterised by these features, and to compare the results thus obtained with the data available on the pathogenesis of the human exanthems.

The recent identification of the virus of infectious ectromelia of mice as the murine representative of the mammalian pox viruses (Burnet and Boake 1946) and subsequent studies on the clinical and pathological features of the disease and its epizootic behaviour (Fenner 1948a) suggested that this disease, mousepox, could be used as such a "model." Cross-protection tests (Fenner 1947a) have given ample evidence of the close relationship of the virus to vaccinia virus. Recent tests of the inhibition of hæmagglutination due to vaccinia and ectromelia viruses by sera from non-vaccinated humans who had just recovered from smallpox † have shown that variola virus also is closely related to ectromelia virus.

Mousepox is spread by contact, the virus usually entering the host's body through minute abrasions of the skin (Fenner 1947b). Seven or eight days after the mouse has been exposed to infection a primary lesion develops at the site of entry of the virus, and this is followed within the next two days either by death, with acute necrosis of the liver and spleen, or by a rash which reaches its apogee in another two or three days. Thus mousepox is caused by a virus closely related to the causal organism of one of the human acute exanthems and is characterised by a relatively long incubation period and a rash.

The pathogenesis of mousepox was studied by inoculating a large number of mice in the pad of the hind foot with a small dose of ectromelia virus, a procedure which closely resembles natural infection. At daily intervals between the second and the twenty-fourth day two mice were killed. The virus and ectromelia anti-hæmagglutinin (E.-A.H.A.) content of the blood, and the virus content of the inoculated foot, the skin of the abdomen remote from the site of inoculation, and the spleen of each mouse was determined. Sections of skin were also studied, Mann's stain being used to demonstrate virus inclusion bodies. The technical methods used and the detailed results obtained are fully described elsewhere (Fenner 1948b). Here a hypothesis of the pathogenesis of mousepox based on these experiments is presented and the pathogenesis of the human acute exanthems is discussed in the light of this hypothesis.

* Present address: Rockefeller Institute for Medical Research, New York.

† These sera were kindly supplied by Dr. F. O. MacCallum.

MULTIPLICATION OF VIRUS AFTER A STANDARD SMALL INFECTING DOSE

In fig. 1 the results of the series of virus and antibody titrations are shown in the form of curves constructed through the individual daily titres, which have been omitted here but are being published elsewhere (Fenner 1948b). The ordinates are logarithmic, one unit indicating a tenfold difference in virus concentration. The appearance of the foot and of the shaved skin, and the density of inclusion bodies in sections of the skin, are also shown.

In the Foot

When the foot was the site of the primary lesion, the virus multiplied there logarithmically between the first and the eighth day and more slowly afterwards, the titre remaining about the same from the ninth to the fourteenth day. After that the titre fell steadily until no virus was detected after the thirtieth day. The fall was unrelated to the masking of virus by antibody.

No macroscopic change was observed in the inoculated foot until the seventh day, when it was slightly swollen in most of the mice. This point, the first clinical evidence of infection, has been taken as the end of the incubation period. The concentration of virus in the foot had reached almost its maximum before there was clinical evidence of infection.

In the Spleen and Blood

The first evidence of blood-stream dissemination of the virus was the demonstration of virus in the spleen on the fourth day. The titre of virus in the spleen then rose steeply. In some animals, which were either moribund when killed or destined for an early death from acute mousepox, the titre rose to a very high level—over 10,000,000,000 infective particles per g. In the other animals a stationary phase was reached at a level of 100,000,000 infective particles per g. on the seventh day, and this continued until the tenth day. Thereafter, coinciding with the rapid increase in circulating antibody, the concentration of virus in the spleen declined rapidly, and none was recovered after the sixteenth day, except in one animal in which the virus titre was higher than usual in the foot and skin and virus was also present in the spleen and blood. The E.-A.H.A. titre was 1000, and in the undiluted blood antibody inactivated the virus present. However, this effect was overcome by dilution of the blood.

Large amounts of virus in the blood were found only in moribund animals. In the others virus was always present in the blood at a relatively low titre between the fifth and the twelfth day. Viræmia in mousepox is probably due to the continual liberation of virus into the blood-stream by necrosis of the infected cells of the spleen and liver and possibly the bone-marrow also.

In the Skin Remote from the Point of Inoculation

The curve (fig. 1) showing the virus content of the skin and its relation to the lesions of the rash and the occurrence of inclusion bodies in the epidermal cells is of considerable interest. Virus was first found in the skin on the sixth day and increased logarithmically until the eighth or ninth day, when the concentration reached a stationary phase which persisted until the fourteenth day. Thereafter it fell rapidly. As in the primary lesion, macroscopic changes were first detected when the virus titre had almost reached its maximum. This is in keeping with observations on other virus diseases (Rivers 1939, Bang 1943, Taylor 1941).

Histological examination of the skin showed that the first change, which was seen on the seventh day, occurred in isolated groups of the basal cells of the epidermis, which showed pyknotic nuclei surrounded by vacuoles. A few inclusion bodies were evident in the cytoplasm of some of these cells. The size and number of affected area

of skin rapidly increased until on the ninth day there were many papules in which most of the epidermal cells were infected, and inclusion bodies were numerous in the cells of the hair follicles and sweat glands also. Massive necrosis of the superficial cells of the papules converted them to ulcers with closely adherent scabs. The dermis showed intense lymphocytic infiltration at this stage. Healing took place by the development of new epithelium beneath the scabs, and the new epidermal cells were not invaded by the virus. The scabs had fallen off by the eighteenth day, and after a further week recovery was complete except for the absence of hairs and sweat glands in the scarred areas of skin.

TIME OF APPEARANCE OF VIRUS IN REGIONAL LYMPH-NODES, BLOOD, LIVER, AND SPLEEN

Certain features of the pathogenesis of mousepox were not established in the experiments just described; so another short experiment was carried out in which mice were infected by rubbing the pinna with a swab soaked in a concentrated virus suspension, and testing the blood and suspensions of the regional lymph-node, the pinna, the liver, and the spleen for the presence of virus. Accurate titrations were not performed, but the methods used were sensitive enough to detect very small concentrations of virus. The results are shown in table I.

Virus was isolated from the regional lymph-nodes eight hours after the application of the virus suspension to the ear, and increased in titre for the next few days. On the third day a small amount of virus was found in the blood, and larger amounts in the liver and spleen. The virus content of the liver and spleen then increased rapidly, and that of the blood increased slightly.

RÔLE OF ALLERGY IN PRODUCTION OF SKIN LESIONS

Most hypotheses of the pathogenesis of the rashes of the acute exanthems have, from the time of von Pirquet (1913), postulated allergy as the basic mechanism by which the rash is produced. However, in the experiments just described, focal multiplication of virus in the skin was shown to cause the rash. An allergic reaction to ectromelia virus could not be demonstrated in these animals until the seventh day after infection—i.e., after the virus had become localised in the skin.

The strongest evidence that allergy is of little importance in causing the rashes of the acute exanthems is derived from the study of cases of congenital variola and vaccinia (Lynch 1932), alastrim (Stott 1945), measles (Kohn 1933), and chickenpox (Shuman 1939). In all these diseases the rash appears to go through its normal course of development in fœtuses infected in utero. The fœtus is probably incapable of forming antibody (Grasset 1929, Burnet 1941); and, though the human placenta is permeable to neutralising antibodies, which probably play a part in controlling the fœtal infection, it is impermeable to sensitising antibodies (Sherman et al. 1940). The production of typical skin pocks three or four days after the inoculation of large doses of vaccinia virus into the bodies of 24-day-old rabbit fœtuses (Gallagher and Woolpert 1940), and of skin lesions and Koplik's spots in simian measles four days after the intravenous inoculation of virus (Blake and Trask 1921), is explicable only on the hypothesis that the skin lesions are caused by multiplication of the virus.

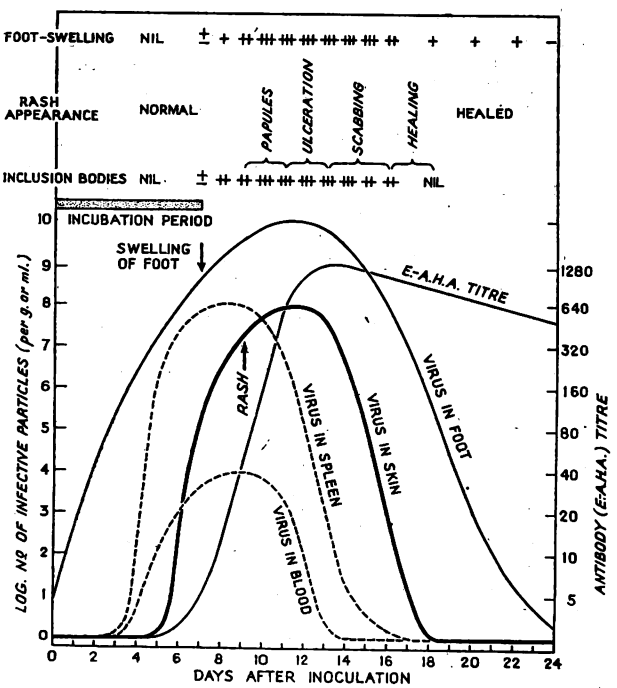

Fig. 1—Growth curves of virus in foot, spleen, blood, and skin of mice inoculated in the foot with a small dose of "Moscow" ectromelia virus. Development and disappearance of primary lesion and rash are shown, as is the occurrence of inclusion bodies in skin in sections stained with Mann's stain.

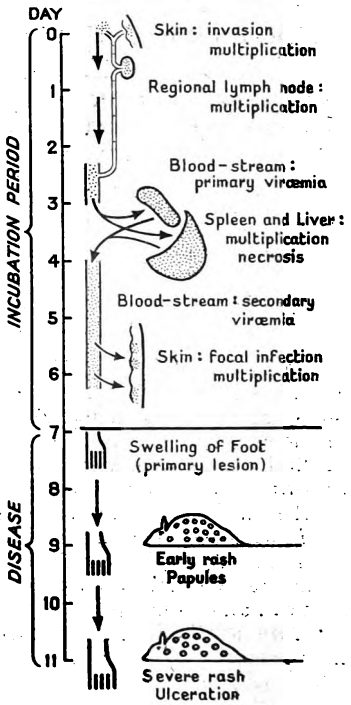

Fig. 2—Diagrammatic representation of pathogenesis of mousepox.

PATHOGENESIS OF MOUSEPOX

The observations just described may be interpreted as shown diagrammatically in fig. 2. Infection with ectromelia virus takes place by the introduction of a few virus particles into the skin of the mouse either naturally through an abrasion or by inoculation. Within eight hours of the establishment of infection virus passes to the regional lymph-node, within which it multiplies for a few days. Necrosis of cells in the lymph-node next liberates virus, which enters the blood-stream but is immediately taken up by the phagocytes of the liver and spleen and possibly the bone-marrow. Contiguous cells of these organs are infected, with a great increase in the concentration of virus. Virus particles are next liberated directly into the blood-stream by necrosis of the infected cells lining the sinusoids of those organs. This secondary viræmia, which is first evident on the fourth day after infection, leads to widespread focal infection of the epidermal cells, virus being first detected in the skin on the sixth day. By this time the titre of virus in the primary lesion has reached a high level, and for the first time there is obvious œdema at the site of entry of the virus, and the incubation period has come to an end.

This œdema increases, ulceration follows, and the mouse liberates virus into the environment—i.e., it is infective. Meanwhile virus multiplies rapidly in the liver and spleen and may so destroy the cells of these organs that both become almost completely necrotic and the mouse dies. Multiplication of the virus in the skin lags behind that in the liver and spleen, for the skin is

not infected until the period of the secondary viræmia developing from the fourth day onwards. If death occurs before the eighth or ninth day, as acute deaths usually do, no skin lesions are found, but the virus content of the skin is high and microscopic sections may show many inclusion bodies within the epidermal cells, the distribution of groups of infected cells being focal. If multiplication of virus in the liver and spleen is less extreme and the animals survive the acute phase of the disease, œdema of the epidermal cells becomes clinically obvious as pale macules, which rapidly become papular and ulcerate owing to necrosis of the superficial cells. The massive liberation of virus which then takes place is responsible for the high infectivity of mice at this stage. By this time the circulating antibody has reached a high titre and skin sensitisation to the virus can also be elicited. Antibody prevents the virus from infecting new cells, and the virus content of all organs and tissues rapidly falls, with recovery of the infected animal.

This picture of the pathogenesis of the virus disease mousepox closely resembles that drawn by Ørskov (1932) (see also Madsen 1937) from his classical investigations on mouse typhoid. The main difference, which is of some importance for our later argument, is that in mousepox the natural portal of entry of the virus is the skin, a tissue for which the virus has a high affinity and in which prolonged multiplication takes place, with the production of a macroscopic primary lesion. In mouse typhoid, and probably in several other bacterial and virus diseases, local multiplication of the micro-organism at the portal of entry does not produce a clinically recognisable primary lesion.

TABLE I—OCCURRENCE OF VIRUS IN SEVERAL ORGANS AT INTERVALS AFTER INFECTION BY THE APPLICATION OF "MOSCOW" ECTROMELIA VIRUS TO THE EAR

Material	Hours after infection				Days after infection				
	1	2	4	8	1	2	3	4	5
Pinna ..	+	+	+	+	++	+++	+++	+++	++++
Regional lymph-node	0	0	0	+	+	++	+++	+++	++++
Blood ..	0	0	0	0	0	0	+	++	++
Liver ..	..	..	..	..	0	0	++	+++	++++
Spleen ..	..	..	..	..	0	0	++	+++	++++

COMPARISON WITH OTHER EXANTHEMS

Table II, which includes much that is speculative, summarises present knowledge of the length of the incubation period, the occurrence of clinically apparent or postulated primary lesions, and the interval between the onset of the disease and the appearance of the rash in many human and a few animal diseases. It is not suggested that in all these the pathogenesis is similar to that of mousepox, but it may be useful to think of them in terms of a primary lesion at the site of entry of the bacterium or virus, an early primary bacteræmia or viræmia, and localisation and multiplication of the organism in some internal organ, which is usually the liver, spleen, or bone-marrow. From here it may be reliberated in much larger amounts into the blood-stream, leading to a second series of foci of infection, which

TABLE II—COMPARISON OF MOUSEPOX WITH VARIOUS OTHER EXANTHEMS

Disease	Usual mode of spread	Site of primary lesion (C, clinically apparent)	Usual length of incubation period (days)	Interval between end of incubation period and appearance of rash (days)	Presence of organisms in lesions of rash
Virus diseases:					
Mousepox	Contact	Skin (C)	7	2	+
Rabbitpox	? Contact or ? airborne	? Upper respiratory tract	5	0–1	+
Smallpox	Airborne	Upper respiratory tract	12	3	+
Inoculation smallpox	Intradermal inoculation (variolation)	Skin (C)	3–4 (local lesion) 8 (symptoms)	6 (from local lesion) 2 (from symptoms)	+
Generalised vaccinia	Intradermal inoculation	Skin (C)	3–4	4	+
Varicella	Airborne	Upper respiratory tract	16	0–1	+
Measles	Airborne	Upper respiratory tract	10	4	+
Rubella	Airborne	Upper respiratory tract	16	0–1	?
Dengue	Intravenous inoculation (mosquito)	? In internal organs	6	4–5	?
Diseases of unknown ætiology, possibly due to viruses:					
Infectious mononucleosis	? Airborne	? Upper respiratory tract (C)	8	7	?
Pityriasis rosea ..	?	? Skin (C) (herald patch)	? 4–10	7	?
Rickettsial diseases:					
Tsutsugamushi ..	Intradermal inoculation (mite)	Skin (C)	12	6	+ (in endothelial cells of capillaries)
Murine typhus ..	Subcutaneous inoculation or inhalation	?	10	5	+ (in endothelial cells of capillaries)
Bacterial diseases:					
Typhoid fever ..	Ingestion	Throat (C, rarely) Intestine	12	7	+
Meningococcal septicæmia (spotted fever)	Airborne	Upper respiratory tract	?	0–2	+
Scarlet fever ..	Airborne	Upper respiratory tract (C)	3	2	– (toxin)
Spirochætal diseases:					
Syphilis	Contact	Skin (C)	28	21	+

may include the epithelial cells of the skin or the endothelial cells of capillaries in the dermis. Subsequent multiplication of the organism in the skin would then cause the characteristic rash.

Rabbitpox and Rabbit Vaccinia

Before discussing the human exanthems it is desirable to consider briefly animal diseases other than mousepox which are characterised by a rash. The only ones on which any detailed investigations have been made are generalised vaccinia of rabbits (Douglas et al. 1929, Pearce et al. 1936), rabbitpox (Greene 1934, Hu et al. 1936), and rabbit plague (Jansen 1946). These diseases are caused by closely related viruses, and the last two may be due to modified laboratory strains of vaccinia virus.

There is no exact information available on the natural mode of spread; possibly the infection is airborne or is transmitted by contact. No statement is possible, therefore, on the site of the primary lesion. A large amount of virus is certainly disseminated by the blood-stream at the latter end of the incubation period, and there is ample evidence that the skin lesions are due to multiplication of virus in the dermis and sometimes in the epidermal cells. In both diseases virus was isolated from the skin lesions, and in certain outbreaks (Greene 1934) inclusion bodies were observed in the epithelial cells. Greene also noted that several crops of skin lesions sometimes developed, corresponding, on our interpretation, to several successive seedings of the dermal cells with virus distributed via the blood-stream.

Ørskov and Andersen (1938) applied the methods of investigation which had been so fruitful in elucidating the pathogenesis of bacterial diseases of mice to the study of the mechanism of infection of vaccinia in rabbits. After intradermal inoculation they found the same process of regional involvement of lymph-nodes on the first day, and multiplication of virus in the liver and spleen, with secondary viræmia, on the third day. In very young rabbits (two and three days old) virus was demonstrated in the liver and spleen on the first day, and in animals which survived long enough hæmorrhagic foci, due to further generalisation of the virus, were noted in the kidneys and skin. In addition, multiplication of virus in the skin at the site of inoculation produced a local lesion there. The parallel to ectromelia in mice is close, but with the doses used the incubation period was much shorter in vaccinia in rabbits than in ectromelia in mice.

Variola and Vaccinia

The closest human analogues of mousepox are undoubtedly smallpox, alastrim, and generalised vaccinia, and these diseases may well be discussed together. In generalised vaccinia and inoculation smallpox the analogy with mousepox is direct, for in all three the primary lesion is in the skin. In natural smallpox and alastrim available evidence suggests that the virus enters the susceptible host through cells of the respiratory tract. Paschen (1932) reported that he had obtained evidence of infection of the throat, with multiplication of the virus in that site in contacts examined during the incubation period. He relied on the demonstration of elementary bodies in stained smears, a technique which is open to error and difficult to put on a quantitative footing. It is highly desirable that this question should be reinvestigated by the chick-embryo method of titrating the virus. In this way definite information on the site of primary infection and the periods of infectivity of variola could be obtained. The infectivity of early cases of variola, before necrosis of the skin has liberated virus there, is almost certainly due to nasopharyngeal lesions, which may be due to the primary lesion there or perhaps to the early ulceration of the secondary lesions when they develop on mucosa.

Paschen suggested that, after multiplication in the throat, the lungs were invaded, with later secondary liberation of virus through the blood-stream and infection of the skin and other organs. It seems more likely that virus particles which entered the blood-stream via the lymphatics to cause the primary viræmia would be taken up generally by macrophages lining the sinusoids of the spleen, liver, and bone-marrow. Titration of the virus content of various organs from fatal cases of variola might indicate their relative importance in this respect.

There is no doubt that the skin lesions of variola and generalised vaccinia are due to multiplication of virus in the epidermal cells, and there is good evidence that this multiplication proceeds in apparently normal skin for some days before lesions become evident. Downie and Dumbell's (1947) plate shows almost universal infection of the epithelial cells in an early smallpox lesion of the human skin, and Dible and Gleave (1934) demonstrated early histological changes with inclusion bodies in the cells in apparently normal areas of skin in a fatal case of generalised vaccinia. Comparison of the histological descriptions of Dible and Gleave with the sections obtained in mousepox makes irresistible the conclusion that the pathogenesis of the rash is the same in the two conditions. The differences in appearance of the lesions can be explained by the much greater thickness of the epidermis in man.

Varicella

Experimental investigations on the virus of varicella are very meagre, Rivers's (1926, 1927) production of lesions with characteristic intranuclear inclusion bodies in the testes of vervet monkeys inoculated with vesicle fluid being the only accepted transmission to experimental animals. Several investigators have produced varicella in children inoculated with vesicle contents, Steiner's (1875) observations being the most reliable. The children that he inoculated in the arm with clear vesicle fluid became feverish on the fourth day. Constitutional symptoms increased and the characteristic rash appeared on the eighth day. The short incubation period parallels that observed in inoculation variola, and is probably due to the larger dose of virus and its more rapid passage to the internal organs than in natural infection. Elementary bodies, which are probably varicella-virus particles, can be demonstrated in the vesicle fluid by differential centrifugation and are specifically agglutinated by varicella convalescent serum (Amies 1933).

Tyzzer (1905–6), investigating the histology of the skin lesions of varicella, found characteristic eosinophil intranuclear, and less commonly intracytoplasmic, inclusion bodies in cells of the dermis and epidermis in affected areas. The earliest changes, which long preceded the appearance of the vesicle and were much more widespread than the vesicles, were seen in the endothelial cells of dermal capillaries. The appearance of inclusion bodies in these very early lesions, and their great multiplication in cells of the epidermis before the characteristic degenerative changes which led to vesicle formation, suggest that the pathogenesis of the rash of varicella is much the same as that of smallpox and mousepox, virus being widely distributed by the blood-stream some days before vesicles develop.

The site of the primary lesion in the natural disease is almost certainly the upper respiratory tract. Mild inflammatory lesions of the nasopharyngeal mucosa appear in the earliest stages (Stokes 1943) and discharge virus. The sites of the internal foci of multiplication of the virus are unknown.

Measles

The primary lesion of measles is undoubtedly in the upper respiratory tract. Cases are infective for at least

five days before the rash appears (Box 1946), and lesions of the throat are the first that can be detected.

In human measles the virus has been demonstrated in nasopharyngeal washings collected when Koplik's spots are plentiful, just before the appearance of the rash, and in blood drawn at various periods extending from just before the appearance of the rash until two days after its appearance (Rake and Shaffer 1940, Shaffer et al. 1941). The most important study on the pathogenesis of measles, however, is that of Blake and Trask (1921) on simian measles. They found that the incubation period of simian measles was about seven days when large amounts of nasopharyngeal washings or tissue suspensions were inoculated intratracheally. By the subinoculation of 10 ml. of citrated blood collected from an inoculated monkey, which subsequently developed Koplik's spots on the eighth and a rash on the eleventh day, these workers could not demonstrate virus in the blood on the second, third, or fourth day of the incubation period, but obtained a positive result with blood drawn on the fifth, sixth, or seventh day. There was no means of deciding which specimen or specimens were positive, since all samples were inoculated into the same monkey. Blood drawn after the seventh day was always positive until the animal was killed on the thirteenth day. When infective blood drawn after the seventh day was inoculated intravenously the incubation period was only four days, suggesting that the interval between establishment of the primary lesion and the secondary viræmia had been eliminated.

The shortening of the incubation period by the intravenous inoculation of large amounts of virus is also seen when the fœtus becomes infected; for, when there is a miscarriage due to measles, it is often found that the fœtus has a rash at about the same stage as that of the mother (Kohn 1933). Some of Shuman's (1939) cases of varicella in the newborn showed the same feature.

Blake and Trask's (1921) investigations also showed that Koplik's spots were part of the rash and not the primary lesion of measles, for they appeared after both intratracheal and intravenous inoculation. Further, virus was demonstrated in the minced buccal mucosa and skin of infected animals.

The data just outlined show that the pathogenesis of measles is similar to that of mousepox, and von Pirquet's (1913) theory that the regular course of the measles eruption was the expression of an allergic response to the measles is untenable.

The internal focus of proliferation of the virus is unknown, but the spleen, which is often enlarged, is probably one such site.

Dengue

Dengue is not usually regarded as one of the acute exanthems. Its incubation period is shorter, and this may be due to the fact that, because the virus is inoculated intravenously by the mosquito, the interval of three or four days between infection and the proliferation of virus in the internal organs is eliminated. The situation may be compared with variola, measles, and chickenpox in the newborn, with Blake and Trask's (1921) production of measles with an incubation period of four days by the intravenous inoculation of monkeys, and with the results (Fenner 1948b) of the intravenous and intradermal inoculation of mice with ectromelia virus. Sabin and Schlesinger (1945) have shown that enormous concentrations of virus occur in the blood; and, though no direct evidence is available, the rash is probably due to multiplication of the virus in the cells of the dermal capillaries.

DISCUSSION

Several of the observed features of the exanthems can be explained by the hypothesis just enunciated. First, the long incubation period of the natural diseases, and the shorter incubation period of the same diseases after intravenous inoculation, and of dengue can be explained by the time necessary for the proliferation of virus in the primary lesion, in the regional lymph-node, and next in the internal focus in the natural disease, and the elimination of the first two stages when intravenous inoculation is the mode of infection. Differences in the reproduction-rates of different viruses and in different tissues are also important in this connexion (Fenner 1948b). Secondly, the delay of several days between the onset of symptoms and the appearance of the rash is due to the fact that symptoms ensue when multiplication in the primary focus or in the internal organs reaches a high level, whereas infection of the epidermal cells during the consequent secondary viræmia takes place at just about the time of the onset of symptoms. Multiplication of the virus in the skin must then proceed for a few days before lesions become evident. Thirdly, the long period of the secondary viræmia provides the massive and universal distribution of virus which leads to the very durable immunity produced by these diseases.

In textbooks of medicine the description of the symptoms of the more severe exanthems, smallpox and measles, is usually divided into the period of incubation, the period of invasion, and the stage of eruption. A consideration of the virus titres in the blood and other organs in mousepox (fig. 1), which is a valid model for smallpox and measles, shows how erroneous is this concept of pathogenesis. "Invasion" presumably means either the entry of virus into the blood-stream or the invasion of the organs by virus spread by the blood-stream. Both these events occur during the incubation period and do not give rise to symptoms. The principle that symptoms and signs develop only when multiplication of the virus has almost reached a maximum is of general application in virus diseases (Rivers 1939). In the acute exanthems the onset of symptoms is probably due to sudden widespread necrosis of the cells of the internal organs in which multiplication of the virus has reached a high level, with the consequent release of abnormal cell products into the circulation and the interference with normal metabolism. When the rash is fully developed, the virus content of all organs and tissues is declining, and in the absence of secondary bacterial infections it is accompanied by a decrease in the severity of general symptoms.

SUMMARY

Mousepox (infectious ectromelia of mice) is a good laboratory model for the study of the acute exanthems.

Multiplication of the virus at the site of entry of the virus reaches almost its highest titre before any lesion is evident macroscopically.

A complicated series of events occurs between infection and the end of the incubation period: the virus passes to the regional lymph-node and multiplies there; small amounts of virus pass into the blood-stream and undergo phagocytosis by cells of the reticulo-endothelial system; the virus multiplies in the organs (liver and spleen) rich in these cells, and necrosis of infected cells adjacent to sinusoids produces a secondary viræmia; and the virus thus distributed causes focal infection of cells of the epidermis. Virus deposited in the skin multiplies for several days before any macroscopic lesions appear. Clinical recovery and the disappearance of virus are closely correlated with the appearance of circulating antibody.

This interpretation of the pathogenesis of mousepox provides a good explanation of the known facts in smallpox, chickenpox, and measles.

It is suggested that the concept of a primary lesion (which may or may not be clinically apparent), an internal focus of multiplication, and a secondary liberation of the virus or bacterium into the blood-stream, with the

production of focal lesions in the skin and elsewhere, may prove useful in studies of the pathogenesis of many human diseases.

The description of the period of the onset of symptoms in smallpox and measles as the stage of "invasion" is erroneous, for the blood-stream and the organs are invaded during the incubation period before symptoms arise.

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SPLENECTOMY IN KALA-AZAR

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SPLENECTOMY has come to be regarded as entirely contra-indicated in the treatment of kala-azar since the introduction of pentamidine and potent pentavalent preparations of antimony, but the successful results recently obtained in three drug-resistant cases show that, combined with specific therapy, it can sometimes be the only method of obtaining a radical cure.

The treatment of kala-azar by splenectomy was first reported by Makkas (1912) in Athens. For three weeks the hæmoglobin and red-cell count improved, but the patient died of an intercurrent pneumonia. Makkas was so encouraged by this temporary improvement that he examined the spleens in a pathological museum and found numerous leishmaniæ in one which had been removed from a patient diagnosed as having Banti's disease. He traced the patient, who had been operated on a year previously, and found him in perfect health.

Cochran (1915) performed splenectomy in three cases of kala-azar in China; all three patients died, though two showed temporary benefit for two months. Leishmaniæ were found in the liver sections.

Kokoris (1915) recorded three cases of infantile kala-azar in Greece in which the diagnosis was confirmed by finding leishmaniæ on splenic puncture. Splenectomy was performed in each case. The first child continued to have fever and died four months after the operation; the second improved temporarily, but later the fever returned and he was removed from hospital by his parents two months after the operation; and the third child improved rapidly and remained well for over three years. This is the first proved case of kala-azar recorded in which splenectomy alone was followed by recovery.

SPLENECTOMY IN UNRECOGNISED KALA-AZAR

There is no doubt that splenectomy has been done in many cases of unrecognised kala-azar and not reported. These cases have invariably been mistaken for Banti's syndrome, and the fallacy of excluding kala-azar on one negative sternal marrow or splenic puncture must be guarded against if this mistake is to be avoided. The modern laboratory aids to diagnosis, such as culture from sternal marrow and spleen punctures on suitable media and the complement-fixation test of Sen Gupta, should in most cases prove sufficient. We have, however, encountered a case where three sternal-marrow punctures were negative and it was only on splenic puncture that the diagnosis was made. Provided specific treatment is instituted as soon after operation as possible, the prognosis is by no means hopeless.

Olmer (1931) records the case of a young man, who had never lived out of France, reporting sick with a pyrexia and a grossly enlarged spleen. A puncture of the enlarged spleen having failed to reveal leishmaniæ splenectomy was performed. Death resulted from hæmorrhage, and at necropsy numerous leishmaniæ were found in the spleen. Kala-azar in young children is common in Marseilles, but this appears to be the first reported case in an adult.

Sweeney et al. (1945) reported a case of kala-azar simulating splenic anæmia. An Italian prisoner-of-war contracted the disease in Sicily. The disease, following a presumptive latent period of two years, manifested itself by pyrexia, gross splenomegaly, and a leucopenia with a relative lymphocytosis. Frequent blood smears were negative for malarial parasites, and numerous sternal-marrow smears were examined for leishmaniæ with negative results. A Napier's aldehyde test was not done. In 1944 the spleen was removed on a tentative diagnosis of Banti's disease. The spleen weighed 1770 g. and on section showed numerous leishmaniæ. A course of 'Neostibosan' was given after the splenectomy up to a total dosage of 4·7 g., and the patient completely recovered.

The following case occurred in a R.A.F. station hospital in 1945.

Case 1.—An airman who had recently returned from India was admitted to hospital with a palpable mass in his left hypochondrium. He was anæmic, and there was a leucopenia. His urine contained a cloud of albumin and some blood. A sternal-marrow smear showed no leishmaniæ, and no malarial parasites were seen in repeated blood films. A surgical consultant advised laparotomy, and at operation a very large spleen was found and removed. Leishmaniæ were present in the smears from the cut surface of the spleen (fig. 1). 'Pentostam' was given on the day after operation, and further courses were given later up to a total of 14·2 g. The spleen weighed 3111 g., and sections showed numerous leishmaniæ. The patient ultimately made a good recovery after a stormy convalescence, during which 11 blood-transfusions were given.

SPLENECTOMY IN DRUG-RESISTANT CASES OF KALA-AZAR

Timpano (1930) reported a case of kala-azar in a child, aged 5 years, who was treated with tartar emetic.

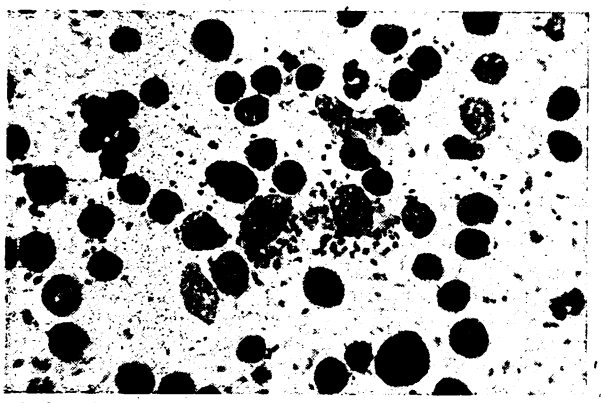

Fig. 1—Leishmaniæ in smear from cut surface of spleen (case 1).

Her condition deteriorated in spite of treatment, so a splenectomy was performed. The fever quickly subsided after operation, and rapid improvement followed. Two months later the child was in good condition and was discharged as cured.

Abrami et al. (1931) reported a case which, though it does not strictly conform to this category, presents some interesting features. A woman, aged 35, who for the past ten years had lived in France, England, and Germany, was found to have kala-azar. It was concluded that the disease had been contracted in France, on the Mediterranean littoral. Because of the advanced stage of the disease splenectomy was performed, and next day 10 cg. of 'Stibenyl' was administered. This was followed by a course of neostibosan, but a blood-transfusion had to be given on the nineteenth day, and a month later a further course of neostibosan was given, followed by complete recovery.

Martin et al. (1935) reported a case of kala-azar in a Russian man, aged 21, which had been contracted in the south of France. A course of neostibosan up to a total dose of 4·6 g. was followed, after six days' rest, by a course of 'Stibyal' up to 0·2 cg. The temperature fell, and the appetite improved, but the anæmia and splenomegaly did not improve. A blood-transfusion was given, but six days later the blood picture showed Hb 45%, red cells 1,800,000 per c.mm., and white cells 3200 per c.mm. A splenic puncture revealed numerous leishmaniæ and was followed by internal hæmorrhage which lasted some hours. Four days later splenectomy was done. A further course of neostibosan up to a total of 6 g. was given and followed by a further 0·84 cg. of stibyal. The patient made a complete recovery.

Burchenal et al. (1947) have reported a drug-resistant case in which splenectomy was undoubtedly the determinant factor in recovery. A negro soldier contracted the disease in North Africa in 1944. Leishmaniæ were found on splenic puncture, and intensive treatment with pentavalent antimony preparations and stilbamidine for the next eighteen months did not effect a cure, and it was only with 85 blood-transfusions of 500 ml. each that the patient was kept alive. Eventually splenectomy was performed, and a spleen weighing 3050 g. was removed, in sections from which leishmaniæ were found. No further specific treatment was given after splenectomy, and the patient made an excellent recovery, being in perfect health two years after the operation.

Case 2 (Prof. L. J. Witts's case).—A soldier who had served for three years in the Sudan and the Mediterranean littoral was taken ill some four months after he had returned to England, and was admitted to a military hospital. He had pyrexia for eleven weeks and was investigated fully during this period, with negative results. A Napier aldehyde test was negative for kala-azar on April 1, 1944. His spleen gradually enlarged until its lower border reached the umbilicus. No diagnosis having been made, he was transferred to the Radcliffe Infirmary under Professor Witts on May 22, 1944. A sternal puncture was done, but no leishmaniæ were seen. He was given a course of neostibosan, which had only a slight effect on his temperature. A second course was begun on July 8, 1944, and two blood-transfusions were given. On June 27, 1944, a blood-count showed 3,250,000 red cells per c.mm., Hb 62%, and white cells 2600 per c.mm. Splenectomy was performed by Mr. D. C. Corry on Aug. 1, after which the patient's temperature subsided, and for his last three weeks in hospital he was afebrile. A course of 'Neostam' was given after the splenectomy. Smears from the cut surface of the spleen revealed leishmaniæ. Sixteen days after splenectomy a blood-count showed red cells 4,790,000 per c.mm., Hb 94%, white cells 8000 per c.mm. (polymorphs 47%), and platelets 1,500,000 per c.mm., a previous count on May 23, 1944, having shown 146,000 per c.mm. The patient was transferred to a convalescent home and was finally discharged from the Service. He was seen again in November, 1946, and there had been a steady gain in weght since his operation in 1944. A blood-count showed Hb 104%, and white cells 10,000 per c.mm. (polymorphs 51%). His erythrocyte-sedimentation rate was 2 mm. in an hour.

This case showed a lymphocytosis following splenectomy which was also evident in the next case.

Case 3.—A corporal, aged 24, developed kala-azar in Calcutta in December, 1945. A provisional diagnosis of typhoid fever was made, but a month later leishmaniæ were found in a sternal-marrow smear, and he was given a course of 'Urea stibamine,' with an excellent immediate effect. His pyrexia subsided, and the spleen was no longer palpable. He received no further treatment until he arrived in England in April, 1945. On examination he had an enlarged hard spleen some 2 in. below the costal margin, his white-cell count was 5000 per c.mm., a Napier aldehyde test was negative, and so was Sen Gupta's complement-fixation test. A sternal-marrow smear was negative for leishmaniæ, and cultures made from the marrow on Alder's media were sterile at the end of three weeks. The patient was feeling well, was apyrexial, and was anxious to go on sick leave. In spite of these negative findings we decided to give him

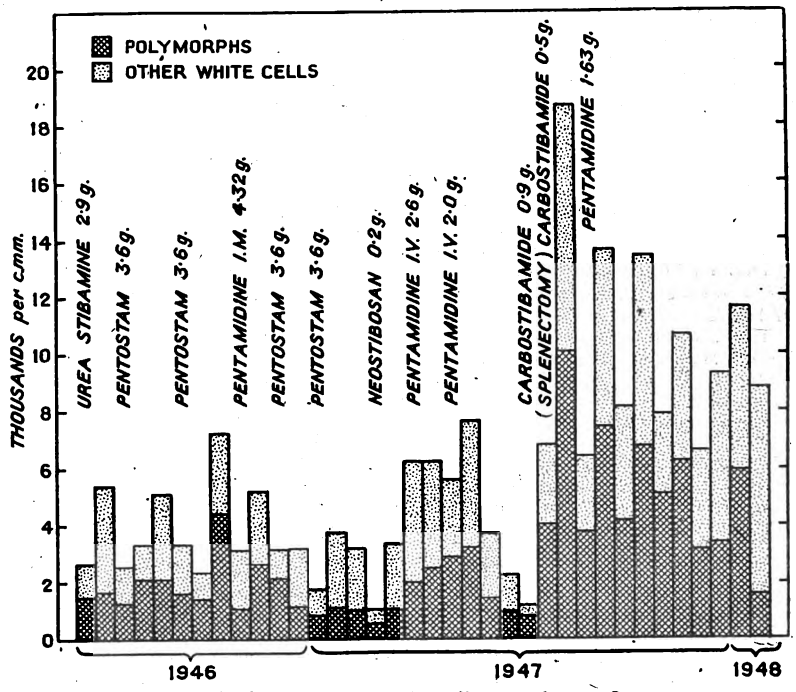

Fig. 2—Treatment and white-cell counts in case 3.

a full course of pentostam forte up to a total of 3·6 g. The course was started on April 24, 1946, and his white-cell count rapidly fell to 2500 per c.mm. This fall, mainly affecting the polymorphs, recurred shortly after the start of treatment with antimony preparations on every occasion (fig. 2) and, though noted, was neither so well marked nor so constant in other cases.

On his return from a month's sick leave he felt well; he had taken his temperature every night, and had only noted it slightly raised once when he had a cold. He had walked five miles a day during the last week of his leave. The spleen was still palpable $2^1/_2$ in. below the costal margin, there was a well-marked gingivitis but no other signs or symptoms, and he was apyrexial. Sternal-marrow smears were, however, positive in the direct smear and later on culture. A further course of pentostam forte up to a total of 3·6 g. was given. Sternal-marrow smears and cultures were negative after this course, and he was given a further month's sick leave.

After this he complained of being easily tired, and his spleen, which had regressed after the pentostam, was 3 in. below the costal margin. It was decided, in view of his intolerance to antimony, to give him a course of pentamidine isethionate intramuscularly up to 4·32 g. Sternal-marrow smears were negative after this course, but to our disappointment leishmaniæ grew three weeks later from cultures made from the sternal marrow. Further treatment was given (fig. 2) from Oct. 10, 1946, with various antimony preparations and pentamidine, with good initial response so far as the pyrexia was concerned and occasional regression of the spleen, but there was a steady deterioration in his condition.

A course of neostibosan had to be terminated hurriedly after two injections, since his white-cell count fell from 3000 to 900 per c.mm. (polymorphs 22%), and he had a severe epistaxis. Pyridoxine was given together with liver injections, with a good effect on his white-cell count, and further intensive treatment was given with intravenous pentamidine preceded by adrenaline hydrochloride min. 10 of 1/1000 solution intramuscularly. Thrombosis of many veins was caused by the pentamidine, but it was possible to complete the courses. The spleen became impalpable, and the irregular temperature which had been running for four weeks subsided. Sternal-marrow smears and cultures were negative, and it was hoped that the intravenous pentamidine had at last effected a cure.

On his return from a month's sick leave his spleen was again enlarged to $2^1/_2$ in. below the costal margin, and a blood-count showed red cells 3,300,000 per c.mm., Hb 60%, and white cells 1800 per c.mm. A sternal-marrow smear was negative on direct examination, even after an hour's search by five observers. A spleen puncture was done three days later, and the splenic smear was found to be packed with leishmaniæ. It was considered that his spleen was the reservoir of his infection, and it was decided to begin a course of 'Carbostibamide' and in the middle of the course to perform a splenectomy, continuing with the course as soon as the patient's condition permitted. A blood-transfusion was given during the operation, and Air-Commodore P. Hall removed an enlarged spleen weighing 2736 g. Smears and sections from the spleen were full of leishmaniæ, and positive cultures were obtained on Adler's medium. There was an immediate rise in the white-cell count after splenectomy. The course of carbostibamide was completed and was followed by a short course of intravenous pentamidine up to a total of 1·63 g.

The patient became completely apyrexial a fortnight after his operation, and has remained so for the last six months. There has been a gradual increase in weight; he now weighs 12 st. and is back at his work as a motor-transport driver. A blood-count shows red cells 5,600,000 per c.mm., Hb 100%, and white cells 7000–10,000 per c.mm. (lymphocytes 55–65%). A similar lymphocytosis after splenectomy has been reported in other cases and is apparently due to the splenectomy. The patient's liver is not enlarged, liver-function tests are satisfactory, and there is no enlargement of lymph-glands.

Case 3 presents several interesting points for discussion.

Drug-resistance.—It was fortunate that successful cultures were obtained early in the disease and again at splenectomy. Inoculation into hamsters, which were treated with pentostam, showed that the strain had not developed "drug-fastness." The fault therefore lay in the patient and not in a particularly antimony-resistant strain of leishmaniæ.

Persistently Negative Complement-fixation Test (Sen Gupta).—The fact that the antigen is made from the Kedrowsky acid-fast bacillus, and is therefore not a specific antigen for kala-azar, weakens the argument that the fault lay in the immunity response of the host; but in fairness to Sen Gupta's test it must be admitted that this was the only positive case of kala-azar in which the test was negative. In many of our cases a strongly positive complement-fixation test gradually became weaker and finally negative during treatment, and we consider that Sen Gupta's complement-fixation test is as reliable as any of the other complement-fixation tests, not excluding the Wassermann reaction.

Inadequate Dosage in the Initial Stages of the Disease.—This we consider to have been an important factor in our case. The initial course of urea stibamine consisted of only 2·9 g., and there was an interval of two months during which the patient was awaiting repatriation. On the other hand, Napier with his unique experience of kala-azar in India, has found no correlation between irregular inadequate treatment and drug-resistance. Some of his most resistant cases were adequately treated as inpatients. Kirk (1947) states that "cases which relapse after insufficient treatment are subsequently much more difficult to treat than primary cases." Manson-Bahr (1945) says of urea stibamine: "If for some reason or other an intermission in treatment takes place, the parasites tend to become antimony-fast."

Spleen as a Reservoir of Infection.—In adequately treated cases resistant to intensive specific chemotherapy we consider that the spleen is the reservoir of infection. Sections in our case showed a diffuse reticulo-endothelial proliferation in the spleen, and it is suggested that, owing to pooling and stagnation of the circulation in the splenic sinuses, an effective concentration of the drug did not reach the parasites in situ. It is suggested that the specific-drugs destroyed the parasites in the bone-marrow, thus explaining the numerous negative marrow smears and cultures in this case. It is significant that marrow smears were negative, but two days later a spleen smear was teeming with leishmaniæ, and it was on this finding that splenectomy was considered. The spleen in section showed numerous leishmaniæ, and since it weighed 2736 g., the extent of the parasitisation is obvious. The splenic fibrosis in these resistant treated cases is possibly due to the antimony and not to the disease.

CHANGES IN THE WHITE-CELL COUNT AFTER SPLENECTOMY

The following white-cell counts before and after splenectomy have been recorded:

	White cells per c.mm. Before	*After*	*No. of days after*
Martin et al. (1935)	3200	5400	16
Sweeney et al. (1945)	1800	12,800	Not known
Burchenal et al. (1947)	2900	22,500	1
Present series:			
Case 1	2200	4300	3
Case 2	2600	8000	16
Case 3	1800	6200	6

Singer et al. (1941) followed up 19 cases in which splenectomy had been done for various diseases, mainly purpura and hæmolytic jaundice, and found that, even after several years, the white-cell count was definitely raised (above 10,000) in 12 cases. The neutrophils were less than 60% in 15 cases, and the lymphocytes and monocytes were generally increased both relatively and absolutely.

Case 3, though a relative and absolute lymphocytosis was present, responded to a streptococcal tonsillar infection with a well-marked polymorph leucocytosis.

SUMMARY

Splenectomy in a very resistant case of kala-azar appears to have effected a cure, after sixteen months of intensive treatment with various pentavalent antimony preparations and pentamidine had been unsuccessful. The splenectomy was done in the middle of a course of carbostibamide, which was completed after the operation. A further course of pentamidine was then given, and fortnightly examinations and blood-counts have been carried out for six months. There is now no clinical or laboratory evidence of kala-azar, and the patient is well and on full duty.

Negative marrow smears are insufficient to exclude the diagnosis of kala-azar.

Splenectomy should be considered in selected drug-resistant cases of kala-azar, and the operation should be followed by a further course of chemotherapy.

Every case of kala-azar should be kept under close medical surveillance for at least six months.

We wish to thank the Director-General of the R.A.F. Medical Service for permission to publish this case; Dr. Everard Napier for his helpful criticism; Professor Witts for allowing us to quote his case; Dr. L. G. Goodwin, of the Wellcome Tropical Laboratories, for inoculating cultures into hamsters and testing the susceptibility of the strain to pentostam; and the patient (case 3) for his coöperation during a long illness.

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THE MALE-TOAD TEST FOR PREGNANCY

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INJECTION of urine into animals has been used for the past twenty years as a test for pregnancy. Many different animal species have been recommended for the purpose, but only a few have been accepted as suitable for routine use in clinical pathology.

The original test, described by Aschheim and Zondek (1928), is widely employed, for it is simple and reliable. From three to five immature female mice are given injections of urine twice daily until five injections have been given, and are killed 90–100 hours after the first injection. At laparotomy the ovaries are inspected. Hæmorrhagic follicles indicate a positive result. Supplies of immature mice are not universally available, and without concentrating the urine a result is not obtained before five days.

Friedman (1929) reduced the time of the test, without losing accuracy, by using segregated virgin rabbits. Urine is injected intravenously, sometimes on two successive days, and the ovaries are inspected 48 hours after the first injection. Some samples of urine are toxic enough to kill the rabbits, which latterly have become costly and difficult to obtain.

Bellerby (1934), in this country, and Shapiro and Zwarenstein (1934), in South Africa, introduced the female clawed toad (*Xenopus lævis*) as the test animal. Subcutaneous injection of urine from a pregnant woman causes extrusion of spawn (oviposition) within 24 hours, usually within 6–18 hours. The chief advantages of this test are the clear and rapidly obtained end-point and the low maintenance costs. The toads may be used repeatedly, and one feed a week seems to be adequate. Up to now this test has not been adopted generally. In nearly all cases previous chemical extraction of the urine (Scott 1940) becomes necessary, and to obtain good results two or three toads should be used for each test.

The early enthusiasm for the rat test (similar in execution to the Aschheim-Zondek test) has lagged, at least for clinical purposes. Bunde (1947) could not confirm the accuracy claimed by Salmon et al. (1942), particularly as the test does not have a clear end-point.

I report here my results of using as test animals male toads of the species *Bufo arenarum* Hensel, indigenous to South America, which was first used for pregnancy diagnosis by Galli Mainini (1947).

PRINCIPLE OF THE TEST

In frogs and toads spermatogenesis and ovulation generally take place only during sexual activity, which usually lasts a few weeks in spring. Nearly all frogs and toads use amplexus without internal fecundation—i.e., the male clasps the female from behind with his fore limbs until spawning is over. The discharge of gametocytes is presumably under hormone control, but the agency which initiates it has remained undiscovered. In the male toad the liberation and expulsion of spermatozoa are controlled by the pars anterior of the hypophysis (Houssay and Lascano Gonzalez 1929). de Robertis et al. (1946) further showed that injection of pituitary gonadotrophins causes spermatogenesis at any season of the year.

In controlled experiments these and other workers, notably Rugh (1937), have followed, by histological examination, the effects produced on the testes. The spermatozoa normally lie in clusters attached to Sertoli cells. The effect of gonadotrophin is first signalled by swelling of the Sertoli cells, followed by detachment of skeins of spermatozoa into the lumen of the seminiferous tubules. These events occur rapidly, are obvious in 10 min., and are often completed within half an hour. The mature spermatozoa next pass quickly through the vasa deferentia into the ureters, whence they may be either voided or stored temporarily in the bladder.

Galli Mainini (1947) gave practical application to these facts when he published results of parallel experiments substituting chorionic for pituitary gonadotrophins. He showed that injection of urine from the pregnant human female effected spermatogenesis in the adult male toad, and that spermatozoa appeared in the toad's urine within a short time (average 3 hours) of the injection. The adoption of these experimental results as a basis for a biological test for pregnancy depends on one further point—namely, that spermatozoa are never discharged into the ureters except in amplexus or as a result of experiment stimulus, as described above. This is true for those species already studied—*Bufo arenarum*, *Bufo marinus*, *Rana pipiens*, and *Bufo d'Orbigny*—and in each test it may be checked by sampling the toad's urine before an injection is given. So far as I am aware, all these species are indigenous to the New World.

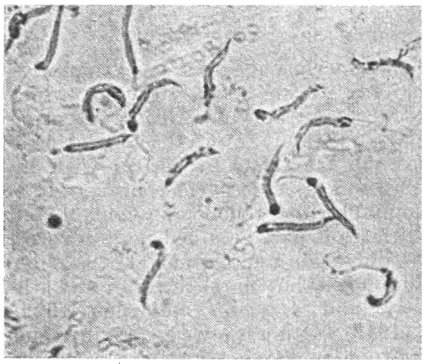
TECHNIQUE

It is desirable to collect the first morning specimen of urine from the patient into a clean bottle. The toads seem to be unaffected by variations in bacterial or cellular content or in the pH of the urine injected. Therefore the urine requires no treatment before injection. I found that urine from patients who had recently undergone general anæsthesia was lethal to the toads (Haines 1948). It is therefore best to avoid injecting urine from women who have recently had anæsthetics or other forms of medication likely to be toxic to toads. Galli Mainini (personal communication) reports a mortality of 1·13% in over 2000 toads injected.

Bufo's skin is warty and usually dry and therefore, unlike xenopus, it is easy to hold. The position in which

it may be held is a matter of choice, because the lymph sac can be reached from many different points. The lymph sac is a potential space between the skin and muscles almost all over the body of the toad; but the skin is firmly attached over joints and bony prominences such as the mandible and midline of the back. I find it convenient to grasp the body and four limbs of the toad in the palm of my left hand. This leaves uncovered an area of dorsal skin through which the injection is made.

The needle is passed into the skin at an acute angle and before reaching the muscle it is directed more horizontally so as to avoid puncturing viscera. The injection (10 ml.) is given slowly to allow the urine to diffuse. The needle is withdrawnafter waiting $^1/_2$–1 min. to prevent reflux of urine through the needle puncture. Each toad is then placed in a separate well-ventilated dish or jar with enough water to allow the toad to soak himself if he wishes. The water should not be enough to cover him. The temperature of the room is important, for in cold weather the test is retarded. Good results are obtained at an average temperature of 22°C.



Positive pregnancy test, showing spermatozoa in male toad's urine after injection of pregnant woman's urine into toad's lymph sac. (No stain.) (×400.)

The end-point of the test is given by the appearance of large numbers of spermatozoa in the toad's urine. Urine may be collected from the test jar if the toad has voided his bladder spontaneously or by catheterisation. This latter procedure is recommended and is simple to perform. In my experience 3 hours is a suitable interval between the injection and the taking of the first sample. This time the toad is held in the hand as before, but with his ventral aspect uppermost. A modified bulbed pasteur pipette is inserted into the cloaca to a distance of 0·5 cm. and not further than 1 cm. Usually a column of clear urine collects in the pipette within a few seconds. If not, gentle agitation of the pipette in the cloaca will cause urine to appear. A drop of the sample is examined microscopically, in the manner usually adopted for urinary deposits. In a positive test spermatozoa are seen in large numbers. They are often motile, but their presence is the criterion of the test. The heads of the toad spermatozoa (see figure) are much longer and narrower than those of man. The hair-like tail appears to be about three times as long as the head. Obviously, samples may be examined at any time during the test. I have taken samples after intervals of 1, 2, 3, and 4 hours. Sampling after 18–24 hours in positive cases showed that sperms were by then absent, or if present were few.

ADVANTAGES OF THE TEST

Before comparing this with other biological tests for pregnancy it is useful to consider what constitutes a good test. The important point is its reliability (see below). Other points are the collection and preparation of the urine for injection, the technique of injection, the speed of reaction, a clear end-point which is easily read, and the supply and maintenance of a stock of animals.

In most tests now in routine use the urine commonly receives some form of preparation before it is injected. This is because it may be toxic to some animals—e.g., mice and rabbits—or because the gonadotrophins need purification and even concentration before a response is obtained in the animals—e.g., the clawed toad (*Xenopus lævis*). Adjustment of pH followed by filtration is always required. Chemical extraction is often carried out if a contaminated specimen is received or a "rapid test" is requested. These procedures, though simple, demand a supply of reagents and apparatus, and add to the time of the test. No such preparation is needed in the male-toad test. Thus time is saved, and the test becomes, from the start, simpler than the others. A single subcutaneous injection is all that is required. In some other tests two or more injections may be needed. The male toad is much easier to hold than the female xenopus.

The earlier tests, Aschheim-Zondek and Friedman, are completed in 2–5 days. The introduction of the xenopus test reduced the time to less than 24 hours; readings are taken in 6–18 hours. With the male toad it is now possible to have consistent readings at the end of 3 hours. In fact, the nature of the reaction and experience show that a test (under the conditions outlined above) which is negative at 3 hours will not become positive later. Thus there is no such thing as a "weak positive reaction" in this test. The xenopus test may be held to have the most clear end-point, but it varies in the degree of response. In some animals only a few ova may be seen; hence two or three clawed toads are needed for each test.

One of the disadvantages in the use of mice, rats, and rabbits is that the end-point is not clearly shown. An experienced worker can make reliable readings in most of the doubtful cases, but occasionally the ovaries may have to be examined histologically. Reading the result of the male-toad test should cause no difficulties. The observation of large numbers of toad spermatozoa in a hanging-drop preparation of the urine requires no special skill. The whole operation of pipetting off the urine and its microscopical examination takes only a few seconds—not much longer than examining a jar for xenopus spawn.

Stocks of male toads have been easy and cheap to obtain. They require no special tanks or boxes. Each animal may be used for several tests. Toads live naturally for several weeks without food. If they are in good supply, those which have been used several times can be discarded before feeding becomes necessary, and a fresh stock obtained. On the other hand, the feeding of rabbits, mice, and South African toads needs care and is often costly. The supply of stock is discussed below.

RELIABILITY OF MALE-TOAD TEST

In his original paper Galli Mainini (1947) reported a parallel series of 99 tests on rabbits and male toads. There were 94 coincidental results, including 47 positives. As controls he used urines from miscellaneous cases and various hormones. Except with chorionic gonadotrophin, negative results were given in all cases. Reports confirming these results have been published by Figueroa Casas et al. (1947), Pinto and Suer Boero (1948), Lima and Pereira (1948), and many other workers in South America. In the U.S.A. the male leopard frog (*Rana pipiens*) is reported to give comparable results. Wiltberger and Miller (1948), after making tests on 200 of these frogs, reported no false positives, and no false negatives except in patients who had been pregnant longer than three months. Robbins and Parker (1948) obtained no false positives in 34 control urines, but there was 1 false negative in 78 urines from women known to be pregnant. This patient was only two weeks beyond her first missed period. Finally Galli Mainini (1948) has reviewed his own and published cases. In 2661 cases of pregnancy the accuracy of the test was 98–100%, including 458 cases of his own with an accuracy of

99·0%. He found no false positives in urine from 960 persons, including non-pregnant females of all ages and males. There were also 543 cases reported by other workers, again with no false positives. Thus, so far, the test appears to be 100% reliable in not giving false positives. The incidence of false negatives has been 0–2%. This apparent error is discussed below.

My experience is based on data obtained from 100 samples of urine and other substances injected into 136 toads (*Bufo arenarum*). Where possible, early morning specimens of urine were used. In all but 4 cases positive results were recorded 3 hours after the injection of urine. This was found to be a convenient time for reading tests, but over the whole series readings were made at 1, 2, 3, 4, and 5 hours after the injection. In only one instance a negative reading after 3 hours was followed by a positive one an hour later. This delay may have been caused by a temporary upset to the animal, because the patient had had an anæsthetic the day before the urine was collected. My results indicate that urine which does not give a positive reaction at the end of 3 hours, or 4 hours at most, never becomes positive under the conditions I use. On the other hand, positive readings were not usually found before 1 hour. But in one case, where the woman's period was nearly four weeks late, a positive result was obtained 45 min. after the toad was injected.

Several of the 11 patients for whom we obtained positive readings at the end of an hour had missed just one or two periods. One of our patients who was being investigated because of infertility was, on admission for the dilatation and insufflation, found to be four days late with her period. (Previously she had often been one or two weeks late.) Conception was confirmed by the male-toad test. Daily samples on three consecutive days gave positive results.

The 4 false negative results require further examination, and it is useful to view them in three groups, according to the duration of pregnancy. Thus in the first three months of pregnancy there were 38 cases with 1 negative result; in the second there were 6 cases with 1 negative result; and in the third there were 6 cases with 2 negative results. The specimen in the first group was obtained in difficult circumstances and was unusually dilute. It has been suggested that this specimen was too dilute to cause a reaction in the toad, but this explanation may not be adequate for I have found positive results after the injection of less than 10 ml.—e.g., 2·5 ml.—of early morning urine. In these early cases simultaneous Friedman tests were performed on 6, with agreement of 5 out of 6. The sixth patient's period was a week late when the toad test was positive, but the urine gave a negative in the Friedman test. Both tests were positive five days later. In this group with a small number of cases, the male-toad test appears to be reasonably reliable.

In the other groups the numbers are very small—6 cases in each. There was 1 negative reading in a case of eighteen weeks' gestation, and perhaps a dilute specimen was used. But it should always be borne in mind in interpreting biological tests for pregnancy later than the first three months, that there is a characteristic dip in the curve representing the excretion level of chorionic gonadotrophin somewhere between the sixteenth and twentieth weeks of gestation (Wright 1945). The effective level falls again towards term; hence the 2 false negatives (a third of the cases) which I recorded need not be scored against the reliability of the male-toad test in particular. As stated by Wiltberger and Miller (1948), it is only in the first three months that the need arises for a biological pregnancy test.

Besides cases of known pregnancy, other types of case were studied. There were 7 cases of clinically unexplained amenorrhœa. These were all in young women who thought they might be pregnant and who had had amenorrhœa for two or three months or less. All these patients gave negative toad tests. Friedman tests were negative in 2 cases, menstruation has restarted in 4, and 1 woman remains untraced. We found the toad test helpful in the differential diagnosis of 2 cases where menstruation has not restarted after confinement—amenorrhœa following pregnancy. One of these women had not menstruated since she had miscarried five months previously. The male-toad test was positive, and fœtal parts were demonstrated by X rays. The other woman had missed two periods after a normal confinement. The toad test and a confirmatory Friedman test were negative.

We studied 2 cases of complete abortion, in which the results of the toad test agreed with the clinical findings and progress of each case:

Case 1.—A primigravida, aged 27, with a gestation of eighteen weeks, was admitted to hospital with a week's history of recurrent vaginal bleeding. Ten days later the bleeding ceased, and it was hoped that the pregnancy might proceed. The toad test then was negative, and next day a macerated fœtus and a placenta were expelled.

Case 2.—A primigravida, aged 38, had had irregular menstruation and infertility. Her present pregnancy had been confirmed by a Friedman test. She was admitted because of threatened miscarriage. A toad test was positive. The test was still positive two days after the placenta had been passed. It became negative 100 hours after the placental separation.

The observations in case 1 have clinical but no scientific value. It is only possible to suggest that the placenta separated a few days before the test was made. However, the findings in case 2, in which clinical data and laboratory tests were carefully checked, agree with the view generally accepted—that biological tests for pregnancy give negative readings about 100 hours after all chorion has been detached. It is notable that Miller and Wiltberger (1948) found a negative reaction as soon as 18 hours after operative removal of a placenta in a case where the fœtus had been aborted 24 hours previously. The male-toad test was positive 6 hours after miscarriage. I feel that their statement "if the test is positive the placenta is still attached and alive" requires qualification.

The association of uterine fibroids and pregnancy is not uncommon and may lead to diagnostic difficulties. I have found positive toad tests in all 6 cases of this group—4 patients aged over 40 and the others aged 23 and 39. Biological tests are of special value in this type of case, because the future safety of the pregnancy can be controlled if an early diagnosis is made. On the other hand, amenorrhœa not associated with pregnancy may come on at the menopause and be accompanied by fibroids; 3 of my 6 cases, those aged over 40 and possibly the woman of 39, were in this category of pregnancy, fibroids, and menopause. The contemplated hysterectomy was not carried out.

I have no available data on cases of chorion carcinoma or vesicular mole other than one negative result in a patient who had passed a vesicular mole two months earlier. Further, it would be unwise to speculate on the results to be obtained in such cases. It should be more widely appreciated that hormone excretion in these cases is uncertain and often capricious. Probably the effective gonadotrophic result is more in keeping with a follicle-stimulating action and less in the luteinising effect associated with a physiological chorion (Zondek 1942).

My series of controls is small. A positive result was obtained at the end of 3 hours after an injection of 500 I.U. of chorionic gonadotrophins ('Gonan' B.D.H.) into the lymph sac. From other experiments it seems probable that 50 I.U. will readily evoke a positive reaction.

I have examined 25 toads at rest and found the urine free of spermatozoa in all of them. Negative results were obtained with urine from 12 patients under hospital care for conditions other than pregnancy, including uterine fibroids (2 cases) and menopausal amenorrhœa (3 cases). Injection of male urine (6 cases) gave negative results.

CONCLUSION

The new test merits further study. The number of cases I have studied is too small to warrant definite conclusions, but the results agree with much that has been published. The whole technique is very simple. One animal will serve for several tests. The end-point is clear and easy to read; it seems to be unique in having no gradations; and, because of the specificity of the basic reaction, false positives are not obtained.

SUPPLY OF STOCK AND MAINTENANCE

My present stock of toads was imported from South America as part of a traveller's luggage. Up to now no other method of supply seems to be available. If the need arises, arrangements for import might be made by travel agencies, as is done with South African toads. However, we should be able to find species of batrachians indigenous to the British Isles which would be just as suitable for this test and avoid the need to import from the New World.

Toads, whether from the New or the Old World, are easy to keep. They are not aquatic like fishes and *Xenopus lævis*. Placed in deep water they will not survive. They should be kept in large cages or glass-walled tanks. The floor of the terrarium is covered to a depth of 4 in, with a mixture of peat mould and sand, which is kept moist. A shallow tray of water is placed in one part of the cage. The toads can clamber in and out of this at will. They spend some hours, mostly at night, soaking in water. They must not be overcrowded, for they easily become asphyxiated. They feed on earthworms, mealworms, and cockroaches and other insects. In captivity they may refuse food, but normally they can exist for long periods without feeding. This is useful because several tests can be made on one batch of toads, which may then be discarded when they begin to lose weight—i.e., when they weigh less than 100 g. It is reasonable to discard a batch of toads in this way, because they have been easy to obtain and are cheap, the estimated cost being 6*d*. each. Each toad may be used again after an interval of six days. The cost of toads will depend on the supply and demand. If indigenous species are found suitable for the test, the price per toad may be expected to rise.

SUMMARY

Adult male toads of the species *Bufo arenarum* Hensel, indigenous to South America, are used in a new biological test for pregnancy.

Injection of 10 ml. of patient's untreated urine can give a positive result in 2–4 hours, indicated by the presence of masses of spermatozoa in the toad's urine.

In cases of pregnancy and in controls the favourable results of other workers have been confirmed. Additional results have been valuable in the study of abortion.

It is a pleasure to record my thanks to the surgeons of the Chelsea Hospital for Women, for their interest and coöperation with this study; to Mr. J. W. Law, A.I.M.L.T., for technical assistance; to the Keeper of Zoology, British Museum (Natural History), and to the Curator of Reptiles, London Zoological Gardens, for their help in identifying species and for advice on the care of the animals; and to Dr. Galli Mainini for help so freely given and for the active interest he has taken in the work.

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HUMAN TOXOPLASMOSIS IN ENGLAND

REPORT OF A CASE

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No case of congenital toxoplasmosis seems to have been reported previously in this country. The condition has been recognised only fairly recently, the first reported case of human toxoplasmosis being described by Janku (1923), the second by Torres (1927), and the third by Richter (1936). In these cases a protozoon was isolated which at the time was not identified as toxoplasma but has since been so identified. Wolf and Cowen (1937) described a case in which they named the organism *Encephalitozoon hominis*, and Wolf et al. (1939) described another case in which the clinical features were similar to the previous five cases, and for the first time identified the causal organism as a toxoplasma. Since then many possible and proved cases have been described in the United States, South America, Continental Europe, and Australia (Pinkerton and Weinman 1940, Pinkerton and Henderson 1941, Sabin 1941, Wolf et al. 1942, Weinman 1944 and 1945, Zuelzer 1944, Dow 1945, Adams et al. 1946, Callahan et al. 1946, Robertson 1946, Syverton and Slavin 1946, Villegas 1946, Abbott and Camp 1947, Binkhorst 1947, Robinson 1947, Kean and Grocott 1948).

DIAGNOSIS

There are two types of human infection—congenital and acquired. The congenital type, which so far has been the more commonly reported, may be manifest at birth, or the symptoms may not appear until several months later.

Hydrocephalus is one of the commoner and more important signs, and may be associated with convulsions, mental change and other signs of involvement of the central nervous system—e.g., "scissors" position of lower limbs and deviation of head (fig. 1). In some cases microcephaly has appeared instead of hydrocephaly.

Chorioretinitis.—In the retina toxoplasmosis affects chiefly the macular region, though it may also affect the periphery of the fundus. White areas surrounded by pigment are seen, the intervening retina being normal. Optic atrophy develops rapidly, but the vitreous remains clear.

Cerebral calcification (fig. 2) may not be present in the very early months but develops later. The most characteristic appearance is curvilinear streaks of calcification in the region of the basal ganglia or the optic thalamus; there may also be multiple rounded deposits 1–3 mm. in diameter.

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Cerebrospinal Fluid.—Though there may be no changes in the cerebrospinal fluid (C.S.F.), the protein content is usually increased, with perhaps xanthochromia.

Neutralising Antibody Test.—Sabin and Ruchman (1942) devised a test for demonstrating neutralising antibodies in the serum. In congenital toxoplasmosis the tests may be strongly positive in the mother and only weakly positive, or even negative, in the infant. In the acquired type Syverton and Slavin (1946) confirmed Sabin's (1941) observation that antibodies may be absent from the serum 7–10 weeks after the onset of the illness, and thus the absence of demonstrable antibodies does not rule out the diagnosis.

Demonstration of Protozoon Toxoplasma.—The commonest sites in which the toxoplasma has been found are the brain, retina, nerves, and skeletal muscle; it has occasionally been found in the C.S.F., lungs, kidneys, spleen, bone, lymph-nodes, heart, stomach, suprarenal glands, pancreas, diaphragm, subcutaneous tissues, and skin (Wolf et al. 1939 and 1942, Pinkerton and Henderson 1941, Guimares 1943, Callahan et al. 1946, Pratt-Thomas and Cannon 1946, Kean and Grocott 1948). Thus, apart from a successful biopsy or a chance finding in the C.S.F., the protozoon can usually be found only after death.

CASE-RECORD

A male infant, aged 4 months, was admitted to the County Hospital, Pembury, with a history of persistent crying, anorexia, and enlarged head. He was born at full term after a normal pregnancy, with a birth weight of 7 lb. There

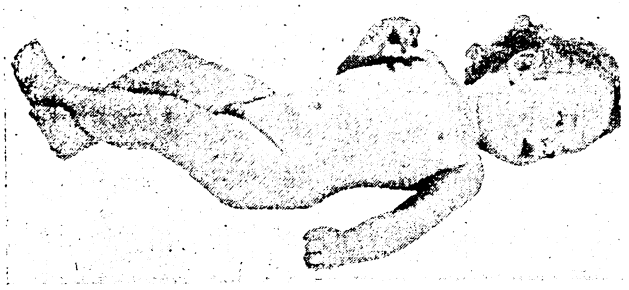

Fig. 1—Child with congenital toxoplasmosis showing "scissors" position of lower limbs, hydrocephalus, and deviation of head to the left.

was no record of the head circumference at birth, and his mother could not say when she had first noted the enlargement. He had had a "stuffy" nose since birth, but had otherwise progressed satisfactorily until a week before admission, when he had gone off his food and begun to cry incessantly.

Family History.—The child's family have lived in their present home for the past seven years. The house was formerly occupied by a veterinary surgeon who practised there. The present occupiers keep no domestic animals, but the house is reported as rat-infested. The mother, father, and three other children (girls aged 7, 6, and $3^1/_2$ years) are all alive and well, and have been examined by us, but no abnormality could be found in any of them.

On examination the child was well-nourished but obviously hydrocephalic. Weight $13^1/_4$ lb., length $27^1/_2$ in., head circumference $17^1/_2$ in. The anterior fontanelle was very large and bulging, and the posterior fontanelle patent. The sagittal and coronal sutures were separated. Nothing abnormal was detected in the heart, lungs, and abdomen, apart from a mild bronchitis and upper respiratory infection. Both eyes were slightly proptosed and deviated to the left, and nystagmus was present. The pupils were equal and reacted sluggishly to light. The fundi showed very extensive chorioretinitis, with a heavy deposit of pigment round parchment-white areas. There was also optic atrophy. So far as could be judged, vision was negligible, but there may have been some appreciation of light. No other abnormality was found in the central nervous system. The only other clinical finding was several small nodules up to $^1/_4$ in. in diameter on the dorsum of both feet.

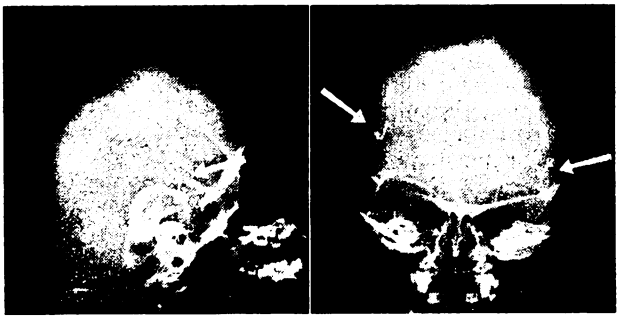

Fig. 2—Radiograms of skull, showing multiple intracerebral areas of calcification.

Radiography of the skull showed appreciable thinning of the bones of the calvarium; in the cerebrum there were small focal areas of calcification and one curvilinear streak (fig. 2). Radiography of the rest of the skeleton and of the chest showed no abnormality.

Blood-count showed red cells 5,200,000 per c.mm., Hb 84% (Haldane), colour-index 0·8, white cells 26,400 per c.mm., neutrophils 34%, lymphocytes 61%, monocytes 5%.

Cerebrospinal Fluid.—Repeated attempts to obtain fluid by lumbar puncture were unsuccessful, so a ventricular tap was performed; the fluid obtained was not xanthochromic; it contained 4 lymphocytes per c.mm., protein 80 mg., chlorides 702 mg., and sugar 57 mg. per 100 ml., Wasserman reaction negative. Pandy's test showed a well-marked increase in globulin. No organisms were seen or cultured.

Blood Tests.—The Wasserman reaction and Kahn test were negative in the infant and in both parents.

Antibody Neutralisation Test.—This was done for us by Dr. Sven Gard, of the Statens Bakteriologiska Laboratorium, Stockholm. The mother's serum showed a positive neutralising capacity of 25 skin-reactive doses, whereas that of the infant gave a weak or dubious positive reaction.

Biopsy of a nodule from the foot showed overgrowth of sweat glands and reactive fibrosis; no protozoa were seen.

Animal inoculation of gastric washings, blood, and C.S.F. did not reproduce the disease.

Progress.—Since the infant's admission to hospital there seems to have been no further progress of the disease. The head circumference remains at $18^1/_2$ in., and the sutures seem to be closing. There have been several recurrences of the respiratory infection, all of which have responded readily to 'Sulphamezathine.'

DISCUSSION

Since this is apparently the first case to be described in England, it is well to point out that there is no reason why cases should not occur here. Infection of the squirrel with toxoplasma was reported in Britain by Coles (1914) and of the snake, fruit-pigeon, and pied bush chat in the London Zoo by Plimmer (1916). Infection of domestic animals in this country has not hitherto been recognised, but a dog in this area of Kent has recently had toxoplasmic encephalitis, proved by identification of the protozoon (D. M. Heeley, private communication). It is worth noting that our patient's home was previously used by a veterinary surgeon, though we have no evidence that this has any bearing on the child's infection.

The diagnosis in our case has not been proved by isolation of the protozoon, but in view of the clinical findings in the infant and the presence of neutralising antibodies in the mother's serum there seems little doubt about the diagnosis. We have tried to isolate the organisms from the blood, C.S.F., and stomach washings, so far without success, but further efforts are being made, including a muscle biopsy. Failure to identify the organisms in no way disproves the diagnosis.

The negative serological reaction of the infant and the positive reaction of the mother are in keeping with the diagnosis. Sven Gard (private communication) informs us that this type of result is common at this early age. Syverton and Slavin (1946) found, in an adult patient,

that antibodies were absent from the serum seven weeks after the onset of the illness. Sabin's views on these unusual results are that they are due either to an immunologically different strain of toxoplasma or to the disappearance of the neutralising antibodies from the blood. He favours the latter explanation, since he found that monkeys lost their antibodies six weeks after the onset of the illness. We suggest that young infants may not have had time to develop neutralising antibodies.

This infant had repeated respiratory infections, and Callahan et al. (1946) found that these were comparatively common among the recorded cases. We have no evidence that the respiratory symptoms are directly due to the toxoplasma. We have made one interesting observation as an indirect result of the treatment of the respiratory infections with sulphonamides. When we first saw the child, his head circumference was 17½ in. and his fontanelles were bulging. Within a fortnight the circumference increased by 1½ in., requiring a ventricular tap to relieve the pressure. The head circumference was thus reduced to 18 in., and during the next four months, in which repeated sulphonamide therapy was used, it increased only ¼ in. No direct claim can be made that this halting of the progress is due to sulphonamides, but Sabin and Warren (1942) have shown that sulphapyridine and sulphathiazole, though having no effect in vitro, have a therapeutic and curative effect in mice and rabbits. Weinman and Berne (1944) state that sulphonamides may cure the acute phase of the disease but do not eradicate the organisms. Robinson (1947) apparently cured a case with sulphathiazole and emetine. Penicillin has been tried (Augustine et al. 1944) and found ineffective.

Though human toxoplasmosis has been recognised only since 1939, increasing numbers of cases are being reported in various parts of the world, and the disease may well be commoner in England than is supposed. For example, cases of chorioretinitis which in the past have been called congenital may well be due to toxoplasmosis. The diagnosis might also be considered in obscure cases of encephalitis and chronic meningitis. Unfortunately there are in England at present no facilities for performing the antibody neutralising test, and in our opinion the provision of such facilities is essential.

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RELAPSE OF PERNICIOUS ANÆMIA DURING MAINTENANCE THERAPY WITH FOLIC ACID

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RECENT work has clarified the value and limitations of folic acid (synthetic pteroyl-glutamic acid) in the treatment of addisonian pernicious anæmia.

The initial hæmatological and clinical improvement is comparable with that obtained with the best liver extracts (Spies 1947, Davidson and Girdwood 1947), though the rate of regeneration of red cells may be slightly slower with folic acid (Frommeyer and Spies 1947). Meyer (1947) and others have claimed that the reticulocyte response is less, and the red-cell and final hæmoglobin levels are lower with folic acid, but most writers, including Vilter et al. (1947) and Heinle et al. (1947a), consider the levels reached with either liver or folic acid to be similar.

The neurological manifestations of pernicious anæmia are not prevented or controlled by folic acid (Davidson and Girdwood 1947, Meyer 1947, Vilter et al. 1947, Wilkinson 1948), and evidence is accumulating that the incidence of subacute combined degeneration of the cord may be increased among patients so treated (Heinle and Welch 1947, Davidson and Girdwood 1948, Ross et al. 1948, Wagley 1948). These disturbances tend to arise early in treatment, often after the blood picture has become normal.

The danger of the development of subacute combined degeneration of the cord in patients treated with folic acid makes it unlikely that many long-term studies will be made of its ability to maintain the hæmatological remissions it produces. Reports suggest that, with rare exceptions, most patients may be kept in adequate remission on a daily dose of folic acid 10 mg. by mouth (Heinle et al. 1947a, Vilter et al. 1947).

The following history of a patient with typical addisonian anæmia who relapsed under treatment with folic acid despite increasing dosage is thus distinctly unusual.

CASE-RECORD

The initial response of this patient to folic acid has been described by Harrison and White (1946). Their report may be briefly summarised.

A man, aged 63, was admitted to Hammersmith Hospital on June 4, 1946, diagnosed as a typical case of pernicious anæmia, in his first relapse. He was given by mouth a total of 200 mg. folic acid, in three separate courses of 100, 50, and 50 mg. A transfusion of 500 ml. of packed red cells was given at the start of treatment.

His initial blood picture was: red cells 840,000 per c.mm., P.C.V. 9·2 ml. per 100 ml., M.C.V. 135 c.μ, Hb 3·1 g. per 100 ml., M.C.H.C. 36%, colour-index 1·2, white cells 2600 per c.mm.

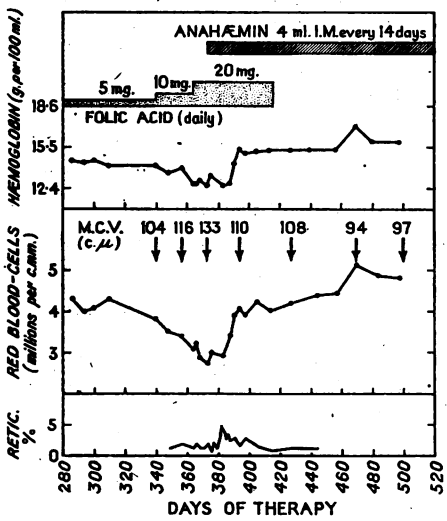
Seventy days after the above-mentioned treatment the blood picture was: red cells 4,200,000 per c.mm., Hb 13·3 g. per 100 ml., colour-index 1·01, white cells 6000 per c.mm. The patient was then put on a maintenance dose of folic acid 10 mg. by mouth twice weekly.

Subsequent History.—This is summarised in the accompanying table and figure. The table shows that, on folic acid 10 mg. by mouth twice a week, his red-cell count averaged 4,500,000 per c.mm. When the dose was reduced to 5 mg. twice a week, the count fell and was not restored by increasing the dose to 5 mg. thrice weekly. The patient's blood picture and clinical condition, however, rapidly improved on 5 mg. daily, and he remained in excellent health for about four months.

At the end of this period his red-cell count began to fall. No reason for this could be found by clinical examination, and an increase in folic acid to 10 mg. a day did not halt the fall. This dose was continued for twenty-three days. Sternal-marrow puncture then showed a reversion to megaloblastic erythropoiesis, and by this time the patient was complaining of anxiety, depression, and fatigue. Physical examination

was still negative. The dose of folic acid was then further increased to 20 mg. a day, but no reticulocyte response followed. The red-cell count continued to fall, and the clinical condition remained unchanged. Eleven days later 'Anahæmin' was given intramuscularly in addition to the folic acid by mouth. There was a reticulocyte response with a peak of 5·5% eight days after the injection of the anahæmin. This was associated with a rapid rise in red-cell and hæmoglobin levels.

The patient continued to receive folic acid 20 mg. daily and anahæmin 4 ml. intramuscularly fortnightly for six weeks. The folic acid was then stopped. The improvement in the blood picture continued, and the patient has since been maintained for nine months on anahæmin alone (now 2 ml. every fourteen days).



Response of pernicious anæmia to maintenance therapy with folic acid.

At no time during treatment with folic acid did the patient show signs of subacute combined degeneration of the cord.

DISCUSSION

Two features of this case deserve comment. The average levels of red cells and hæmoglobin during the period of successful folic-acid therapy were slightly lower than those reached later on liver therapy. The amount of folic acid required to induce the initial remission was small, and the patient was kept in excellent health for eight and a half months on the maintenance doses given. However, it is possible that, if larger maintenance doses had been given, the red-cell and hæmoglobin levels would have reached those attained with liver extract.

Of greater interest is the fall in red-cell count which began after the patient had been receiving folic acid 5 mg. daily for about four months. This trend could not be reversed by a fourfold increase in the dose of folic acid. Larger doses might possibly have been effective, but it did not seem justifiable to withhold liver extract any longer.

Very few cases of increasing insensitivity to oral folic acid have been described. Vilter et al. (1947) described two cases in which increasing doses of folic acid were needed to maintain the patients in remission. The patients did, however, respond to the increased dose. Wilkinson (1948) describes similar cases. Hansen-Pruss (1947) gives histories of two cases very similar to that of the patient now reported. One of his patients whose initial red-cell count was 1,200,000 per c.mm. responded to a daily dose of folic acid 20–30 mg. by mouth; his count reached 3,600,000 per c.mm. in about forty-five days. He was kept in fair remission for two or three months on 10 mg. daily, but his red-cell count subsequently fell, and an increase of folic acid to 30 mg. daily did not halt this relapse. The other patient responded well to a similar initial dose of folic acid, and his red-cell count reached 4,500,000 per c.mm. in about eight weeks. He also was kept in remission for about four months on 5–10 mg. daily but relapsed at the end of this period. Again this deterioration was not arrested by increasing the dosage of folic acid to 45 mg. by mouth daily. Both cases responded satisfactorily to liver extract afterwards.

The exact function of folic acid in the pathogenesis of pernicious anæmia is still obscure. The work of Welch et al. (1946) and of Bethell et al. (1947) suggested that the primary defect in pernicious anæmia might be an inability to liberate free folic acid from conjugated forms, and that liver extract given parenterally corrected this abnormality. The evidence to date does not justify complete acceptance of this attractive hypothesis. Heinle et al. (1947b), in fact, consider that the more recent experimental evidence does not support the idea of a direct relationship between folic acid and the anti-pernicious-anæmia principle of liver. They suggest that these two substances may function by unrelated pathways.

RESPONSE OF PERNICIOUS ANÆMIA TO MAINTENANCE THERAPY WITH FOLIC ACID

Days of therapy	Therapy	Total folic acid per week (mg.)	Duration of therapy (days)	No. of blood-counts	Red blood-cells (millions per c.mm.)			Hæmoglobin (g. per 100 ml.)		
					Average	Range	Final count of period	Average	Range	Final value of period
71–126	Folic acid 10 mg. by mouth twice weekly	20	55	20	4·5	4·2–5·0	4·5	13·9	12·5 to 15·3	13·7
127–150	Folic acid 5 mg. by mouth twice weekly	10	23	7	4·3	3·9–4·5	4·2	12·8	12·2 to 13·6	12·2
151–179	Folic acid 5 mg. by mouth three times a week	15	28	5	3·8	3·5–4·0	4·0	13·0	11·5 to 13·9	13·9
180–214	Folic acid 20 mg. by mouth twice weekly	40	34	9	4·2	3·5–4·8	4·0	13·7	13·1 to 15·0	14·4
215–339	Folic acid 5 mg. by mouth daily	35	124	13	4·2	3·9–4·9	3·8	14·3	13·1 to 15·0	14·5
340–363*	Folic acid 10 mg. by mouth daily	70	23	4	3·4	3·8–3·0	3·0	13·7	13·3 to 14·0	13·3
364–375*	Folic acid 20 mg. by mouth daily	140	11	3	2·9	3·2–2·7	2·7	13·0	12·9 to 13·2	13·0
376–416*	Folic acid 20 mg. by mouth daily and anahæmin 4 ml. fortnightly	140	40	8	3·7	3·0–4·3	4·0	14·5	12·8 to 15·5	15·5
417–532	Anahæmin 4 ml. fortnightly	..	115	7	4·0	4·2–5·4	5·2	16·3	15·4 to 17·5	16·2
533–662	Anahæmin 2 ml. fortnightly	..	130	8	4·6	4·2–4·9	4·9	16·4	14·8 to 17·5	17·0

* The detailed results for this period are shown in the figure.

Case-records such as that reported here and those described by Hansen-Pruss (1947), and the instances of almost complete insensitivity to folic acid in patients with apparently typical pernicious anæmia in relapse mentioned by Heinle et al. (1947a), further underline the complexity of the relationship between addisonian anæmia, folic acid, and the liver principle.

SUMMARY

Details are given of a patient with addisonian pernicious anæmia, who, after a good initial response, relapsed ten months later while still under treatment with folic acid. He did not respond to a fourfold increase in the dosage of folic acid but responded well to anahæmin.

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HYPERDURIC PREMEDICATION

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PREMEDICATION is now considered essential to any operation, but the main difficulty is to estimate the correct time for the injection to be given. Often an apparently long case is started, found to be inoperable, and terminated, and consequently the premedication of the following case cannot be given at the ideal time—i.e., 45–75 min. before operation.

Messrs. Allen & Hanburys Ltd. have introduced a salt of morphine and atropine which is more slowly absorbed than the tartrate or the sulphate. We have investigated this product, which is called "Hyperduric Morphine and Atropine" and consists of a mixture of the mucates of morphine and atropine.

Mucic acid is a dibasic hydroxy-acid which may be regarded as a homologue of tartaric acid; it bears the same relationship to adipic acid as tartaric acid does to succinic acid:

CH_2COOH | CH_2COOH Succinic acid	CH.OH COOH | CH.OH COOH Tartaric acid
$CH_2\ CH_2\ COOH$ | $CH_2\ CH_2\ COOH$ Adipic acid	CH.OHCH.OH COOH | CH.OHCH.OH COOH Mucic acid

Toxicity.—The toxicity of mucic acid is low, and though it has no peculiar pharmacological action of its own it prolongs the action of bases with which it is combined.

Baumgarten (1906) reported the administration of 50 g. of mucic acid by mouth to a patient without any observable ill-effects. Rose and Jackson (1926) found that massive doses of 5–19 g. by mouth occasionally produced nephritis in fasting rabbits. A statement was made by Lumière (1925) that sodium mucate acted as an anticoagulant at a concentration of 0·4% and was completely non-toxic.

C. J. Eastland (personal communication) has found that in rats the L.D. 50 for subcutaneous injection of mucic acid in the form of its triethanolamine compound is 3 g. per kg. of body-weight. With regard to the L.D. 50 by the intravenous route, the largest permissible volume of the solution (0·25 ml. per 10 g. of body-weight) led to no deaths. This corresponds to a dose of mucic acid, in the form of its triethanolamine compound, of 0·75 g. per kg. of body-weight.

H. O. J. Collier (personal communication) has further determined by the method of Miller and Tainter (1944) the acute toxicity in mice by subcutaneous injection of a suspension of sodium mucate in water, and of solutions of sodium tartrate and sodium citrate. He found that the acute L.D. 50 of sodium mucate was equivalent to $1{\cdot}47 \pm 0{\cdot}17$ g. of mucic acid per kg. of body-weight; of sodium tartrate was equivalent to $5{\cdot}97 \pm 0{\cdot}32$ g. of tartaric acid per kg. of body-weight; and of sodium citrate was equivalent to $3{\cdot}715 \pm 0{\cdot}18$ g. of citric acid per kg. of body-weight.

Since injection solutions of mucic-acid compounds do not contain more than 0·025 g. per ml., it seems reasonable to describe the injection as non-toxic.

Prolongation of the action of bases with which mucic acid is combined was first noted in this country during the early stages of the late war after many different compounds of morphine had been examined in a search for one which would have a more sustained action and therefore be of particular value for air-raid and Service wounded (Eastland 1944).

Subsequently it was found that Régnier (1938) had called attention to the variations in activity of any given base according to the acid combined with it. Later, when the liberation of France rendered correspondence possible, Professor Régnier stated, in a private communication made in 1945 to C. J. Eastland, that using narcotic bases he had studied the effect of the formation of salts with two types of acid, such as phenyl-propionic and phenyl-butyric acids on the one hand and gluconic and mucic acids on the other. Salts formed with the first group of acids he described as "sels rapides"—i.e., salts having an immediate and more profound action—and compounds formed with the second type of acids he termed "sels lents"—i.e., those developing the specific activity of their base slowly.

More recently Régnier (1946) described the prolongation of morphine narcosis when the base was used clinically in the form of mucate.

Our first investigation was with morphine mucate gr. $^1/_4$ and atropine mucate gr. $^1/_{150}$, but we found that, though this dosage was ideal in most respects, in some cases, when irritant drugs—e.g., ether—were used, an excess amount of mucus was produced. We therefore increased the amount of atropine mucate from gr. $^1/_{150}$ to gr. $^1/_{75}$ and have found that now the drying of secretions is excellent.

We have used the mucates of morphine and atropine in 1380 cases—480 with atropine gr. $^1/_{150}$ and 900 with atropine gr. $^1/_{75}$, both combined with morphine gr. $^1/_4$.

RESULTS

Drug action started in about $^1/_2$ hour, reached its peak in about $1^1/_2$ hours, and lasted up to 8 or more hours. This is an advantage in that the action of atropine sulphate usually starts to abate in about 45–60 min., with the result that, if for any reason an operation is delayed, a further injection of atropine is necessary. In our series with hyperduric morphine and atropine no second injection of atropine was required. When using the mucate salts we have been in the habit of giving all

the premedications at 8.30 A.M. for operation lists which start at 9.30 A.M. and extend to 4.30–5 P.M. The nursing staff state that this has effected a great saving of time, since all premedications for the day can be given during what is a relatively quiet period, without constantly interrupting the ward routine.

Drying of secretions is excellent with the combination containing atropine gr. $^1/_{75}$, but not too viscid and equal in effect to scopolamine gr. $^1/_{150}$. Bronchoscopy was done on three thoraco-abdominal resections of stomach 3–6 hours after premedication, and no excess mucus was found, the small amount present being non-viscid.

Sedation was satisfactory, but very few patients had complete amnesia.

Respiratory depression was not pronounced and was certainly less than after morphine sulphate gr. $^1/_6$.

Postoperative sedation was excellent. Most patients, including abdominals and thoracics, required no postoperative morphine for 8–30 hours after premedication. A few patients of exceptional muscular build required postoperative morphine about 6 hours after premedication. Patients of normal physique, aged 16–60, usually did not require any postoperative morphine until about 8–12 hours after premedication; they were not drowsy or depressed, and many sat up in bed and read the evening papers. Those of frail physique and at the extremes of age required postoperative morphine much later, about 15–20 hours after premedication. They were sleepy but not depressed and could talk coherently during our evening visit. Finally, those of very frail physique required postoperative morphine about 24–30 hours after premedication; these were very sleepy but were easily aroused and not depressed. All postoperative morphine was given as sulphate not mucate. The surgical ward sisters are unanimous that postoperative morphine is required much later after premedication with hyperduric morphine and atropine than after any other type of premedication, and that the patients were less restless on regaining consciousness and were in no way depressed. We feel that this tends to decrease postoperative chest trouble in that, with an early return to consciousness and coöperativeness, a minimum of respiratory depression, and an absence of pain, the patients will do their breathing-exercises and thus ventilate their lungs.

Age Limits.—The patients were aged 11–82 years. Every patient in this series received hyperduric morphine gr. $^1/_4$ and atropine gr. $^1/_{75}$ or $^1/_{150}$ to determine whether there was any undue depression or untold side-effect. We noted that those in the extremes of age and in poor or frail physique were more influenced but not unduly depressed. The age-distribution was as follows:

Percentage age-distribution

Age (years)	11–16	16–40	40–60	Over 60
Male	2·0	22·3	30·8	9·1
Female	1·5	12·1	17·4	4·8
Total	3·5	34·4	48·2	13·9

Vomiting was minimal. Many non-abdominal patients within an hour of waking were eating a small lunch with no residual nausea or vomiting. All these patients had been anæsthetised with drugs of minimal toxicity and maintained in the lightest possible plane of anæsthesia with regard to the requirements of the operation, and most had gained their reflexes before they left the theatre. This must have explained in part the almost complete lack of vomiting noted by the nurses and ourselves.

Hypersensitivity.—One case of hypersensitivity was noted. An apprehensive man, aged 23, started vomiting $^1/_2$ hour after the injection and vomited five times in the next 3 hours. He gave no history of sensitivity to morphine, and a postoperative dose of morphine gr. $^1/_4$ caused no further vomiting. We considered this vomiting to be psychogenic.

Anæsthetic Agents.—All the patients had a thiopentone induction, followed either by nitrous oxide and oxygen with 'Trilene' or ether added as necessary, or by cyclopropane. Relaxation in all abdominal cases was obtained with 'Tubarine.'

SUMMARY

The mucates possess advantages over other salts of morphine and atropine, the greatest asset being a very much slower rate of absorption and hence the resulting action is much prolonged. This longer action, especially with atropine, makes it an ideal premedication for patient, anæsthetist, and nurses.

We wish to thank Messrs. Allen & Hanburys Ltd. and particularly Dr. G. R. Boyes, of their medical department, and Mr. C. J. Eastland, of their research department, for supplying most of the drugs with which this investigation was done and for their technical advice.

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Reviews of Books

Clinical Diagnostic Methods

or The Examination of Patients. C. G. LAMBIE, M.D., F.R.C.P.E., professor of medicine, University of Sydney; J. E. ARMYTAGE, M.B., M.R.C.P., demonstrator in clinical laboratory medicine in the university. Sydney: Grahame Book Co. 1947. Vol. I. 1948. Vol. II. Pp. 1138.

THESE two volumes, written for the senior student and hospital resident as well as for the beginner, cover in about 1000 pages the bedside methods of examination and all those laboratory and specialist examinations which may fairly be regarded as part of clinical diagnosis. A new book on this subject ought either to present the groundwork of clinical medicine in a fresh and original way or to combine comprehensively in one textbook what is usually scattered in several. These objects are partly, though not wholly, attained here. For the way in which precise practical details of different examinations are given the book deserves nothing but praise. Such procedures as percussion and auscultation, as well as such techniques as lumbar puncture, are very well described, and excellent photographs (some helpful, some redundant) accompany the text. On the other hand the student who is given a good account of radiography and several pages on electro-encephalograms may feel a need for more than one page and one diagram on electrocardiography, and would probably like to have some account of actual methods of measuring the basal metabolic rate. The authors did not intend to deal with elaborate specialised techniques and no doubt found it difficult to draw the line. Their teaching is thoroughly sound, and the book deserves success.

Hormones and Behaviour

A Survey of Interrelationships Between Endocrine Secretions and Patterns of Overt Response. FRANK A. BEACH, professor of psychology, Yale University. New York: Paul B. Hoeber. London: Hamish Hamilton Medical Books. 1948. Pp. 368. 32*s.* 6*d.*

THE manuscript for this publication was written while the author was chairman of the department of animal behaviour at the American Museum of Natural History in New York. He intended to present a summary of the existing knowledge of hormones and behaviour as a useful aid for workers in this field. Although he describes the book as a "compendium of what others have done and concluded" it is much enriched by the results of his ten years' experimental work on behaviour in animals. The material is arranged arbitrarily in general categories, such as courtship and mating, migration, generalised aggression, emotion, conditioning

and types of learning, developmental aspects, the rôle of nervous stimulation, and interpretations of hormonal effects. Naturally enough, sexual behaviour gets much attention, partly because it is here that the effects of hormone action are particularly evident and specific. Though the book is meant as a work of reference, and "the final responsibility of ascertaining the reliability of any data cited therein is left to the reader," every section contains information of absorbing interest. Thus it seems that German shepherd and saluki dogs have highly active thyroids and excitable natures, but that thyroidectomy reduces their alertness (p. 111); while female rats, according to one observer, are less timid than males, and castration has no influence on this difference. The emotions of women are strongly affected by gonadal hormones, and characteristic psychic changes have been noted during menstruation: thus "girls who were learning to walk a tight-wire showed a deceleration of the learning curve during menstrual periods." Male puppies, if injected with androgen, lift one hind-leg during micturition at 8 weeks, in contrast to the normal dogs, which do it at 19 weeks, and dogs castrated as puppies, which never do it at all. From a study of the hormonal control of learning, and of sexual and maternal behaviour, Professor Beach is led to believe that "the affinity of particular mechanisms for given hormones has resulted from a long, slow process of evolutionary development"; which few will be disposed to dispute. The very full glossary will be appreciated by those who do not know that *Bufo cognatus* is a Great Plains toad, or *Dolichonyx oryzivorus* a bobolink.

Radiotherapy and Cancer

A. G. C. TAYLOR, M.R.C.S., F.F.R., chief radiotherapist Wessex Radiotherapy Board; JOAN LASSETTER, M.B., D.R., and T. K. MORGAN, M.B., D.M.R.T., radiotherapists of the board. London: H. K. Lewis. 1948. Pp. 81. 7*s*. 6*d*.

THIS little book is the result of work by a team of radiotherapists in the area which includes the Royal South Hants and Southampton Hospital and the Royal Victoria and West Hants Hospital, Bournemouth. The classification of malignant disease which they have agreed to use is set out and their views are given on the methods of treatment likely to be most effective. The book is designed for the medical and surgical staff of the hospitals which they visit, and the general practitioners whose patients they treat, but it will also prove a useful quick-reference work for many people interested in radiotherapy. Not all will agree with the terms used, and some will prefer other methods of treatment; but the book is generally sound and shows that a high standard of treatment is being maintained.

Soviet Biology

T. D. LYSENKO. *A Report to the Lenin Academy of Agricultural Sciences, Moscow.* London: Birch Books 1948. Pp. 51. 2*s*. 6*d*.

THE controversy between two schools of genetics in the U.S.S.R. has been followed with interest and emotion by biologists and others in many parts of the world. Those who wish to find out exactly what Acadamician Lysenko has to say on behalf of one school will be grateful to the translators of his recent official report. The type of biological thinking he advocates is forcefully expounded. Darwinism is said to have been debased by the teachings of Weisman, Mendel, and Morgan, because (among other things) "one of the greatest acquisitions in the history of biological science," the principle of the inheritance of acquired characters, has been thrown overboard. That heredity is determined not specifically by the chromosomes but by the metabolism of the whole body is claimed to have been demonstrated by the study of vegetative hybrids, produced by grafting according to methods elaborated by Michurin. Detailed descriptions of these experiments are not easily available, and their validity has been disputed by many Russian biologists of high repute. Consequently, Lysenko says, Morganism-Mendelism has been taught in most Soviet universities and colleges, while the Michurin trend in science has not been taught at all and "remains in the shade."

As a further argument against Mendelism, Lysenko points to the uselessness to the practical farmer of experiments in drosophila genetics, such as those carride out intensively by Dubinin. Similar objections could, of course, be raised against other erudite types of scientific inquiry, which are unlikely to be of immediate value in the advancement of social welfare or medicine. It is difficult for students of genetics, who have been schooled to regard the attractive hypothesis of inheritance of acquired characters as very improbable, to appreciate Lysenko's enthusiastic advocacy. Careful reading of the report, however, suggests that he sincerely believes that this assumption is essential for the most rapid and efficient development of agriculture.

Epithelia of Woman's Reproductive Organs

GEORGE N. PAPANICOLAOU, M.D., PH.D., professor of clinical anatomy, Cornell University; HERBERT F. TRAUT, M.D., professor of obstetrics and gynecology, University of California; ANDREW A. MARCHETTI, M.D., associate professor of obstetrics and gynecology, Cornell University. New York: Commonwealth Fund. London: Oxford University Press. 1948. Pp. 53. 55*s*.

THE investigation over thirty years ago of the œstrus cycle in the guineapig by Stockard and Papanicolaou laid the foundations for the bio-assay of œstrogens. Since then Papanicolaou has continued to study cytology in relation to sex physiology, and between 1939 and 1943 he joined with Traut in working out the diagnosis of uterine carcinoma by vaginal smears. Since then, these two authors have been joined by Marchetti in a histological study of the normal cyclical changes of the female reproductive epithelia.

The chapters on the graafian follicle and corpus luteum, the tubal mucosa, and the endometrium follow the generally accepted descriptions. There are some advances in the account of the cyclical changes in the endocervical glands. The longest section (6 pages) deals with the alterations in the epithelium of the vagina and the outer surface of the cervix. These are discussed under the headings of the two epithelial types, the glycogenic and the keratinised, and the changes are correlated with those in the vaginal smear. This section is of most interest because of its relation to the new diagnostic methods in carcinoma.

The authors offer an interpretation of the histological appearances in relation to function. The tubal epithelium reaches its fullest development at the time the ovum is discharged and passes down the tube. The endometrium reaches its peak of activity at 7–10 days after ovulation, and then degenerates if nidation has not occurred. The endocervical glands show their most characteristic changes shortly before ovulation, which is the time at which intercourse is most likely to be followed by conception. Similarly the vaginal epithelium has its greatest proliferative activity during the follicular phase, and regresses after ovulation.

Apart from the section on the vaginal epithelium, the book does not offer much new knowledge, and as a work of reference in the special field it carries us little further than the standard textbooks. It is well illustrated with 23 coloured plates, which presumably account for the high price.

A New Theory of Human Evolution

Sir ARTHUR KEITH. London: Watts. 1948. Pp. 451. 21*s*.

Sir Arthur finished this book on his 81st birthday, but his readers will hope that the theme will be further developed, especially in the light of recent discovery. While concurring with Darwinian theories, at least to the point of agreeing that the human stem sprang from a simian root, he propounds a "group theory" which stresses the importance in evolution of small isolated groups each with its own particular genes; for "we are linked with our simian ancestry by a continuous trail of gene-containing germ plasm." This theory is worked out by a mass of argument supported by a tremendous bibliography. Later chapters are devoted to nationalism and racialism as factors in human evolution, and review the cases of Egypt, Wales, South Africa, Scotland, the Irish Free State, and the Jews. The lucidity of the writing helps to sustain interest both in the innumerable facts presented and in the explanations offered.

THE LANCET

LONDON: SATURDAY, DEC. 11, 1948

Attack By Virus

MUCH is now known about viruses, but less about the way in which they cause diseases. In the acute exanthems, for instance, it has been usual to recognise an incubation period and a period of invasion; but we do not know what is happening behind the scenes during these phases. Following the precedent of investigations of bacterial diseases, it should be useful to detect the virus, and measure its amount in various organs at different stages of the illness; and at the front of this issue Dr. FENNER describes such a study of the virus infection known as ectromelia or mousepox. This disease of mice is apparently the biological equivalent of vaccinia and variola, resembling vaccinia in its incubation period, its primary lesion at the site of infection, and its generalised rash at a later date. The virus has serological affinity with those of vaccinia and variola, and its attack on the cell is made manifest by an acute necrosis of cells in viscera such as the liver and spleen and by brilliant eosinophil intracytoplasmic inclusions in the skin. For these and other technical reasons mousepox seems an ideal "model" on which to study the mechanism of virus infection, in the hope of throwing light on the processes at work in the virus exanthems of man.

Mousepox is spread by contact, and the virus enters the body through minute abrasions of the skin. After an incubation period of about 7 days a local lesion appears at the site of entry, and within 2 more days an acute fatal necrosis may develop in the liver and spleen, or else a widespread papular rash breaks out on the skin. FENNER shows that the virus passes rapidly from the portal of entry to regional lymph-glands and thence to the blood-stream, from which it is removed by the liver and spleen. Virus proliferation then proceeds actively in the liver and spleen, and from the 5th to the 12th day the virus is present in the blood as a result of continued liberation from necrotic cells in these organs. The skin first shows virus on the 6th day after infection, and from then onwards its virus content rises rapidly to a maximum at the time when the rash appears on the 9th day. *Pari passu* with the appearance and rise in titre of antibodies in the circulation from the 10th day onwards, the amount of virus in all the organs rapidly decreases though virus is still to be found in the skin up to about the 16th day. This course of events bears little resemblance to the classical concept of the infective process, for it consists essentially in a period of initial invasion followed by multiplication of the virus in internal viscera during the incubation period. The rash is clearly the result of focal infection of the epidermal cells, and this is caused by the secondary viræmia initiated by necrosis in the liver and spleen. Clinical phenomena lag behind the multiplication of virus, and symptoms do not appear until after virus proliferation has reached its peak, when the battle may be already lost. The incubation period is thus revealed as the most vital of all the phases of the disease. Focal infection of the skin, causing a rash, is seen in cases where the internal attack has been less fierce, and it is the means whereby the virus is shed from the body to seek fresh hosts. The prolonged viræmia is doubtless responsible for effective stimulation of the antibody mechanism and may therefore be the reason for the staunch immunity which follows such a disease.

Passing from experimentally verifiable facts to deduction, FENNER postulates a similar mechanism in other acute exanthematic diseases. He notes the similarity of the process outlined to that described by ØRSKOV in mouse typhoid and by ØRSKOV and ANDERSEN in experimental vaccinia in the rabbit. Smallpox differs from both mousepox and vaccinia in having no apparent primary lesion, though this may be present in the respiratory tract; but the skin lesions of variola are known to be associated with virus multiplication, and thus the rash at least resembles that of mousepox. The evidence concerning varicella is much more tenuous, though virus has been demonstrated in the skin lesions. In variola, varicella, and measles the incubation period is shortened if the infection is conveyed by direct inoculation, and in measles the blood is well known to be infective during the incubation period. The shortness of the incubation period in dengue is attributed by FENNER to early viræmia following intravenous inoculation of the virus by the mosquito. To his list of other diseases in which the mechanism of infection may be similar we may perhaps add typhus fever, in which the demonstration of rickettsiæ in the skin has been utilised for diagnosis.[1] The primary lesion and secondary rash of such diseases as scrub-typhus and fièvre boutonneuse also suggest that FENNER's observations may apply to rickettsial infections. In whatever direction they ultimately prove to be applicable they are bound to affect our endeavours in prevention and treatment. In measles, for example, if viræmia precedes the rash and causes widespread infection of cells during the incubation period, anti-measles serum cannot be expected to prevent the disease completely unless given soon after infection. The question arises whether this new concept of virus infection reduces the prospect of successful chemotherapy. All that can be said at present is that theoretically the most effective time for therapy would be that which precedes the onset of symptoms; for once these are present, it can do no more than limit the viræmia and thus diminish continued infection of new cells. Happily the results now being obtained with chloromycetin in the treatment of scrub-typhus[2] suggest that such an effect will be worth having.

Meanwhile readers who find difficulty in visualising the intimate processes of the virus infection of individual cells would do well to study the remarkable pictures obtained by the latest technique of electron-microscopy using "shadowed" objects. Photographs of bacterial cells crumbling into masses of bacteriophage particles,[3] and tadpole-like bacteriophage

1. Mandelbaum, H., Hollander, G. *Amer. J. Med.* 1947, *3*, 515.
2. Smadel, J. E., Woodward, T. E., Ley, H. L. jun., Philip, C. B., Traub, R., Lewthwaite, R., Savoor, S. R. *Science*, 1948, **108**, 160; see *Lancet*, 1948, i, 953.
3. Edwards, O. F., Wyckoff, R. W. G. *Proc. Soc. exp. Biol., N.Y.* 1947, **64**, 16.

elements swarming to the attack on bacteria,[4] give a vivid idea of the kind of battle between cell and virus that is going on inside our patients.

Towards Better Statistics

THE International List of Causes of Death, whose object is to secure comparability between the vital statistics of the different countries in the world, has to be revised every ten years to keep pace with advancing knowledge. At the last revision—the sixth—a major advance was made by including the causes not only of death but also of non-fatal diseases, minor ailments, and injuries. With the aid of the International Manual, accepted by the World Health Organisation and now being printed at Geneva in three languages, morbidity statistics can in future be tabulated and presented much more uniformly than has hitherto been customary or possible. In much of the heavy preliminary work involved in this achievement Dr. PERCY STOCKS, chief medical statistician of the General Register Office, played a major part. In the later stages, however, the Minister of Health appointed a special committee, with Sir ERNEST ROCK CARLING as chairman, to study the proposed list and to recommend amendments or additions. The critical examination of some thousand groups of causes of sickness or death was no light task, and it had to be carried out relatively quickly. Now that the detailed and lengthy list has been compiled, there would obviously be advantages in keeping such a body of experts in being, to observe the imperfections in the list that are bound to become apparent, the changes that advancing knowledge will require, and the extensions that research makes advisable. When the seventh revision falls due in another ten years' time we should then be well prepared.

This idea has led the Registrar-General to appoint an Advisory Committee on Medical Nomenclature and Statistics, whose members are named on p. 944; but it will be seen that the committee is not to restrict its activities to the International List, or even to nomenclature in general, but is also asked to assist the General Register Office in any matters concerning medical statistics that may be referred to it. This is an excellent plan. The increasing demands of users of medical statistics are undoubtedly evoking a certain resistance on the part of the producers—the people who fill in the forms. This antithesis between users and producers is of course as false as the antithesis between pedestrians and riders in motor vehicles: we are all both at different times. No doubt most doctors are mainly producers; but very few of us are not also consumers of medical statistics in one way or another, and we are annoyed if the particular information that we ourselves want is not available. The very treatment of the patient must, indeed, be based on previous numerical results—namely, the ratio of successes to failures. What often inspires our resistance as producers is the feeling (*a*) that many of the statistics asked for are useless or unnecessary, (*b*) that nothing will be done with them when they have been collected, and (*c*) that the same, or almost the same, information is being asked for by a number of different persons all oblivious of one another's activities. Such feelings too often have a just, or partially just, foundation; and, though the General Register Office has never been an offender in these ways, one of the possible benefits of the Registrar-General's committee is that it may prevent waste of effort. Its members have obviously been chosen for their widely diverse interests—public health, medicine, surgery, pædiatrics, psychiatry, obstetrics and gynæcology, general practice, and so on, in addition to the professional statisticians and members of Government departments. It should therefore be able to give the Registrar-General sound advice over this very wide field: to say when and how it would be appropriate for him to make some statistical venture; to keep, so far as the General Register Office is concerned, the demands made upon those actively practising medicine within reasonable bounds and to prevent overlapping demands; and to ensure that the kind of information that doctors from time to time require from the national registers has in fact been collected, and collected in the best and most informative way.

The need for research on a problem in medicine has quite often been first revealed by the tabulation of statistics—sometimes, indeed, quite crude statistics. So long as the practitioner in medicine is satisfied that his returns of sickness and death are in this way of real value as a stimulus to research and in its prosecution, and will in the long run contribute to the advance of medicine, he will not grudge the time that must be given to accurate diagnosis and to the recording of it. Indeed, it is a sign of the times to find specialists from every main departent of medical practice accepting an invitation to deliberate on —statistics.

Toxoplasmosis

TOXOPLASMA has been recognised for forty years as a separate genus of protozoa, pathogenic for various animals; but it was not until 1939 that WOLF and his colleagues [1] in New York established that the organism was a cause of human disease. The protozoan was first described in 1908, when it was found in a rabbit by SPLENDORE [2] and in the North African gondi by NICOLLE and MANCEAU,[3] who proposed the name toxoplasma. All the toxoplasmata since isolated probably belong to one species.[4] In smears from affected organs they are usually crescentic, pointed at one end and rounded at the other (see figure), and measure 4–7 × 2–4 μ. The protoplasm is very delicate, staining pale blue. The nuclear chromatin occupies about a third of the parasite, near the rounded end, and stains red to purple with Giemsa. The organism divides by binary fission. In tissue sections "pseudocysts," representing aggregates of parasites in a host cell whose nucleus has disappeared, are sometimes seen.

Smear from peritoneal exudate of a mouse infected with toxoplasma, kindly provided by Dr. Albert Sabin. (× 1350.)

1. Delbrück, M., Delbrück, M. B. *Sci. Amer.* 1948, November, p. 46.

1. Wolf, A., Cowen, D., Paige, B. H. *Science*, 1939, **89**, 226; *Amer. J. Path.* 1939, **15**, 657.
2. Splendore, A. *Rev. Soc. sci. S. Paulo*, 1908, **3**, 109.
3. Nicolle, C., Manceau, L. *C.R. Acad. Sci., Paris*, 1908, **147**, 763.
4. Sabin, A. B., in Advances in Pediatrics. New York, 1942; vol. I.

The human disease takes five forms: (1) a congenital necrotising encephalitis, (2) an acquired encephalitis in older children, (3) an acute toxoplasmosis with maculopapular rash in adults, (4) a chronic encephalitis in adults, and (5) symptomless infection. Of the clinically manifest types the congenital encephalitis is the commonest. The symptoms of this may be present at birth or may develop after a few weeks or months. Hydrocephalus (which may be demonstrable in utero[5]) or occasionally microcephaly, twitching or generalised convulsions, chorioretinitis, and cerebral calcifications are the main features. Jaundice is present in about half the cases and when accompanied by enlargement of the spleen and liver may suggest icterus gravis neonatorum. Splenic enlargement is less frequent than jaundice and is seldom gross. Hæmorrhagic diathesis is present in about a third of cases, and it may dominate the clinical picture and simulate hæmorrhagic disease of the newborn.[6] The chorioretinitis produces progressive blindness and shows itself in irregular white spots with pigmented borders on the retina. The cerebral calcifications are seen as dots or curvilinear shadows in the X-ray film. The blood picture is normal, but in active cases the cerebrospinal fluid shows a moderate or pronounced pleocytosis and often a considerable increase in protein; the fluid may be xanthochromic and this may suggest a spinal block. The infants may survive for several years, but they will be mentally deficient and are likely to be blind. At necropsy the cerebral cortex, pons, and medulla often show multiple opaque whitish or yellowish areas of necrosis, 1–2 cm. in diameter, with calcification and sometimes cysts. These areas contain many compound granule cells, and lymphocytes and polymorphs are also commonly found. Other findings are scattered miliary granulomata, perivascular cuffing, and subependymal granulomata with ulceration of the ependymal lining. Occasionally there is a widespread encephalomalacia, and the brain may even be a "collapsed gelatinous, almost shapeless mass."[7] Malacic changes may be found, more rarely, in the spinal cord. The parasites are usually easily demonstrated in the central nervous system, and they have been reported in the lungs, muscles, kidneys, and elsewhere, with or without any inflammatory reaction.[6–9] Neonatal cases clinically and anatomically resembling toxoplasmosis have been described[10] in which no parasites could be found, and it seems likely that there are other causes of granulomatous or necrotising encephalitis acquired in utero.

The acquired toxoplasmosis of childhood, first described by SABIN,[11] produces vomiting, headache, fever, and convulsions, suggestive of meningitis or encephalitis, and there may be some enlargement of spleen and lymph-glands. Some cases of this group present symptoms of brain tumour.[4] Toxoplasmosis in adults was first reported by PINKERTON and HENDERSON[12] in South America and very few examples have been published. In acute cases the onset is sudden with rigors, fever, respiratory symptoms, and a maculopapular eruption not unlike the rash of rickettsial infections. The main post-mortem changes are in the lungs—interstitial pneumonia and focal necroses—though foci of necrosis are also found in the heart muscle, and the liver, spleen, and other viscera seem to be more commonly affected than in infantile toxoplasmosis. In the chronic adult form the symptoms are mainly related to the central nervous system, and areas of encephalomalacia surrounded by parasites have been found at necropsy. In one unconfirmed case the patient died of heart-failure, and parasitic "cysts" were found in the myocardial fibres.[13] Lastly there are the symptomless infections, discovered serologically, of which there have been many examples among adults and a few in children.[4] The mothers of babies with congenital toxoplasmosis have of course been infected, and neutralising antibodies can usually be found in their serum, yet they show no signs of disease.

However suggestive are the clinical, ophthalmoscopical, and radiological findings, the diagnosis of toxoplasmosis must rest on the demonstration of parasites and the serological tests. During life toxoplasma has only exceptionally been demonstrated in the cerebrospinal fluid.[11] Post mortem the discovery of parasites in smears and sections, and their propagation in suitable animals, is the decisive finding. Mice should be inoculated intracerebrally with 0·02–0·03 ml. of a tissue suspension or the deposit of centrifuged cerebrospinal fluid; guineapigs with 1–5 ml. intraperitoneally and intramuscularly; and rabbits with 0·2 ml. intracerebrally and 0·1 ml. intracutaneously. Lesions in the inoculated animals must then be examined for parasites. In vivo the most important diagnostic investigation is the test for neutralising antibodies, described by SABIN.[11]

The brains of infected mice are ground with ten times the amount of Tyrode's solution. From the supernatant fluid dilutions of 1 : 5, 1 : 50, and 1 : 500 are made. The original supernatant fluid and the three dilutions are then mixed with an equal amount of the serum to be tested, or, for controls, with the same amount of Tyrode's solution. The final dilutions are therefore 1 : 20, 1 : 100, 1 : 1000, and 1 : 10,000. Intracutaneous injections of 0·2 ml. of each serum and control dilution are then made into the depilated back of a rabbit. Reactions usually appear in 5–9 days. The highest dilution with Tyrode's solution which produces a skin lesion is a skin-reactive dose. By comparing the two series of lesions the number of skin-reactive doses (if any) in the serum under test can be estimated.

For this test a strain of toxoplasma continually propagated in suitable animals—usually mice—is required, and unfortunately no such strain exists in Britain. Sending sera abroad for testing is unsatisfactory because the neutralising antibodies often disappear in a few days. Toxoplasma cannot be cultivated on synthetic media, but propagation on minced chick embryo suspended in Tyrode's solution has been successful,[14] and lately MACFARLANE and RUCHMAN[15] have cultivated the organism on the developing chick embryo. The infected membranes

5. Wolf, A., Cowen, D., Paige, B. H. *Science*, 1941, **93**, 548.
6. Callahan, W. P. jun., Russell, W. O., Smith, M. G. *Medicine, Baltimore*, 1946, **25**, 343.
7. Kean, B. H., Grocott, R. G. *J. Amer. med. Ass.* 1948, **136**, 104.
8. Hertig, A. T. *Amer. J. Path.* 1934, **10**, 413.
9. Zuelzer, W. W. *Arch. Path.* 1944, **38**, 1.
10. Parsons, L. G. *J. Obstet. Gynæc.* 1946, **53**, 1. Baar, H. S. *Brit. med. Bull.* 1946, **4**, 178.
11. Sabin, A. B. *J. Amer. med. Ass.* 1941, **116**, 801.
12. Pinkerton, H., Henderson, R. G. *Ibid*, p. 807.
13. Kean, B. H., Grocott, R. G. *Amer. J. Path.* 1945, **21**, 467.
14. Sabin, A. B., Olitsky, P. K. *Science*, 1937, **85**, 336.
15. MacFarlane, J. O., Ruchman, I. *Proc. Soc. exp. Biol., N.Y.* 1948, **67**, 1.

could be stored at 4°C for as long as a month, so this technique may make it possible to obtain a strain for continuous propagation in this country.

Hitherto most cases of toxoplasmosis have been reported from America, though there have been reports from Czechoslovakia, Holland, Australia, and recently from Sweden[16] and Italy.[17] The first case in England is reported by JACOBY and SAGORIN in this issue. The observation by HEELEY of a toxoplasmic encephalitis in a dog, which they quote, is the first known example of the infection in a domestic animal in this country, though toxoplasma has been found in other animals. This observation is important, for animals appear, whether directly or through insect vectors, to be responsible for the human infection.

Annotations

TO ADVISE ON CHILDREN

THE new Advisory Council on Child Care, appointed by the Home Secretary in accordance with the Children Act, is fortunate in its chairman. Dr. Alan Moncrieff is Nuffield professor of child health in London University, and has great understanding of the physical needs and potentialities of children. The council includes Lady Allen of Hurtwood, whose letter in the *Times* four years ago led ultimately to the appointment of the Curtis Committee, and hence to the Act. The names of the remaining members, which are printed in our Parliamentary columns, also inspire confidence, for they represent both Church and lay voluntary societies interested in children's welfare, psychiatry, the juvenile courts, education, and local government. The Act is founded on the children's officer, conceived as the personal friend of the children under her care; and it is administered by the Home Office (which has a long tradition of serious regard for childhood), now advised by a body of people whose experience and deeds have proved their sympathy with children. The Act was specifically devised for the welfare of individuals, and the new council should help to guarantee the individual approach.

PREVENTION OF RUBELLA

A FEW years ago it would have seemed laughable for a research institute to expend time and funds on rubella prophylaxis; but the establishment of a connexion between maternal rubella and congenital defects, stillbirths, and miscarriages has entirely changed the position. The production of a simple, safe, and effective rubella prophylactic for pregnant women exposed to infection would relieve anxiety and prevent an appreciable proportion of fœtal deaths and deformities. In Britain and the United States research on this subject has been hindered by the absence of extensive outbreaks in adults since 1940–41. But the disease has been prevalent in Australia, where an epidemic in the naval base at Flinders, Victoria, provided Prof. F. M. Burnet, F.R.S., Dr. S. G. Anderson, and their colleagues at the Walter and Eliza Hall Institute, Melbourne, with material for virus studies and a large amount of convalescent serum.[18]

Attempts to cultivate the virus on the developing chick embryo were unsuccessful, but the disease was transmitted to 9 out of 16 women student volunteers by getting them to inhale filtered throat-washings atomised by compressed air. None of the remaining 7 students developed rubella, despite close contact with the infected ones; so it seems probable that they were already immune. It was shown that the virus is present in high concentration in throat-washings taken from patients at the height of their rash; such washings remain active indefinitely if frozen, and they can be used to produce infection when desired. It should thus be practicable to infect a young woman at will and at a convenient time, instead of waiting for an epidemic, and virtually to guarantee her immunity from rubella during any subsequent pregnancy. Burnet mentions the possibility of a seaside holiday camp where women could spend a fortnight to be immunised without any risk of their infecting others. Active immunisation could also be practised in a resident institution such as a girls' boarding-school.

The convalescent serum collected was processed by the Commonwealth Serum Laboratories, and the gamma globulin extracted was given to 22 presumably susceptible pregnant women, all of whom had been in proved or possible contact with rubella. None developed a rash. This passive method would of course be a far simpler way of protecting pregnant women against rubella than artificial infection, but it must also be far less certain, since in a susceptible woman the fœtus may well be damaged before she knows herself pregnant—and indeed there are now several reports of congenital defects arising when the mother has had rubella shortly *before* conception. It would be useful to know whether gamma globulin will modify an induced infection without interfering with the subsequent immunity (experience with measles suggests that it will). If so, it may greatly increase the popularity of active immunisation; for unmodified rubella, though very rarely serious in girls or young women, often makes them unpleasantly ill.

THE MENTAL HOSPITALS

THE report of the Board of Control for 1947 hardly paints a reassuring picture. Overcrowding in public mental hospitals, though somewhat less than it has been, remains in the board's words "one of the main difficulties which have to be overcome." At the end of 1947 there were 144,736 people under care, compared with 145,391 in 1946; 128,817 of these were in public wards and 14,668 of them were overcrowded "on the basis of recognised standards," compared with 16,662 at the end of 1946. Even "recognised standards" are not necessarily the best that could be wished. It is a fault of our mental hospitals, built for the most part at the height of the Gothic revival, that the large wards with their gloomy narrow windows look at once crowded and bleak. The mentally ill are at present obliged to spend their days in close contemplation of others as sick as themselves; and it is a matter for speculation how much mental disorder is perpetuated by this necessity. Even a mentally normal person convalescing from a physical illness would find his mood and outlook affected by such surroundings; the sick mind finds in them a giant obstacle to recovery, as those who have been mentally ill can attest. Overcrowding of a mental hospital ward means not merely that these depressing circumstances are reinforced, but also that there is a falling off in individual care, and an increase in offensive sounds and smells—even sometimes of squalor. At present more than 14,000 mentally sick people are enduring it.

The reasons for the lack of beds are clear enough: no fresh building has been done since 1939; a growing population has meant an increase in the numbers (though not in the incidence) of the mentally sick; at the end of 1947 over 5000 beds were still diverted to war-time purposes, and of 4908 beds returned during the year nearly 4000 still needed re-equipping; and nearly 2000 beds were out of use for lack of nursing staff. This situation has had a most unfortunate secondary effect:

16. Magnusson, J. H., Wahlgren, F. *Acta path. microbiol. scand.* 1948, **25**, 215.
17. De Toni, G. *Min. Med.* 1948, **39**, 157.
18. Report of the director of the institute for 1947–48.

to keep overcrowding within limits many hospitals have restricted themselves to certified cases and have declined all voluntary patients—a practice detrimental to the whole scheme of voluntary treatment. It is encouraging, however, that taking the country as a whole, voluntary admissions have continued to mount in relation to certified admissions, and during 1947 accounted for 54·5% of the total of 39,223 admissions. There were signs, too, that staffing difficulties were not as bad as they had been, at any rate in some areas. The incidence of tuberculosis among patients showed an increase from 6·5 per 1000 in 1946 to 8·8; this may be compared with the average of 8·1 over the last ten years. In public mental hospitals the death-rate was 7·62 per 1000 daily average population of the hospitals, as against 7·35 for 1946.

Some useful work has been done by the British Red Cross Society and the Order of St. John in supplying books to patients; and the Women's Voluntary Services have organised social activities. An interesting experiment is the Council for Music in Hospitals, founded by Sir Steuart Wilson. This body arranges good concerts, and was giving them in ten hospitals by the end of the year.

DEATH FROM EXPOSURE TO BERYLLIUM

AT an inquest in London last week on a 36-year-old physicist, the jury returned a verdict of death by misadventure as a result of heart-failure and granulomatous fibrosis of the lungs from exposure to compounds of beryllium.

The coroner remarked that this was probably the first case of its kind in the country. He ascertained that the man was exposed to compounds containing beryllium oxide between December, 1941, and December, 1942; the compound in question here was zinc beryllium manganese silicate. The man's first symptoms had not come on until three years later, in December, 1945.

Dr. W. W. Woods stated that death was due to granulomatous fibrosis of the lungs and failure of a hypertrophied right heart. The microscopical appearances in the lungs somewhat resembled silicosis and sarcoidosis, but were not typical of either. The picture was not one which Dr. Woods had met before, but in view of the recent reports from the U.S.A. he considered that death was due to beryllium poisoning.

Dr. John Agate said that the deceased man's condition had gradually deteriorated since he first saw him in February, 1948. He had been suffering for three years from cough, breathlessness, and extreme loss of weight. Diagnoses of miliary tuberculosis and sarcoidosis had been made and later abandoned; there was little doubt now that the true diagnosis was granulomatous fibrosis of the lungs, brought about by exposure to the dust of beryllium compounds.*

Questioned by the coroner about preventive measures, Dr. Agate said that he thought that the best procedure was to abandon the use of beryllium wherever possible. It would be possible to extract the dust from processes, but he was not quite sure whether perfect safety could be achieved by this means in ordinary manufacturing works. The deceased had been exposed to risk while doing research on fluorescent lamps; at that time the delayed form of pneumonitis due to beryllium compounds was not recognised, so he would not have taken special precautions.

A representative of the employers said that preventive measures had been adopted and would be increased. New fluorescent powders which did not contain beryllium were being evolved.

* This case was reported in an article by Dr. Agate on Oct. 2 (p. 530).

SALARIES OF PROFESSORS AND LECTURERS

AT a time when academic salaries are being vigorously discussed, in our correspondence columns and elsewhere, it is useful to have the University Grants Committee's account of the principles they have followed.[1] Before the war salaries in universities remained well below the level the committee would have thought satisfactory; though it has never been their view, or the view of the universities, that academic rewards should be comparable with financial prizes in commerce, industry, or the competitive professions. "The expectation of a large income," they note, "is not among the motives which lead to the adoption of an academic career." The man who enters it should have the same prospect of marrying and maintaining himself and his family as any other moderately successful member of other learned professions, and of providing satisfactorily for the education of his children. The committee thought, also, that academic salaries should also take into account the need to accumulate a private library, to join learned societies, and perhaps to travel abroad. These principles are still sound, they believe; for, if salaries are insufficient to meet these basic needs, teachers without private means—and that includes most of them—are obliged to supplement their incomes by doing extraneous work. It seems that, before the war, few universities could pay their lecturers on a scale sufficient to spare them this necessity; and the rise in the cost of living which followed the war made matters worse. Thanks to an increased Treasury grant it then became possible to revise salaries with these principles and difficulties in mind.

In 1938–39 professors were paid, on an average, £1115, an advance of about £20 on the figure for 1934–35. In 1946–47 the corresponding figure was £1534. Before the war salaries varied, being highest in universities with the greatest income from endowments: these in the main were the universities with large departments and heavy teaching and administrative duties. In some universities higher salaries were paid to professors in some scientific subjects and in engineering, where there was serious competition with industry. The committee had to decide whether these relative differences should be retained; they finally agreed to reduce but not abolish existing inequalities, and followed the plan of recognising for all institutions a standard rate of professorial salary (distinguishing, however, between universities and university colleges) and assessing for each institution an appropriate sum to be expended in raising these salaries above the standard rate. They decided on £1450 a year for universities and £1350 a year for university colleges. The supplementary amounts were assessed according to the number of chairs in the university, the numbers of students to be taught, and the proportion of chairs in scientific and technological subjects. The committee made no attempt to assess the salary to be paid to a particular professor: that is the affair of the university. Many universities think it just to pay more to professors with large departments and heavy administrative responsibilities; and competition with industry may make higher salaries necessary in some scientific subjects.

Readers' and lecturers' salaries are naturally related to the scales paid to professors. Thus the salaries of readers now range from £800 to £1200 a year, and those of senior lecturers from £900 to £1100; while assistant lecturers and demonstrators now receive £400–450, as compared with about £300 before the war. Those ex-Servicemen who were appointed at the end of the war are given higher salaries, appropriate to their age and family responsibilities. Nearly all universities now

1. University Development from 1935 to 1947. London: H.M. Stationery Office. 1948. p. 45 et seq.

have a system of family allowances for their staffs; and teachers on retirement receive pensions through the Federated Superannuation System for Universities.

PENICILLIN INHALATION FOR POSTOPERATIVE COMPLICATIONS

THE inhalation of penicillin aerosol produces effective penicillin levels in the sputum, and its value is undisputed in pulmonary disease associated with sensitive organisms.[1] The place of this therapy in the treatment of postoperative pulmonary complications is not so certain. It is generally believed that collapse of the lung after operation derives mainly from mechanical and physiological disturbances of respiration brought about by the operation itself and by the anæsthetic. Subsequent invasion by bacteria is probable, and in certain circumstances—for example, in old age or with toxæmia or pre-existing lung disease—bronchopneumonia may ensue.

The influence of penicillin inhalation in preventing this bacterial invasion has been investigated by Taplin and his colleagues.[2] They found that most postoperative pulmonary infections are caused by organisms already present in the respiratory tract before operation, and that nearly all the organisms normally residing in the tract are sensitive to penicillin or streptomycin. Though not impressed by the aerosol method, they believe that these drugs can be effectively inhaled in the micropulverised (" micronised ") form, the powder having a particle size of about 1 μ. . In this powder the vehicle is dextrose, which may act as an expectorant since, when first dissolved, it forms a hypertonic solution. The treatment is apparently well tolerated by patients, who quickly learn how to inhale the powder properly and to avoid coughing. Penicillin and streptomycin assays of peripheral pulmonary tissue from patients who had undergone thoracotomy showed that the powder penetrates to the terminals of the bronchial tree; and Taplin and his associates suggest that this form of inhalation therapy should be started some time before operation, so as to reduce or eliminate the bacterial population in the upper respiratory tract.

A few weeks ago Holborow and Spriggs[3] reported in these columns that nebulised penicillin did not significantly reduce the incidence of chest complications. Thus it seems to be agreed that penicillin aerosol is disappointing. Micropulverised powder containing penicillin and streptomycin seems more promising; perhaps with it the treatment of the ubiquitous postoperative " chest " will be taken one step further.

THE DENTIST'S EARNINGS

THE Spens Committee on the remuneration of dentists thought that an efficient single-handed dentist working 33 chairside hours a week should be able to earn a net income of £1600 a year at the 1939 value of money. A general medical practitioner on a comparable standard of full but not unusually heavy work would, they thought, command £1800, the difference being justifiable because the doctor would have less leisure and less time entirely off duty. If 20% is added for betterment, the Spens income of £1600 becomes £1920; and if the practice expenses of a dentist are reckoned at 52% he will require a gross income of about £4000. The Ministry of Health accepted £3800 as a reasonable figure for the gross earnings of a dentist working 33 chairside hours, and recognising that for many dentists the volume of work makes longer hours necessary it sees no reason why an additional £1000 should not be earned, making £4800 in all. But it is well known that some dentists in the National Health Service are in fact earning far larger incomes, particularly in industrial areas, where gross takings at the rate of £7000–8000 are said to be not uncommon; indeed here and there the rate is as high as £12,000 a year. Accordingly the Ministry has decided that from the start of next year gross annual earnings beyond £4800 by dentists in the service will be reduced by half. The relatively high incomes are attributable not only to long hours of work, but also to scales of fees which have proved more generous in practice than was expected. A thorough review of the scales is to be undertaken. Meanwhile officials of the dental organisations have protested that an investigation, with the dental profession participating, should precede any change; and that the change now announced will discourage dentists from working the longer hours required by the public need. It yet remains to be shown how the general medical practitioner is to obtain the advantage in remuneration to which the Spens Committee thought he was entitled.

THE MEDRESCO HEARING-AID

OVER 3000 of the hearing-aids designed by the electroacoustics committee of the Medical Research Council[1] have so far been distributed through the National Health Service. An efficient and quite powerful valve-amplifying aid of the portable type, the Medresco is about the most powerful instrument for its size at present manufactured. The microphone and valve circuit are housed in a small plastic container, while the batteries are in a separate leather pack—a little bulky because the batteries are designed to give a long service. The two batteries, high-tension and low-tension, have different shapes of plug fitting so that no mistake is possible in connecting the wires. As ear-piece the patient can choose between a crystal insert and a telephone: the former is the more efficient and can readily be attached to a plastic meatal mould which is made in several sizes. The volume-control has a good range but is somewhat clumsily built. The instrument as a whole naturally lacks the finish and some of the refinement of the best commercial aids of this type, but it is easy to use and is robust enough to stand up well to wear and tear.

THE KING'S HEALTH

The following bulletin was issued from Buckingham Palace last Monday:

The King's general health continues to be good, and he devotes a considerable proportion of his time to the conduct of affairs of State.

The process of restoration of the arterial circulation to the feet is proceeding slowly, and since the bulletin of Nov. 29 a further small but encouraging improvement has occurred.

In order to secure the rest and the warm environment which are indispensable for the re-establishment of the circulation, his Majesty is remaining in his apartments and spends most of the time in bed.

MAURICE CASSIDY
THOMAS DUNHILL
J. R. LEARMONTH
MORTON SMART
JOHN WEIR.

Dr. ARTHUR ROBINSON, emeritus professor of anatomy in the University of Edinburgh, died at Eastbourne on Dec. 3, at the age of 86.

Dr. F. B. PARSONS, physician to Addenbrooke's Hospital, Cambridge, died in London on Dec. 4, at the age of 46.

We also regret to announce the death on Dec. 4 of Sir EDWARD STEWART, K.B.E., M.D., a former vice-chairman of the British Red Cross Society. He was in his 92nd year.

1. Mutch, N., Rewell, R. E. *Lancet*, 1945, i, 650. Humphrey, J. H., Joules, H. *Ibid*, 1946, i, 221.
2. Taplin, G. V., Cohen, S. H., Mahoney, E. B. *J. Amer. med. Ass.* 1948, 138, 4.
3. Holborow, E. J., Spriggs, E. A. *Lancet*, Oct. 30, p. 688.

1. *Lancet*, 1947, ii, 801.

Special Articles

THE PATHOLOGICAL SERVICE OF A DISTRICT HOSPITAL

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T.D., M.B., B.Sc. Edin., F.R.C.P.E., D.P.H.
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MEDICAL and pathological facilities have rapidly developed at this hospital, particularly in the latter part of the eighteen years of its control by the Middlesex County Council. The administrative lessons, and indeed the ethics, of this development may be of topical interest in view of the probable expansion of hospital services in the National Health Service.

The main function of a hospital laboratory service is to help the clinician in diagnosis and in the scientific control of treatment. This demands close coöperation with the clinician, and laboratory help must be available day and night. The laboratory must also undertake public-health duties for the hospital, such as watching the efficiency of the sterilisers and the quality of milk supplied to the hospital, and the laboratory staff must play a part in the clinical activities of the hospital—attending scientific meetings of the staff, collaborating with the clinicians in original investigations, and assisting in the teaching of students and nurses.

Each group of hospitals under a regional board needs a pathological service capable of undertaking all routine examinations. Highly specialised work, such as examinations for filtrable viruses, phage typing of staphylococci, and the estimation of ketosteroids, may be referred to various centres either within the hospital region or throughout the country. Already certain individuals are recognised not merely as specialist pathologists but also as experts in one type of examination, and they are usually willing to help their colleagues, and at the same time to enlarge their experience in their "ultra-specialty."

In this hospital of 800 beds the amount and variety of the work require three senior pathologists—a morbid anatomist and histologist, a bacteriologist, and a "clinical biologist" who undertakes the biochemistry and hæmatology—and they are supported by three junior pathologists.

The laboratory of a hospital of this size is suitable for training junior pathologists. A 24-hour laboratory service was started last year, and the three junior pathologists take turns to carry out for a week at a time the urgent examinations outside laboratory hours. They are resident when on duty. One of them, in addition, has charge of the hospital blood-transfusion service under the supervision of the hæmatologist.

TECHNICAL STAFF

The staff consists of one chief technician, six technicians, ten laboratory assistants, two orderlies, and two clerks. The attendants of the animal-house and the post-mortem room are seconded from the steward's staff.

The junior technical staff is mainly recruited directly from school, and the possession of the School Certificate is essential. The local schools send an intermittent stream of youths and girls seeking employment in the laboratory. Informal talks allow a much better appreciation of suitability than do formal interviews, and permit the young person to ask questions and see the work and the staff. A few of the more promising applicants are allowed to visit the department regularly for a week or a fortnight to give them a better idea of the work. The care and time spent in this sifting process are amply rewarded by the collection of technicians and trainees who are the justifiable envy of many other laboratories for their ability, personality, and esprit-de-corps.

All trainees accepted are urged to join the Institute of Medical Laboratory Technology as student members. They are interchanged at suitable intervals among the different sections of the department to give them all-round experience in their preparation for the intermediate examination of the institute after three years in the laboratory. This interchange also helps the laboratory to meet emergencies caused by illness, holidays, or a sudden rush of work in one section. The National Service Acts do not interfere with the training of the male students, for it has been arranged that their call-up be deferred for three years. Later, in preparation for the final examination admitting to the associateship of the institute, tuition is given by the various pathologists. The conditions of service are good, and the allowance of time off duty for approved study in addition to their tuition in the laboratory is much appreciated.

Members of the technical staff attend the scientific meetings of the London branch of the Institute of Medical Laboratory Technology and the meetings of their own Middlesex County Technicians' Society. Further, they can attend the weekly clinicopathological demonstrations held by the medical staff of the hospital, particularly when their own technical work is concerned. Taking part in such meetings increases the interest and raises the status of their work, and provides a useful opportunity for the medical staff to meet them.

ADMINISTRATION

Each of the three pathologists is in charge of his own section of the department. Problems affecting one section only, such as techniques used, are entirely within the discretion of the individual pathologist. For administration one of the pathologists is recognised as the normal channel between the department as a whole and outside persons and bodies. He is justified in discussing problems, technical and personal, with his colleagues, but his advice and opinions need not necessarily be adopted. Weekly informal meetings of the three pathologists ensure a uniformity of policy, a continuity of control, and a means of friendly discussion of technical problems.

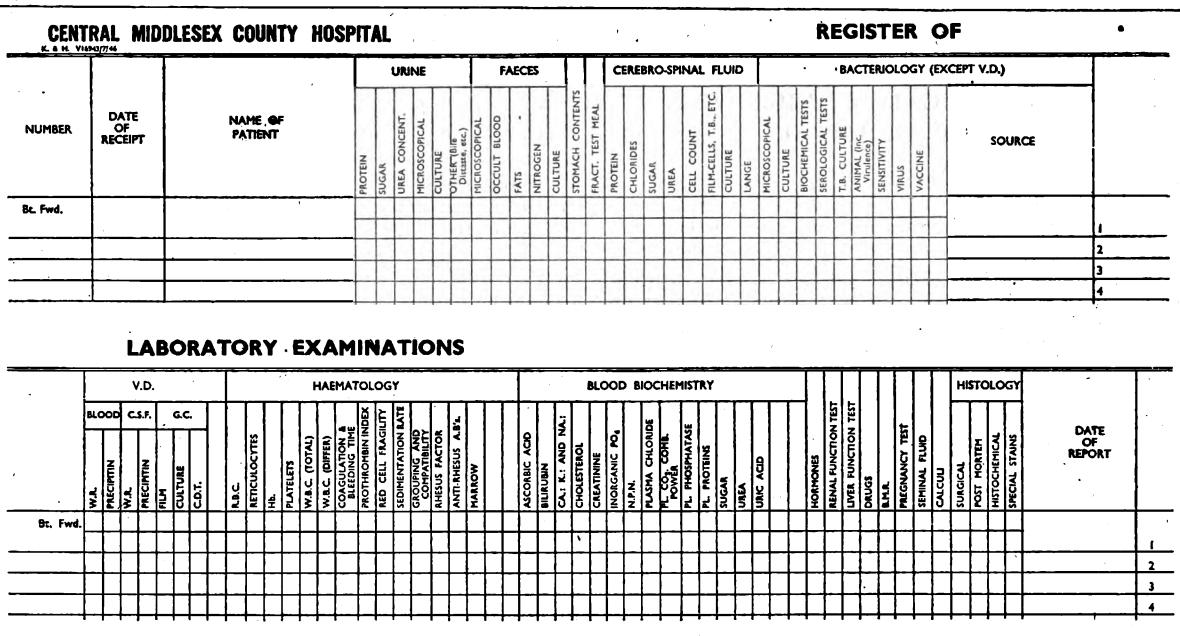
It is important that the pathologists keep their knowledge up to date, and good library facilities supplied by the hospital are invaluable. Besides the general medical and surgical journals available in the hospital library (Avery Jones 1948) there are the *Journal of Pathology and Bacteriology*, the *Journal of Bacteriology*, the *British Journal of Experimental Pathology*, the *American Journal of Pathology*, and *Biological Abstracts*. Lately the hospital has been placed on the list of institutions privileged to borrow from the Science Library books on pure and applied natural science which are not in any of the medical libraries.

It is very desirable that the senior staff should attend meetings of societies such as the Pathological Society of Great Britain and Ireland and the Association of Clinical Pathologists, according to the particular interests of each worker. Further, the pathologists of the Middlesex County Council formed last year an advisory group. The meetings are informal and allow of discussion and the interchange of ideas.

PRACTICAL WORKING OF LABORATORY

Every effort has been made not to allow restrictions in building and in the use of materials to impede the work, but expansion of the department is urgently required. The best use has therefore been made of the available space.

Part of a corridor partitioned off makes an office for the receipt of specimens, the dispatch of reports, and the keeping of records. One of the store-rooms, made light-tight and



Headings of front and back of form.

fitted with an air-extractor and safe light is a photographic dark room. A fan and chimney help to ventilate the overcrowded media room. Part of that room is partitioned off as a dust-free space for the pouring of plates. An unused portion of the roof, walled off and covered in, houses a large refrigerator, centrifuge, and clothes lockers, &c. Numerous additional electric and gas points allow use to be made of tables and benches hitherto wasted. Fluorescent lighting facilitates work in corners previously dark. Extra shelves allow of the clearing of benches, and an old shed, enlarged and made rat-proof, has increased the accommodation for animals.

Work which can reasonably be deputed should not be undertaken by a skilled and highly paid worker. This does not mean that the juniors should act as cleaners, but skilled technicians should not, for instance, have to spend a large proportion of their time cleaning glassware. The preparation of glassware is a major problem in a laboratory, and carelessness in cleaning one batch of universal containers may cause numerous complaints from all over the hospital as well as invalidating work done. Several unsuccessful experiments showed that washing up is best done by women employed as department orderlies similar to the female ward orderlies on the matron's staff. The laboratory trainees must, of course, learn the preparation, cleaning, and sterilisation of glassware as part of their training, and they now have before them an example of cleanliness and order resulting from intelligent and conscientious work in the wash-up room.

A remarkable wastage of the time of workers trained and in training is seen in the use of members of the medical and nursing staff for the transmission of specimens to the laboratory, and the appointment of a porter for this purpose is recommended.

In 1938, 16,665 specimens were examined. The number rose to 31,378 in 1942, 48,279 in 1945, and 69,579 in 1947. The variety and nature of the examinations are becoming increasingly complicated, but the rapid assessment of new methods has in many instances saved time. For instance, the adoption of Chown's technique has shortened to 10 min. the time required for the determination of A,B,O, and Rh groups, and is therefore specially useful for obstetric emergencies. The dangers, immediate and remote, of transfusing rhesus-negative preclimacteric women with rhesus-positive blood are reduced by the preliminary screening with anti-D serum of the samples taken for the Wassermann and Meinicke tests from all patients attending the antenatal clinics. Unfortunately, however, many of the emergency obstetric patients received by the hospital have not been seen before their need for transfusion arises; so a blood bank of some 60 pints of rhesus-positive and 3–8 pints of rhesus-negative blood is maintained.

The 24-hour service allows the fullest use to be made of these new methods, and has been justified by the requirements of the transfusion service alone. The frequent need for speed in transfusion does not allow of delay in summoning non-residents during the night, and therefore necessitates the use of resident staff. In one week alone 63 pints of blood were transfused. Of these, 24 were used outside laboratory hours. The immediate availability of the resident pathologist ensures speed as well as accuracy. Emergency transfusions are often required for young women after abortion, and rhesus-incompatible transfusions can now be eliminated. Apart from the occasional lives thereby saved, the sensitisation of rhesus-negative women and the resulting hæmolytic disease of their newborn children are obviated (Discombe and Hughes 1948).

The day-and-night service is much appreciated by the clinicians, who can always obtain an emergency estimation of blood-sugar in a difficult diabetic case, or of urinary diastase in an acute abdominal case, or an examination of cerebrospinal fluid in suspected meningitis. Throat swabs and blood-cultures can be undertaken with the minimum of delay, and there are many research projects which are greatly facilitated by these pathological facilities during the night as well as the day.

The service is of real value for the training of young pathologists, who have the opportunity of assisting in a responsible rôle in the management of many emergencies.

RECORDS AND REPORTS

Particular attention has been devoted to method and accuracy in the filing and reporting of the work of the laboratory. Request forms accompanying each specimen are used to take a carbon copy of the report, and are filed in alphabetical order. Though the carbon copies may not be so satisfactory as cards, this saves the employment of an additional clerk. When a specimen is received, the clerk stamps the request form, the blank

report form, and the left-hand column in a register with the numbering machine, which automatically advances after every third stamp. The register of examinations is kept in a large loose-leaf file. The headings are reproduced in the accompanying figure. There are horizontal spaces for thirty different specimens, and two extra ones for "brought forward" at the top and "totals" at the foot of the page. The clerk inserts the date and the patient's name, and hands the specimen to the technical staff, who insert on the carbon of the report a letter and a number—e.g., U indicates urine, 1 protein, 2 sugar, and so on, to help the clerks to record accurately the examinations by figures in the appropriate spaces. The register is of value in tracing the receipt of specimens and dispatch of reports, and allowing an accurate estimation of the total numbers of examinations done.

COÖRDINATION WITH OTHER WORK OF THE HOSPITAL

Medical Staff.—Close contact is maintained with the clinicians, and every possible help is given them. Their visits to the laboratory are welcomed, and if they miss attending a necropsy in which they are interested they can see the specimens at demonstrations held in the early afternoon. For junior newcomers and some of the nurses a pamphlet has been prepared giving brief details of the amount and nature of the specimens required for different estimations, along with a table of average results of the more infrequent tests. In it the necessity of full clinical details is emphasised.

The medical staff of the department takes a share in the weekly clinicopathological meetings of the hospital staff, showing naked-eye and microscopic specimens, and introducing some of the discussions.

General Practitioners.—Fortnightly meetings are run by the hospital staff, including the pathologists, for the local general practitioners. One of the staff gives an informal talk on his own subject, with illustrations from the ward or laboratory, and a discussion follows.

Undergraduates.—A few undergraduates are attached to the department for periods of three months, each spending three weeks in each of the four sections. The students see the daily routine and can repeat the work themselves.

Nurses.—Elementary bacteriology can be most profitably taught to nurses, not just to enable them to pass their examinations but to instil the general principles to make them act intelligently rather than by rule of thumb.

The Medical Research Council's memorandum on the control of cross-infection in hospitals (1941) shows how bacteriological knowledge should be used in the everyday life of a hospital, and outlines a course of practical bacteriology for nurses. The chief characteristics of bacteria, such as their size, numbers on solid or in liquid media, motility, staining reactions, habitats, methods of spread, and relation to disease are described.

An important practical lesson is conveyed by demonstrating to nurses their own bacterial flora. One nurse has her fingers rubbed with a swab moistened in sterile saline and the organisms grown on blood-agar, and the experiment is repeated after washing the hands in soap and water. A second nurse is made to speak continuously over an open plate and to repeat the process after donning a face mask. A third brushes her hair over uncovered medium to illustrate the value of a covering of sterile gauze.

PUBLIC RELATIONS

One of the pathologists acts as press officer and is responsible for publicity in the local press, not only for medical but also for social information. This has appreciably helped the local drive for blood donors.

ECONOMIC CONSIDERATIONS

Ffrangcon Roberts (1948) has drawn attention to the economics of the accelerated expansion in the expenditure of money and man-power on medical services in spite of our present economic plight. When a pathologist was first appointed to this hospital ten years ago, the staff of the department consisted of two technicians, who had been appointed the previous year. Today it consists of three senior pathologists, three junior pathologists, and twenty-one technical and clerical staff. In the first place the increase may be regarded as part of the development of the whole hospital from a poor-law institution in 1929 to a modern general hospital in 1948. During that period the proportion of acute to chronic patients became inverted, and the need for pathological services increased accordingly. Secondly, the scientific control of treatment has advanced very considerably in recent years, and the many different sulphonamides have made necessary estimations of sensitivity and assays in body fluids. The use and study of penicillin and streptomycin have required much laboratory assistance. The treatment of a difficult hæmatemesis, of oliguria, or of jaundice may make heavy demands on the transfusion and biochemical workers of the department. But vigorous transfusion or the careful check on blood chemistry now help to save patients whose cases would have been assumed to be hopeless less than ten years ago. Routine rhesus testing will in time reduce the incidence of erythroblastosis fœtalis by eliminating the sensitisation of women in the reproductive period of life. Other new methods requiring careful laboratory control, such as the treatment of thrombophlebitis with heparin and dicoumarol, can shorten the illness and the stay in hospital. The increase in staff needed for the adequate laboratory control of such treatment is offset by the advantages to the patient, the clinician, and the hospital service.

The study of the natural history of disease and the response to new methods of treatments is an important function of any large district hospital. It necessitates heavy demands on laboratory workers to make investigations for the purposes of records rather than for the control of treatment. The pathologist is entitled to view critically all such demands on his department to make certain that such results are actually used. A slight hurdle in the laboratory to be negotiated by those interested in research may act as a useful stimulus for the collection and analysis of results already obtained.

Clinicians are apt to persist in certain ritual investigations long after the need for them has ceased. This may be the result of habit and innate conservative outlook, or because their assistants think they want them. For instance, Himsworth (1948) has shown that, in the treatment of thyrotoxicosis, the determination of the basal metabolic rate is unnecessary save for diagnosis. It is highly probable that many other routine investigations could be reduced or even abandoned, except perhaps at certain research centres, and there is sometimes unnecessary duplication of work when patients are admitted from the outpatient department.

Pathologists in district hospitals with access to abundant human pathological material are in a position to help colleagues in research institutes and university departments less favourably situated as regards material. Contacts so made stimulate a more scientific outlook on medical problems by the hospital staff, and this in turn increases the demands on the laboratory. It must be remembered, too, that any reorganisation or development can only be made if there is a slight surplus of staff over routine requirements.

CONCLUSION

The development of the pathological services of a hospital which is being upgraded can be extremely rapid. Whole-time staffing allows a useful liaison between the pathologists and clinicians far closer than if they were part-time workers.

A well-developed pathological laboratory greatly increases the amount and standard of the original work of which the hospital staff is capable.

Thanks are due to Dr. F. Avery Jones, Dr. George Discombe, and Dr. Horace Joules, and numerous other colleagues for their generous collaboration in the development of the pathological services of the Central Middlesex Hospital and for their help in the preparation of this account of its growth.

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Himsworth, H. P. (1948) *Ibid*, p. 61.
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Roberts, F. (1948) *Brit. med. J.* i, 485.

INDUSTRIAL HEALTH RESEARCH BOARD

THE Medical Research Council have appointed the following to serve as members of the board during the next three years:

Sir FREDERIC BARTLETT, C.B.E., F.R.S., professor of experimental psychology, University of Cambridge (chairman); Sir CHARLES BARTLETT, managing director, Vauxhall Motors; R. V. CHRISTIE, M.D., D.SC., F.R.C.P., professor of medicine, University of London; C. R. DALE, social insurance department, Trades Union Congress; A. N. DRURY, C.B.E., M.D., F.R.S., director of the Lister Institute of Preventive Medicine; Sir LUKE FAWCETT, O.B.E., general secretary, Amalgamated Union of Building Trade Workers; THOMAS FERGUSON, M.D., D.SC., F.R.C.P.E., professor of public health, University of Glasgow; Sir CLAUDE GIBB, C.B.E., D.SC., F.R.S., chairman and managing director, C. A. Parsons & Co., Newcastle-on-Tyne; A. BRADFORD HILL, D.SC., professor of medical statistics, University of London; ESTHER M. KILLICK, M.SC., M.R.C.P., professor of physiology, University of London; R. E. LANE, M.B., F.R.C.P., Nuffield professor of occupational health, University of Manchester; ARTHUR MASSEY, C.B.E., M.D., chief medical officer, Ministry of National Insurance; E. R. A. MEREWETHER, C.B.E., M.D., F.R.C.P., H.M. senior medical inspector of factories, Ministry of Labour and National Service; J. M. ROGAN, M.D., F.R.C.P.E., Medical Research Council headquarters staff; DONALD STEWART, M.D., F.R.C.P., chief medical officer, Austin Motor Co.; Mrs. JOAN M. FAULKNER, M.B., Medical Research Council headquarters staff (secretary).

The board is appointed to advise and assist the council in the part of their research programme which relates to occupational health. The detailed consideration of research work is in the hands of scientific committees dealing with such subjects as occupational medicine, occupational physiology, occupational psychology, industrial pulmonary diseases, toxicology, and statistics. These committees report directly to the council for purposes of immediate action. The function of the board itself is that of a reviewing body considering general policy for research over the whole field.

"... The greatest of researchers have had the rare quality of genius ... a genius is often unappreciated by his contemporaries. He cannot be organised into any scheme, for he creates his own world. ... Yet it would be wrong to suggest that discovery is dependent on genius, for this could serve as a soft excuse for inaction. ... As genius is unpredictable, so also is chance. Nor can it be planned for, otherwise than by creating environments in which it can be exploited. ... There is one inauspicious quality, however, that does appear to have a significant association with research; that is eccentricity, or sometimes rather a reputation for eccentricity. The memory of Hughlings Jackson was curiously erratic. He could never remember a patient's name, nor could he find his way to his own wards without a guide; but he could remember in the minutest detail any fact that bore on one of his own doctrines. Henry Cavendish, the millionaire investigator of hydrogen and many other things, was so morbidly shy that the mere introduction to him of a stranger at Sir Joseph Banks's house was sufficient to make him turn and run in terror ... eccentricity may not necessarily be part of the make-up of a great researcher, but it is a risk to which intense devotion to a specialised field is apt to expose him."—Dr. E. H. DERRICK in a lecture on the Spirit of the Researcher, *Med. J. Aust.* Nov. 27, p. 621.

Medicine and the Law

Artificial Insemination and Incapacity to Consummate Marriage

WHEN Mr. Cecil Binney addressed the Eugenics Society on artificial insemination last October,[1] he seemed to favour the view that, where the husband is the donor, the law of nullity was unlikely to be applied. In L. *v.* L., tried before Mr. Justice Pearce on Nov. 30, the unlikely has occurred. A wife, artificially inseminated by semen from the husband, was awarded a decree of nullity on the ground of his incapacity to consummate the marriage. An unhappy consequence is that the child, conceived as the result of the artificially assisted intercourse between a married man and his wife, becomes illegitimate. There was no marriage; the offspring is therefore a bastard.

In summarising the history of the material events, the judge stated that the husband's trouble was largely psychological. The wife had persisted in the marriage for five years. Besides her natural desire for a child, she had hoped that a child would help their relationship and enable him to overcome his difficulty. Eventually she left him; at that moment she did not know that, as the result of the artificial insemination to which they had had recourse, she was in fact pregnant. When she took proceedings for a decree, the husband not unreasonably contended that her conduct in voluntarily undergoing the artificial insemination was an approbation of the marriage, and that, not only in the interests of the parties but also in the interests of the public, the marriage should not be annulled. In addition to this reliance upon public policy he urged that, if the marriage were continued, there was hope of his condition being cured; and he drew attention to the illegitimacy of the child which would result if the petitioner's application was successful.

Mr. Justice Pearce observed that the marriage had hopelessly broken down; the wife had tried her best to make it a success in circumstances which inflicted strain and humiliation such as a sensitive woman could not endure indefinitely without serious injury to her health. She could never, he thought, bear to go back to her husband. "I see no hope of happiness by keeping these two people married." If he granted a decree of nullity, the mother might marry again; the husband might conquer his inhibition and enjoy normal married happiness. It was better for the child that a decree should be granted than if it were brought up by an embittered mother tied for life to a marriage which had "never been real" and which "only through the unnatural aid of science had produced the fruit of ill-marriage." It was regrettable, concluded the judge, that the child would become illegitimate; "but sons were not now judged by the errors of their parents." The few who would know the circumstances would probably know the full facts; there was nothing that reflected any dishonour on either side of the parents or the child.

There is much matter for discussion in all this; the ruling may in some form be reviewed some day by a higher court. Meanwhile it is to be noted that this was not a case of A.I.D. (artificial insemination by a donor other than the husband), that impregnation by the husband is not inconsistent with the legal idea of impotence, that a wife can voluntarily undergo artificial insemination and yet (in a sense) repudiate the performance, that a child conceived during a marriage as the consequence of a sexual act (however unnatural and however artificially produced) between husband and wife, can nevertheless be illegitimate, and that the courts have ceased apparently to give much weight to the prospect of bastardy.

1. See *Lancet*, Nov. 6, p. 738.

Public Health

PRIMARY MULTIPLE-PRESSURE VACCINATION OF INFANTS

COMPARISON WITH SCARIFICATION

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IN clinics and centres in this country vaccination is usually done by scarification. Various other methods have been introduced from time to time—e.g., intracutaneous injection—but they have not produced a definite and essential area of vesiculation and scarring and have therefore been abandoned. On the other hand, in the United States and Canada (Leake 1930) vaccination by multiple pressure has been in general use for a long time.

At Guy's Hospital we have used multiple pressure, on occasions, with satisfactory results, and about a year ago we set out to compare the efficiency of this method with that of scarification in primary vaccination. Since the Ministry of Health (1947), in its recent memorandum, recommends multiple pressure as the method of choice for general use, our findings may be of interest.

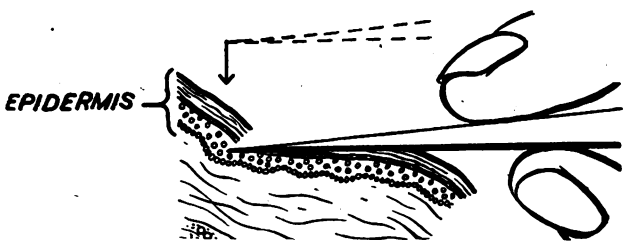

Fig. 1—Multiple-pressure vaccination by rapid up-and-down movement of flat side of needle against skin to break epidermis.

Method

Primary vaccination is carried out as a routine in this department at the age of 3 or 4 months. The vaccination is done on the arm, since vaccination performed elsewhere is associated with more severe reactions or secondary infection. The left arm, just below the posterior border of the deltoid muscle, is the choice, unless the parent insists on some other site.

A volatile antiseptic, either ether or acetone, is used to clean the skin. A drop of lymph is placed on the skin at the prepared site. A freshly sterilised straight needle of the Hagedorn type is used for each child. It is held tangentially to the arm between the thumb below and the forefinger and middle finger above. The side of the needle is pressed firmly into the drop of lymph and then lifted out, clear of the skin, in a plane perpendicular to the skin surface (fig. 1). This movement is repeated rapidly about ten times. It is important to remember it is pressure with the side of the needle that pulls down epidermis over the point so allowing lymph to be forced into the deeper layers of the epidermis. The rapidly repeated pressures are made approximately in the same spot. The operation is painless, there is usually no bleeding, and the only visible sign is a small area of hyperæmia.

The lymph is left to dry for 2 min. before a light sterile dressing is applied. The infant comes up for routine inspection and re-dressing on the seventh and fourteenth days after vaccination.

The method is simple and rapid, and bleeding is less likely to occur than with scarification. It involves so little trauma that the risk of a severe local reaction or secondary infection is very small. The exact number of pressures is not important. We have used successfully about 10; the American reports give 10–30. The important point is to make sure the pressures are made firmly. At this centre, where we are teaching students to vaccinate, a student often fails to get a successful take when first using the method and making 10 pressures, whereas later, when he gets accustomed to the pressure required, 10 are sufficient.

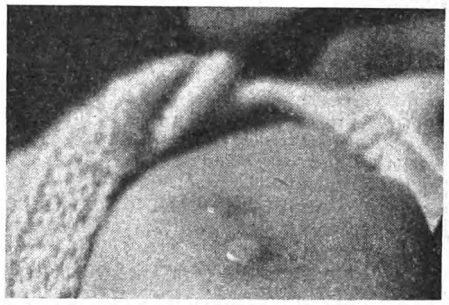

Fig. 2—Vaccination lesions on seventh day: upper lesion by scarification; lower lesion by multiple pressure.

Investigation.—A hundred unselected infants attending the clinic for primary vaccination were vaccinated by both scarification and multiple pressure. The left arm was used, as described above, and two drops of lymph from the same capillary tube were placed on the arm, 1 in. apart, one above the other. In the upper drop a 1/4 in. scarification, and in the lower drop multiple pressure, was performed. The arm was examined on the seventh and fourteenth days, and the results were recorded. Failures were revaccinated by both methods.

TABLE I—GENERAL RESULTS OF VACCINATION OF A HUNDRED INFANTS BY BOTH MULTIPLE PRESSURE AND SCARIFICATION

Ordinal position of vaccinations	No. of vaccinations	Number of takes			
		Total	By multiple pressure	By scarification	By multiple pressure and scarification
First ..	100	83	79	63	59
Second ..	17	8	7	1	0
Third ..	5	0	0	0	0
Total ..	122	91	86	64	59

TABLE II—DISTRIBUTION OF SINGLE TAKES IN A HUNDRED INFANTS VACCINATED BY BOTH MULTIPLE PRESSURE AND SCARIFICATION

Ordinal position of vaccinations	Single take	
	By multiple pressure only	By scarification only
First	20	4
Second	7	1
Third	0	0

Results

The general results show that a primary take by multiple pressure is equal in size to that of a 1/4 in. scarification, though the area of epidermal rupture appears so much smaller (fig. 2). The normal progress of vaccination is slightly slower by multiple pressure, particularly up to the seventh day. There seems to be no significant difference in the local reaction around the primary take in the two methods, and neither method gave rise to a generalised reaction in this series. Sepsis has always been rare in this clinic, and in this series of 122 vaccinations by both methods only 1, by scarification, became mildly infected.

The results (tables I and II) show definitely that multiple pressure is a successful method. In this series it was superior to scarification as regards

the number of both successful primary takes and successful revaccinations. Of the 83 primary takes 79 were by multiple pressure, including 20 by multiple pressure only, and there were only 4 takes by scarification which were not accompanied by takes by multiple pressure. The 17 infants in whom both methods failed on the first attempts were revaccinated by both methods, leading to 8 takes, 7 of which were by multiple pressure and only 1 by scarification. Altogether 5 of the 9 infants in whom both methods failed on the second attempts were revaccinated by both methods a third time but none was successful.

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Leake, J. P. (1930) *Publ. Hlth Rep., Wash.* **45**, 2793.
Ministry of Health (1947) *Mon. Bull. Min. Hlth P.H.L.S.* **6**, 164.

Mineral Oils in Food

Two Sheffield confectioners were fined last week for making jam tarts with mineral oil instead of vegetable or animal fats. The *Manchester Guardian* (Dec. 6) reports that one confectioner said that he had used purified paraffin, which formed a third of the fatty matter in his tarts; the other had used petroleum jelly, which comprised 96% of the fatty matter.

Committee on Medical Nomenclature and Statistics

This committee has been appointed to advise the Registrar-General on questions affecting the International Statistical Classification of Diseases, Injuries, and Causes of Death, and any other matters concerning medical nomenclature or statistics which may be referred to it. The members are:

Sir ERNEST ROCK CARLING, F.R.C.S., F.R.C.P. (chairman), Sir ALLEN DALEY, F.R.C.P., K.H.P., medical officer of health and school medical officer, London County Council; ERNEST FINCH, F.R.C.S., emeritus professor of surgery, University of Sheffield; F. H. K. GREEN, F.R.C.P., assistant secretary, Medical Research Council; C. F. HARRIS, F.R.C.P., dean of the medical college, St. Bartholomew's Hospital; A. BRADFORD HILL, D.SC., professor of medical statistics, University of London; A. J. LEWIS, F.R.C.P., professor of psychiatry, University of London; ARTHUR MASSEY, C.B.E., M.D., chief medical officer, Ministry of National Insurance; P. L. MCKINLAY, M.D., superintendent of statistics, General Registry Office, Edinburgh; W. C. W. NIXON, F.R.C.O.G., professor of obstetrics and gynæcology, University of London; W. N. PICKLES, M.D., general practitioner and M.O.H. for Aysgarth, Yorkshire; A. H. T. ROBB-SMITH, M.D., Nuffield reader in pathology, University of Oxford; PERCY STOCKS, C.M.G., F.R.C.P., chief medical statistician, General Register Office; R. E. TUNBRIDGE, O.B.E., F.R.C.P., professor of medicine, University of Leeds; Sir LIONEL WHITBY, C.V.O., M.C., F.R.C.P., regius professor of physic, University of Cambridge; ALBERTINE WINNER, M.D., medical officer, Ministry of Health; and L. M. FEERY, General Register Office, (secretary).

Notification of Infectious Diseases

ENGLAND AND WALES

Disease	Week ended Nov. 6	13	20	27
Cerebrospinal fever	21	33	32	36
Diphtheria	171	159	154	141
Dysentery	55	133	49	72
Encephalitis lethargica	..	2	..	1
Measles, excluding rubella	6177	6910	6923	8547
Ophthalmia neonatorum	42	45	36	43
Paratyphoid fever	3	8	4	1
Pneumonia, primary or influenzal	496	579	732	716
Polioencephalitis	2	3	6	5
Poliomyelitis	73	60	46	42
Puerperal pyrexia	106	92	100	82
Scarlet fever	1471	1450	1835	1544
Smallpox	..	..	..	..
Typhoid fever	4	5	9	3
Whooping-cough	2240	2481	2680	2747

In England Now

A Running Commentary by Peripatetic Correspondents

THE Memorandum on Mental Health Statistics just issued by the Ministry of Health should prove a source of great comfort to those who have to compile them. Such comfort will derive not only from the optimistic use of the word *Health* in the title, rather than the word *Ill-health*, but also from the evidence therein of the care and helpfulness with which our administrators are watching over our work. Our awareness of this care developed into gratified amazement as we studied the 12 typed foolscap pages of instructions drawn up to help us fill in a natty little record sheet arranged in the familiar box formation.

When we have completed part IA (boxes 1 to 29), we are told that there should be an entry in every box, except that:

22 (Patient related by blood to first spouse)
23 (First spouse's mental state) ..
27 (Age at and duration of first marriage) ..
28 (Age of first wife at marriage to patient)
29 (Married more than once) .. .. ..

Should all be left blank if the patient has never married

Furthermore, 27 (Age of first wife at marriage to patient) *should be left blank if the patient is a female*; a simple little hint which will readily appeal to all.

In part B the good intentions revealed by the above excerpt are combined with tact and delicacy in the remark that box 36 (Address to which patient left) *should be left blank if the patient has died*; and with adaptability to changing circumstances in box 37 (Cause of death; was a P.M. performed?) *which*, we are informed, *should be left blank when the patient has not died.*

Great Stuff as this undoubtedly is, it failed to enthuse the perfectionist member of our staff, who merely remarked acidly that the Ministry had omitted to mention that the whole form, part I, II, and III, A, B, C, and all, should be left blank if it should become apparent that the patient never had existed.

It may be ungrateful to cavil at an attempt to produce foolproof statistics, but we could not help asking ourselves whether a fool would read and understand twelve pages of instructions; especially as, if typed on foolscap, they may well prove to be above his head.

* * *

All the windows in the laboratory were shut, but nevertheless the fog had managed to creep in, making the staff sniff and cough as they met for afternoon tea. The professor cleared his throat partly for the same reason and partly as a signal that he was about to hold forth.

"'Tis somewhat ironical," he said, "that these dense fogs of ours are due to fine weather not merely elsewhere—the North Sea or the Continent—but also above our very heads. They develop round the fringe of an anticyclone and are caused by an inversion of the temperature of the air. Normally, the higher one flies the colder, but in fog-producing conditions something has happened to the adiabatic lapse-rate, the upper air is warmer, and the cold air at ground level, together with the smoke there produced, is prevented from rising. Hence the murk.

"Twenty years ago the London fogs were much blacker, because more coal and less electricity were used; and fires were lit in the streets to warm the air so that it could rise and take the fog away with it. FIDO was invented for military purposes, but it is far too expensive for ordinary civilian use. Obviously some device is required by which the warm air above can be brought down to ground level, from which it will promptly rise again. It's a wonder nobody has invented one."

"It's funny you should say that," said the psychiatrist, "because only today my pet altruistic paranoiac brought me a sketch showing how to do this. The essence of the scheme, you will all observe, is a pilotless aircraft electronically controlled to fly a circle of given radius at a predetermined height selected after consultation with the meteorological office. This aircraft carries a jet apparatus by which the warm air is sucked in and pumped down an airtight hose or tube anchored to the ground through a ball-and-socket joint. From this point on the ground the warm air is distributed to any desired distance through radial pipes, which can be left permanently in

position. Where the air leaves the pipes upward currents are immediately formed. All you want besides is an open space. Almost any London park would do. And of course the same arrangements could be used for sending us cold air in a heat-wave. Indeed the only problem that remains to be solved is what to do with our aircraft and pipes when there are no heat-waves or fogs. Any ideas?"

"Pneumatic delivery of telegrams"—"Collection of salvage in the reverse direction"—"Irrigation of flower-beds in the parks"—"Free distribution of ices in summer and hot dogs in winter" (this from the lab. boy)—suggestions hurtled through the foggy air. "But those don't employ the aircraft," objected the professor; and he rose and placed his empty cup and saucer on a pile of petri dishes as an intimation that it was time to get back to more serious matters.

* * *

Your comparison of two reference systems shows that neither can overcome the disabilities imposed by unselective authors and permitted by inattentive editors.

* * *

Therapy Through Interview [1] shows what could be done by the likes of you and me had we only the requisite vigour and enterprise and lived in the States. It is an entrancing book of dialogues to which, for sheer human interest, those of Plato can't hold a candle. Take, for instance, the story of Joe told in eight racy episodes: Joe has an ulcer; Parents (you might have guessed that they had something to answer for); Joe's History: Joe enters the Second Phase of Therapy (not to be confused with Captain Shotover's seventh degree of concentration); Joe makes Progress; Joe Ends the Second Phase; Joe Tries it Just Once More (meaning psychotherapy); and lastly Joe's Separation (from the apron strings of the psychiatrist, that is; not from his wife).

The hero of the book is You, a small-town physician who, as a sideline, gives psychiatry a whirl. What is particularly satisfactory about Joe's case is that he came to You in the first place because Dr. Brown, a mere somatic but none the less a keen competitor of Yours, lost patience with him. At the end of it all Brown won't have it that You cured Joe by mere talk. "If You've got something new for ulcers and don't let me in on it, You and I are no longer friends," he says. Convinced at last, Brown actually offers to hand over to You a couple of neurotics, being himself too busy to try the psychiatric stuff.

Bill's story (Bill and his Father were Buddies) is hardly less impressive than Joe's. You got him round the corner and soon had him going fishing trips with Joe. Sally's Heart Trouble was the merest chicken feed; but You fell down on Gloria, who proved too tough a nut for You to crack; she was a real high-class psycho-neurotic. However, You were soon up and coming again and brought home the bacon all right in the case of Donald, who got a fracture falling off a stolen bicycle (what a moral the Victorians would have drawn from that) and still more in the case of Harvey, a nasty boy who exposed himself in public because his parents had put him wrong about Sex.

Now and again the question of Your fees and whether You are worth the outlay, crops up during interviews, and You are acutely aware of the competition of other physicians, not only in Your Town but also in the Big City, all selling therapy of one sort or another and ready to pounce on any patient of Yours with whom You fail. Indeed, Yours is a stimulating life if You don't weaken; and of course You don't. The Big Day is when You decide to quit general physician in the Small Town, migrate to the Big City and commence psychiatrist.

You have got there.

* * *

Your newest peripat, a primigravida of 28 weeks' duration, is at last finding the teaching of Mr. Blank, learnt the hard way as his house-surgeon, coming into its own. His special continuous suture is invaluable for finishing off the woolly parts of a layette.

1. By Dr. Stanley G. Law, of the Minnesota Psychiatric Institute. London and Toronto: McGraw Hill. 1948. Pp. 313. 27*s*.

Letters to the Editor

THE UNIVERSITIES AND THE HEALTH SERVICE

SIR,—Professor Dible in your issue of Nov. 27 makes many statements with which one can agree entirely: professors usually are appointed for the reasons he gives, but are nowadays overloaded with administrative responsibilities; these "extramural" (if one may use the word) responsibilities have crowded out his proper academic responsibilities to an increasing extent since July 5; and the Spens report has raised salary problems of national importance. But there are points which might be regarded differently.

Between June, 1947, and August, 1948, of 160 vacancies in non-clinical (excluding premedical) departments, 62 (39%) were unfilled. To 17 vacancies medically unqualified personnel were appointed (comprising 13 in biochemistry and 4 in anatomy or pathology). Of the remaining 81 posts (to which medically qualified individuals were appointed) in 30 there was only one applicant. The mass of the present professoriate of the faculties of medicine in Great Britain are, like Professor Dible, men and women who have elected to work in the less lucrative branches of the profession for the interest of the work. But it is also clear that there are not enough idealists coming forward to meet the requirements of the academic side of the profession under modern conditions. The increased demand is not because of the National Health Service alone, but largely because of the expansion of necessary knowledge and the increased subdivision and specialisation of the older branches of medicine. Put briefly, the past financial directive towards clinical branches of medicine has imposed hardships which have been accepted by idealists. Now, however, the increased directive arising out of Spens plus the post-war cost of living is so impairing recruitment that we are extinguishing our laboratory departments.

There is, however, a much more important matter raised by Prof. Dible out of the two passages:

"certain medical professors have . . . to carry a burden of responsibility for the care of patients, or for the whole gamut of modern clinical diagnostic tests, or for the provision of a post-mortem service to a hospital."

"For myself, however, the position is clear. If a choice is to be made between on the one hand, the large financial gains offered to hospital specialists, with which must be coupled the conditions of service under the Ministry of Health, and on the other the status and emoluments of a professor with the traditional freedom and privileges of that office, even at a much lower salary, I should not hesitate to accept the second."

A whole-time member of a university staff cannot work for more than 24 hours a day. His official working hours are fixed, but they are all the same whatever the post. University duties are teaching and research. Therapeutic responsibilities are properly not university ones but are now clearly National Health Service duties. In so far as these are performed in university hours they should be remunerated proportionately by the Ministry. But there is no good case for the residual university portion of the time being remunerated at any greater rate in any one department than another. An authoritative anatomist is as much entitled to his "hire" as an authoritative surgeon is for his hire in surgery so far as the dual duties of teaching and research are concerned.

In fact the complexity of directing and conducting research with many workers on a departmental staff is as great a problem for the professor of physiology or anatomy as for the professor of pathology or surgery. The problems are equally difficult of correct solution, and, if efficiently tackled, have equal biological disregard for timetables, vacations, and weekends. There is even a case for increased salary in the non-clinical subjects since the non-clinician is often a D.SC. as well as a medical man; he is often doubly qualified, medically and scientifically.

I am not a lover of the principle of "hard-lines pay"—namely that the laboratory worker in the clinical years deserves extra salary because he has so much work to do in treating or diagnosing patients that he has no time for research that would receive academic awards. If he wants to do research, he organises his establishment

and his staff so that no-one has an excess of N.H.S. routine and everyone has adequate time for academic university work of teaching and research. In fact the man who pleads hard lines is worthy, in university terms, of salary deprivation rather than increases.

There is, of course, the strongest possible case for equality of university salaries in all faculties: each man is an authority in his own subject, more he cannot be: Lascelles Abercrombie, Gilbert Murray, Sherrington, Osler, Hopkins, Le Gros Clark, Rutherford, Robinson, are equals, not interchangeables.

The problem before the University Grants Committee to which Professor Dible refers is the problem of reward for extramural work in the N.H.S., when encroaching on university time and duties, and also the problem of maintenance of a qualified university staff in the faculty of medicine when they are attracted by outside interests of guaranteed high salaries without the adventure and gamble of free-lance business. This of course exists in other faculties.

St. Mary's Hospital Medical School, London, W.2. A. ST. G. HUGGETT.

SIR,—Professor Dible raises important and controversial points, but does little to suggest a solution. A possible conclusion to be drawn from his article is that the universities should have little if anything to do with the health service—that no possible benefit could accrue to them. Surely this is a defeatist attitude, which from a purely practical point of view could only be considered in the case of such subjects as pathology and bacteriology. It is hard to believe he advocates that the professors of medicine, pædiatrics, surgery, obstetrics, and psychiatry should do no clinical work in their own field. That would herald a return to the medicine of the Middle Ages—a barrier of suspicion between the academic and the practising man. Those of us who recently served in the Forces discovered that the ideas of the laboratory are difficult to transmit to the man in the field and vice versa. With rare exceptions such transmission is successfully done only by a man experienced and active in both fields. This is equally true of civilian medicine.

In the past the professors and many of non-professorial rank in clinical subjects have been members of hospital staffs. Under the National Health Service the fundamental difference is that the Minister of Health and his Scottish counterpart have decided that those undertaking hospital work should be paid for it. The payment for hospital work does not mean that the person paid must undertake more hospital work than he did in the past, or serve on innumerable committees. The opinion or advice of a laboratory worker or clinician will often be of value to committees, but this surely does not mean that the only possible person to give such help is the professor. The wise professor would delegate some of his authority so that he did not become overburdened by routine clinical work or attendance at committees. Mr. Churchill in his conduct of the recent war showed how superbly this could be done.

Professor Dible is on sure ground when he states that excessive administrative appointments are productive of verbiage in the form of long memoranda and reports. Associated with this is the excessive use of standing committees. For example, in the Act provision is made for each region to set up a medical education committee. In the regions based on a university this would be a duplication of a committee already in existence—the medical faculty, whose chief if not only concern is medical education. It is probable that other duplication may occur, and in that case the universities might well suggest how some existing committee could fulfil a dual function.

Leaving aside the financial problems which have already received much publicity, there are many ways in which the universities and hospitals can benefit by a close linkage and mutual sharing of staff. Sir William Osler believed in a quinquennial brain-dusting; and there is provision for this in some at least of the temporary contracts issued by regional boards. It is up to the universities to see that their staffs have such a brain-dusting, and up to the professors to see that they are not so overburdened with routine as to have no time for reflection and experiment. This is no time to shrink from responsibility, and provided the universities are ever on the alert there seems no reason why they should not coöperate in every possible way with the regional hospital boards to keep British medicine in the forefront of world medicine.

Medical School, Dundee. JOHN GRIEVE.

THE GENERAL PRACTITIONER

SIR,—May I say a word about the plight of the would-be general practitioner? In order to start his practice he must obtain two things—a house and the consent of the local executive council. If he manages to obtain a house he has to sit and wait for the decision of the executive council. This may take up to 3 months or more, and only when the word "go" arrives can he put up his plate and prepare to receive patients. His first cheque appears at the end of the quarter, which means that 4–6 months have elapsed before any income is obtained. Judging from the comments of established general practitioners, this cheque will probably pay one month's rent on his new house.

Suppose, on the other hand, that after the 3 months' wait the executive council refuse to permit him to practise. He appeals to the Minister, who upholds the council's decision. So at the end of, say, 4 months our hero—for that is what I think we must call him now—finds himself still unemployed, with a house he does not now want and the prospect of going through the entire procedure again in another district.

The only work for which a general practitioner is suited is general practice. If this is denied him he must remain not only unemployed but also—and especially if he is over 35—unemployable. Assistantships postpone but do not solve the problem. Incidentally the time-interval of 3 months may be an underestimate. I have so far waited almost 14 weeks, and my letter of inquiry to the executive council written 5 days ago has not yet produced a reply.

I suggest the solution is to be found in the penultimate paragraph of your leading article of Dec. 4—namely, an increase in the capitation fee and limitation of doctors' lists to provide more openings for new entrants to practice. This would enable executive councils to arrive at a decision after somewhat less lengthy deliberations.

London, N.W.10. DANIEL FELDMAN.

YOUNG SPECIALISTS IN SEARCH OF A JOB

SIR,—"The need is twofold, more specialists and a better distribution of them." So said the white-paper which preceded the publication of the National Health Service Bill. The Hospital Survey (Sheffield and East Midlands Area) published in 1945 got down to details:

> "One of the most striking points arising from our survey is the inadequacy of the numbers of available consultants. In Sheffield, not only is the number of consultants too small for the town itself, but the problem is made even more difficult because these consultants visit a large number of hospitals within a radius of twenty miles and cannot by reason of their numbers give the desirable amount of attention to all."

The same report explained why there were too few specialists:

> "The number of consultants in any area has necessarily been determined hitherto by the amount of available private consulting practice by which they live."

Its conclusion for this region was:

> "In general terms it may be said that consultant staffs could be at least doubled and there is especial need for physicians and the adequate development of 'medicine.'"

The Hospital Surveys for the other regions came to similar conclusions.

Since July 5 the number of advertised appointments for whole-time or nearly whole-time surgeons and physicians has been disappointingly small. In spite of assiduously studying the advertisements in THE LANCET, I have noticed only one vacancy for a surgeon and one for a physician in this region since July 5. Surely it is time that some sort of establishment programme was formulated, preferably centrally and right away from any possible local "interests." It might be decided, for example, that the normal establishment should be approximately one full-time surgeon and one full-time physician for every 40,000 of the population. The

regional hospital boards and boards of governors should then be asked to staff up to this level as quickly as possible and thus help to remedy the obvious defects in the specialist services so clearly revealed by the hospital surveys.

CRITIC.

MULTIPLE ABDOMINAL CATASTROPHES

SIR,—I should like to congratulate Mr. Glaser on the successful result in the case described in your issue of Nov. 27. Both the patient and the surgeon must have had great courage and staying power.

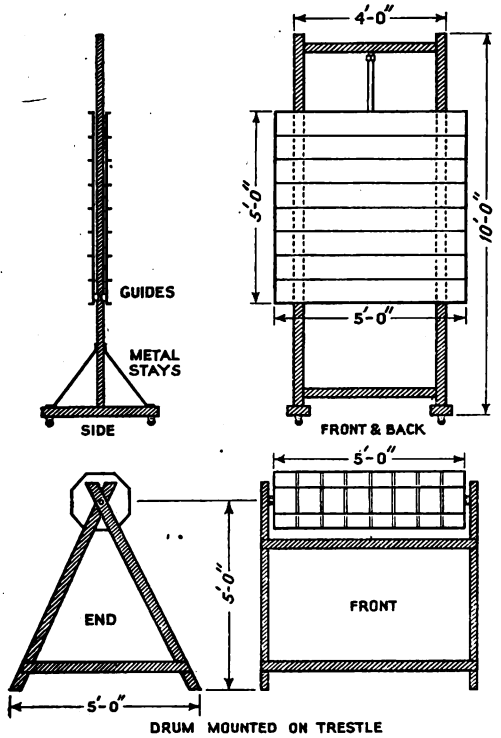
I was particularly interested in his method of dealing with intestinal fistulæ by a dressing with adequate protein, carbohydrate, and fat so as to use up the enzymes in the succus entericus and thus prevent the skin becoming sore. I have not used this method myself but certainly intend to try it on a case under my care at present. I would strongly recommend, however, the use of continuous suction for treating intestinal fistulæ. An apparatus can quite easily be set up so that the intestinal contents are immediately sucked away and no appreciable quantity of them remains in contact with the skin. Should Mr. Glaser have another case of intestinal fistula I would suggest that he should combine suction with his method of dressing. The frequent renewals of the dressing to which he refers would not be necessary if suction were used, since the bulk of the fluid would be sucked away.

London, W.1. JOHN HOSFORD.

CANCER AND RADIOGRAPHIC MUSEUMS

SIR,—Much of the ignorance among general practitioners about the possibilities of radiography is due to there being no place where a fully representative collection of radiographs can be viewed. When the G.P. knows what is suitable for this form of diagnosis, the radiologist will have far less unsuitable material to deal with.

Many hospitals have museums, but these are one-sided, containing films only. The chief object (as yet unattained) of my book *A Descriptive Atlas of Radiographs* was the establishment of such museums. So far as I am aware, none such exists anywhere in the world, the nearest approach being the Wellcome Museum of Medical Science, Euston Road, London, W.C., where radiographs are given the necessary background of clinical notes, specimens, photographs, and microscopical slides. Yet this does not profess to be a radiographic museum.



The ideal radiographic museum would be a place where the common, and therefore important, diseases are depicted. Rarities, save congenital ones, would be shown sparingly. The museum should show routine radiographs since these are the ones which the G.P. encounters; perfect radiographs defeat their object. Films alone should be used in making the original diagnosis, since there is considerable loss in definition in making the print—e.g., loss of skin contour, necessitating silhouette process. But the fact remains that the G.P. likes to see bones and opaque meals as opacities rather than radiolucencies. The ordinary photographic film is a poor thing compared with the print. Prints are much easier to display than negatives, which require viewing-boxes for their display. Reduced prints are a necessity owing to the small amount of space available. They are quite satisfactory; unlike publishers' blocks they show a minimum loss of definition and may, with advantage, be magnified with a lens.

A hall at least 60 by 40 ft. is required; and even then special features have to be adopted so that all the pictures may be at eye level. The first essential is the provision of "photoboards" consisting of sheets of three-ply wood or of duralumin 5 ft. square hung from roof girders 10 ft. high. These boards have ledges to take half-plate reductions; each board accommodates twelve horizontal rows of 8 half-plate radiographs, making 96 for each side. Thus 15 photoboards would accommodate nearly 3000 radiographs. The prints are mounted on aluminium sheets, a layer of paper separating the print from the metal, the whole being bound by passe-partout, with a tag permitting easy removal. Mounted on ledges, each could be taken out easily for closer inspection. They would be slung at right angles to the room so as to form bays each lighted by a vertical window. The window sills would be used to house specimen-jars, models, &c., appertaining to the radiographs. A chain (thrown over the roof girder) would permit the board to be raised or lowered so that the pictures could be seen at eye level.

A knowledge of the normal is imperative; therefore radiographs of such are mounted on photoboards and placed on an easel. The easel consists of two stout uprights secured on a 3-ft. base with metal stays or heavy timber. Two photoboards are slung from the top bar so as to counterbalance one another. They resemble a guillotine, the boards being the knife, moving upwards and downwards so that the radiograph under examination is at eye level; guides are provided to keep them straight. If the easel is likely to be moved from room to room, the uprights are cut in the middle and fitted with hinges and long bolts. By using both sides of the photoboards nearly 400 reduced prints can be displayed.

Another means of displaying the normal is on a hexagonal or octagonal roller, such as shops use for picture postcards, but lying on its side with its axle supported on a 5-ft. trestle. Such a drum, 5 ft. long, would accommodate 48 or 64 reduced prints. (I am grateful to Mr. R. E. S. Ramsay, D.A., for preparing these scale drawings and for useful suggestions.)

The inclusion of the name "cancer" in the title of these museums should aid in their financing. A special cancer section would be devoted to pictures and specimens of skin cancers and the results of treatment. Internal cancers would take their place in the main body of the collection of radiographs.

A historical section would show types of early apparatus. It is surprising how this apparatus is being forgotten in the mass of beautiful apparatus being turned out by the manufacturers.

A canteen at first sight appears to be ridiculously unimportant, but this is not so. Often more knowledge is shared over a quiet cup of tea than is gained from a lecture. Hospitals providing tea are more patronised by postgraduate students than others which do not.

Conclusion.—The creation of radiographic museums at the teaching hospitals is urgent. For smaller hospitals, often giving much postgraduate teaching, they would form useful centres of culture where men could meet and where lectures or, rather, discussions could take place.

Maxwelltown, Dumfries. A. P. BERTWISTLE.

ENTEROGASTRONE

SIR,—In last week's annotation you observe that treatment of peptic ulcer with enterogastrone has proved wholly disappointing. May I give some reasons why this was easy to foresee? Enterogastrone is obtained by the oily extraction of duodenal mucous membrane, and the rationale of its use is based on the observation that it has the same effect as fat in inhibiting gastric secretion and delaying gastric emptying. For the achievement of this effect, which still appears to be the sole consideration in the approach to the problem, would it not be more logical to administer fat itself rather than the result of its metabolic stimulation?

That enterogastrone is not alone in its specific action on the functions of the stomach is shown by urogastrone which has similar effects. Furthermore, the existence of an inhibitory motor reflex of the stomach—the "entero-gastric reflex"—mediated almost entirely by the vagus was postulated by Thomas and Mogan.[1] Day and Webster [2] have shown that the introduction of even neutral fluid into the duodenum inhibits gastric secretion, while Thomas, Crider, and Mogan [3] observed that not only hydrochloric acid, hypertonic salt solution, or alcohol but even chemically inert materials, when introduced into the duodenum inhibited the movements of the stomach. There appears to be no specific reaction for fat, the only difference between the effect produced by these substances being the duration of the reactions, which is longest for fat. Finally, may I point out that the ulcers produced in Mann-Williamson dogs have yet to be shown to be relevant to the problem of peptic ulceration in the human.

London, W.1. J.-JACQUES SPIRA.

A WALKING-CHAIR FOR SPASTIC CHILDREN

SIR,—The appliance for the training of spastic children described by Mr. Wrightson in your issue of Nov. 20 is one which might have a much wider field of usefulness in rehabilitation.

As suggested by Mr. Wrightson, the appliance, which might be described as a "travelling gantry," has the merit of providing a mobile support for a predetermined proportion of the body-weight, and because of this it may be expected to give confidence to an insecure patient. Its value, then, is clear in those cases where, after accident, operation, or illness producing local or general weakness or incoördination of muscles, full weight-bearing is undesirable, but in which the mental picture of normal movement is undisturbed.

In the case of spastic children, however, a normal movement pattern in the brain has either never been formed or has been destroyed, and the major problem in treating these cases is the establishment of such a pattern. This can be done only by painstaking concentration by patient and therapist on the production first of movements at single joints and then by the synthesis of these movements into patterns which can be utilised by the child for progression.

The "gantry" may well get spastic children walking sooner than they otherwise might. But the therapist must realise that the apparatus is introduced to reduce the strain on her own musculature rather than as a form of treatment for the child; otherwise the grotesque gait which is so characteristic of the untreated child will certainly result. That the aim is *normal walking* must not be forgotten. I feel that this point, which was not stressed by Mr. Wrightson, is fundamental.

Middlesex Hospital, London, W.1. W. F. DUNHAM
Assistant,
Department of Physical Medicine.

SIR,—The apparatus described by Mr. Wrightson, though ingenious, involves perpetuation of acquired deformity and implies a belief that in these cases ordinary motor behaviour can be gained by persistent practice.

This apparatus and the more elaborate model now being designed might indeed be valuable in conditions where the cerebral pattern of movement is undisturbed and it is desirable to avoid or minimise weight-bearing: but the treatment of spasticity and allied disabilities of cerebral origin with such an instrument betrays acceptance of a disability which, in fact, responds to careful training directed to the creation of correct motor patterns and normal skeletal postures.

Such an apparatus defeats its own ends by causing a child with defective motor ability to "walk" while retaining poor skeletal posture due to his inability to move normally, and by further distorting that posture (and action) through motion which ignores his motor dysfunction. Further, fear of falling may be eliminated while mechanical protection lasts; but surely the inventor of this machine does not visualise it in use all over the country wherever our thousands of cerebral-palsied children and adults happen to live.

Attention is perhaps better directed to prevention of skeletal deformity and the acquisition of correct motor patterns, to enable handicapped children to dispense entirely with mechanical devices and to protect themselves against fear of falling by developing independent stability and motility. Early and effectively treated "spastics"—without being specifically taught—walk and perform all other normal functions while they are being trained to compensate for their defective motor ability. Of course in the occasional cases with an added mental disability satisfactory treatment is precluded, and there may then be a place for this device.

IRENE COLLIS
Chief Therapist, Cerebral Palsy Research and Diagnostic Clinic.
Queen Mary's Hospital for Children, Carshalton.

1. Thomas, J. E., Mogan, C. J. *Proc. Soc. exp. Biol., N.Y.* 1931, **28**, 968.
2. Day, J. J., Webster, D. R. *Amer. J. Digest. Dis.* 1935, **2**, 527.
3. Thomas, J. E., Crider, J. O., Mogan, C. J. *Amer. J. Physiol.* 1934, **108**, 683.

HOSPITAL BIOCHEMISTS

SIR,—The letter from "PH.D." last week raises a point of great importance to professional biochemists. The advertisement to which he refers, offering £1500 per annum to a medical graduate with experience in biochemistry, but only £750–1000 to a science graduate, is not an isolated case. Several advertisements in similar terms have recently appeared.

If discrimination of this nature is to become part of the policy of the National Health Service it can only result in friction and dissatisfaction. The biochemist who has chosen biochemistry as a career from the commencement of his training will find himself working among colleagues who are all paid at a much higher rate than himself, which can hardly fail to lead to unhappiness.

Hospital biochemists sometimes suffer from other forms of discrimination of a humiliating character. It is not uncommon to find that the most junior and recently appointed member of the medical staff is asked to serve upon committees, in the work of which the biochemist has never been invited to participate. This might be interpreted as evidence that the professional, or even social, status of the science graduate is regarded as lower than that of his medically qualified friends.

M.SC., PH.D.

LOCAL TREATMENT OF BURNS WITH A DIAMIDINE

SIR,—The experience of Dr. Kohn and Dr. Cross with a diamidine, 'Dibrompropamidine' (M. & B. 1270), reported in their article of Oct. 23, corresponds to my own in the treatment of burns with this substance. I have used this compound in 19 cases of burns which, though not extensive, were severe enough to require admission to hospital. All the patients were nursed in general wards and received local applications of M. & B. 1270 up to the time of skin-grafting.

On admission the treatment of shock was the primary consideration. Various dressings had been applied before admission—penicillin cream, M. & B. 1270 cream, or saline or dry dressings. In the ward local application was made of 1% M. & B. 1270 in either the base devised by Todd [1] or a carbowax water-soluble base (see table). There is evidence that Todd's base inhibits the action of this diamidine. With the second base burns dry more rapidly and dressings tend to adhere to granulations.

1. See Clark, A. M., Colebrook, L., Gibson, T., Thomson, M. L., Foster, A. *Lancet*, 1943, 1, 605.

The preparation was applied to burns without any preliminary cleaning, and was left untouched until the patient's general condition had improved. Dressings were then changed, in the ward, 2–3 times a week by a nurse who observed aseptic precautions. If the burnt area involved joints, exercises and dressings were done in a saline bath, a physiotherapist supervising the exercises.

Age (yr.)	Cause, burn or scald	Depth and extent (%)	Region	Organisms cultured	Treatment * and result
6	S.	Superficial and deep 10	Face, neck, back	*Staph. aureus*; *Staph. albus*	A. Skin graft, 2 weeks; healed, 4 weeks; full function
30	S.	Superficial 15	Face, neck, both arms	*Staph. albus*; non-hæmolytic strepto-cocci	AS. Healed, full function, 6 weeks
41	S.	Superficial, with small area deep 20	Both arms, face, neck	*Staph. aureus*; non-hæmolytic strepto-cocci	AS. Healed, full function, 6 weeks
3½	S.	Superficial 10	Rt. abdo-men, chest	*Staph. aureus*	A. Healed, full function, 2 weeks
2	S.	Superficial 5	Forehead, lt arm	*Staph. albus*; hæmolytic strepto-cocci	A. Healed, full function, 3 weeks
40	S.	Superficial 10	Lt. arm, lt hand	*Ps. pyo-cyanea*	A. Healed, full function, 10 days
48	B.	Superficial and deep 15	Lt arm, hand, lt leg	*B. coli*; *Proteus*	AS. Skin graft, 4 weeks; slight residual stiff-ness in lt hand; fair function
32	B.	Superficial 7	Both hands, lt forearm	None	A. Healed, full function, 10 days
1½	B.	Superficial 10	Rt face, rt leg	*Staph. aureus*	A. Healed, full function, 4 weeks
1⁶/₁₂	S.	Superficial 10	Face, neck, lt arm	None	A. Healed, 8 days
7	B.	Superficial 10	Face, lt arm	None	A. Healed, 1 wk; full function
22	B.	Superficial 15	Face, legs	None	A. Healed, 10 days; full function
11	..	Superficial 5	Lt foot	*Staph. aureus*; *B. coli*	A. Healed, full function, 3 weeks
3	S.	Superficial and deep 20	Back, neck, lt arm, lt leg	*B. coli*; *Proteus*; hæmolytic strepto-cocci; *Staph. albus*	B. Split skin graft to neck, 4 weeks
2	S.	Superficial 10	Rt leg, rt arm, back	Hæmolytic strepto-cocci; *Staph. albus*	B. Skin graft to back, 16 days
20	S.	Superficial and deep 15	Both legs	*Staph. albus*	BS. Skin graft, rt leg, 3 weeks
1	S.	Superficial and deep 20	Both legs, abdomen	*Proteus*; *Staph. albus*	BS. Skin graft rt leg and chest, 2 weeks
57	S.	Superficial and deep 5	Rt arm, rt hand	None	B. Healed, full function, 7 weeks
5	B.	Superficial and deep 10	Back, lt thigh, axilla	*Staph. albus*	B. Skin graft to rt leg and back: 1st, 5 weeks; 2nd, 8 weeks. Healed, 10 weeks. Full function

* A = M. & B. 1270, 1% in Todd's base. B = M. & B. 1270, 1% in carbowax soluble base. S = Saline baths.

Swabs for culture were taken at the first dressing and once a week thereafter. The organisms cultured were as follows: *Staph. aureus*, *Staph. albus*, *Strep. hæmolyticus N*, *Pseudomonas pyocyanea*, *Bact. coli*, and *Proteus*. It is thus evident that, in the concentration used, M. & B. 1270 will not completely eliminate either gram-positive or gram-negative organisms.

There were no deaths, and no cases showed significant evidence of infection. A few patients had slight pyrexia until skin grafting was undertaken. The average healing-time was 30 days, and with one exception full function was regained in every case.

Of the 19 cases, 7 were of deep burns requiring skin grafts. In every instance postage-stamp split-skin grafts were used. Grafts were made, on average, on the 22nd day, and healed, on average, by the 44th day. All grafts were 70–100% successful except one, the partial failure of which was due to inadequate fixation of the dressings. If the local application of M. & B. 1270 was used after successful grafting, the graft became soggy and healing was delayed; so from the time of grafting until final healing penicillin powder and tulle gras were applied. No toxic effects from local applications of M. & B. 1270 were observed, but a few patients complained of a slight stinging sensation for a short time after application.

Though there was little change in the bacterial flora in the first weeks after the burn, clinical progress was very satisfactory.

I wish to thank Messrs. May & Baker Ltd. for supplies of M. & B. 1270.

King Edward VII Hospital, Windsor. G. P. ARDEN.

CARCINOGENIC AND ANTICARCINOGENIC SUBSTANCES

SIR,—Professor Dodds in his remarkable review of this subject (Nov. 27) mentioned some work of mine on the treatment of breast cancer and its secondaries with testosterone propionate. He questions, however, the theoretical basis of the treatment, maintaining that the assumption that "a male hormone might possibly inhibit the growth of cells in the female body" is unwarrantable.

Excess of either androgens or œstrogens may in certain circumstances favour cancer development; and, though it sounds paradoxical, both may be anticarcinogenic. This explains the well-known beneficial effects of surgical or X-ray castration on mammary and prostatic cancer and is the basis of the stilbœstrol treatment of the latter condition, found by Huggins one year after I had published my observation on male hormone in mammary cancer.

The female/male hormone ratio in the blood and tissues may be an all-important factor. If this ratio is disturbed in favour of the female or the male hormone a *causa movens* for cancer development may arise, superimposed on a *causa remota*. The determination of the female/male hormone ratio in the body would give this theory a practical and more sound basis. An endocrine disturbance of the female/male hormone ratio occurs normally at the onset of the menopause (45 years) corresponding with the peak incidence of breast carcinoma. The second highest peak in the development of breast cancer is in the 60–61 years age-group at the very end of the menopause, when more androgen principles, as in every ageing woman, are elaborated in the adrenal cortex—the sexual gland of the ageing. Whereas at the beginning of the menopause there may be a preponderance of female principles with a carcinogenic action (here male hormone would be anticarcinogenic) at the end of the menopause the ratio may be disturbed in favour of the male hormone which acts carcinogenically (and here the female hormone would be anticarcinogenic, as indeed it is).

This may be an assumption—and here I agree with Dodds—though clinical experience confirms the theory in part, but there are certainly also some facts which speak in favour of the hypothesis. Male hormone slows down and inhibits, in massive doses, development

of human endometrium.[1] One can exactly determine the amount of male hormone needed to neutralise the stimulating action of the female hormone; 25 mg. of testosterone propionate neutralises 0·5 mg. of stilbœstrol in the vaginal epithelium (ratio 50 : 1), and 600 mg. testosterone propionate neutralises 16 mg. of stilbœstrol in the endometrium (ratio 30 : 1)—which proves that male hormone in the female body has an action against cell growth. That is an undeniable fact.

No-one would claim that testosterone is a cure for mammary cancer (I recommended male-hormone therapy as a prophylactic method against secondaries after a total mastectomy). No-one would say that stilbœstrol is a cure for prostatic cancer, although it brings about very beneficial effects, just as testosterone does very often in mammary carcinoma.

Therapy with endocrines—and here again I agree with Dodds—is not an ideal one, but the results so far obtained surely confirm my assumption which Dodds considers "unwarrantable"; and the therapy should be still further tried until biochemists can give us the necessary anticarcinogenic tool.

London, W.1. A. A. LOESER.

CHANGING ENDS OF SOCIAL MEDICINE

SIR,—Your leading article last week reminded me of something I said in 1941 in my presidential address to the Welsh branch of the Society of Medical Officers of Health. Having described what had been done in the past and what it was still hoped to do in the development of our health and social services, I said:

> "But when we have finished it there will remain the greatest problem of all—the problem of man himself, who has it in his own power at any time to ruin his health and happiness however much may have been done for him by way of organising all kinds of social-welfare services for his benefit. Even for this problem there are optimists in our midst—the psychiatrists, the child-guidance experts, and the like—and we have a new kind of clergyman who is part psychologist and part minister. In days gone by we had debates on church versus science. In the new era, church and science must march together, labouring in harmony for the moral and spiritual as well as the material betterment of mankind. . . . Shall we this time have learnt the lesson that a vigorous social purpose shall inspire a community no less than the will to win survival?"

Cardiff. J. GREENWOOD WILSON.

RESPIRATORY OBSTRUCTION DURING ANÆSTHESIA

SIR,—Respiratory obstruction in general anæsthesia is common enough, but the following case seems to present some unusual features.

The patient, a boy of 13, was about to undergo an exploratory thoracotomy for congenital heart disease. Anæsthesia was induced with nitrous oxide, oxygen, and cyclopropane, using a Waters to-and-fro absorption technique. Induction was smooth as far as the second stage, when ether was added gradually. Mild laryngeal spasm resulted, but respiration was otherwise regular and the jaw muscles were well relaxed. At this point it was observed that the whole of the right side of the chest was immobile, whilst air was freely entering the left side. Prior to operation there had been no abnormal physical signs in the lungs. No pharyngeal airway had been used, nor had there been any noticeable secretion of mucus. During inspiration the intercostal spaces on the right side were seen to be drawn in. No mechanical explanation could be advanced for the complete failure of gases to enter the right lung, especially as there was no obstruction whatever on the left side. The head, which up to now had been turned over to the right, was then straightened and a Macintosh laryngoscope easily introduced. During this manœuvre the right side of the chest suddenly began to inflate as fully as the left. An endotracheal tube was passed and no further abnormality in respiration occurred throughout the operation. Convalescence was uneventful.

In the absence of any obvious cause of mechanical obstruction, such as a plug of mucus, it must be concluded that a reflex bronchial spasm was the explanation of the condition described. The precise moment at which the spasm started is not known as it was only accidentally detected when the towels were removed from the chest. It would be interesting to know whether any of your readers have seen any similar cases which might throw light on the nature of the condition.

St. Thomas's Hospital, London, S.E.1. J. D. LAYCOCK.

1. Loeser, A. A. *Lancet*, 1938, i. 373.

THE MEDICAL CIVIL SERVICE

SIR,—You are, of course, correct in pointing out that only a small proportion of the weekly National Insurance payment is devoted to the National Health Service. That, however, does not really affect the point which I wished to make—namely, that the average individual finds that he is paying some £10 a year in National Insurance, on which he may not live long enough to enjoy a distant return in the form of a pension, while his funeral, though paid for by the State, does not seem to promise much enjoyment, the only obvious immediate benefit which he sees being his ability to call on the doctor without further payment.

There is thus an inherent tendency in the system to call on medical services for trifling ailments for which previously the help of the chemist, or not even his, would have been enlisted.

While sharing Mr. Patey's general dislike of anonymity, I would emphasise your editorial reference to the debt of English literature to that well-known author, "Anon," and to his close relative, the pseudonymous writer—e.g., Junius and Currer Bell; but, in this particular case, for reasons already stated, beg again to subscribe myself

CHIRURGICUS.

DENGUE IN EARLY PREGNANCY

SIR,—I have recently seen a case where a European lady had dengue (a virus infection) during what proved to be the first month of pregnancy. The baby has now been born, and as far as can be told is completely normal and certainly is not deaf.

R. B. WADDY
Medical Officer of Health, Northern Territories.

Tamale, Gold Coast.

INDEPENDENCE IN RESEARCH

SIR,—I should like to comment upon some of the points raised by Sir Ernest Graham-Little in his letter of Nov. 20.

In the first part he is obviously advocating the "laissez faire" system in medical research. I am not a research-worker, but I should have thought that most research-workers would prefer to work as members of a nation-wide, coördinated team, rather than in isolation, very often unnecessarily duplicating each other's work. It seems to me that Graham-Little, and others who think like him, are under the impression that freedom, including freedom in medical research, means the "absence of restraint." This is a fundamental mistake. Freedom comes through coöperation, together with restraint on individuals which coöperation necessarily entails. This is true despite the obvious contradiction.

However, whilst I disagree with him on the organisation of medical research, I do agree with him that the reference to research in the National Health Service Act is meagre. What is more to the point is the actual Government expenditure on medical research compared with other Government expenditure—for example, the expenditure of £1,173,000 on medical research compared with the expenditure of £67,185,000 on military-science research over the same period, and compared with a total expenditure of £154,500,000 on Greece.

Graham-Little concludes with an attack on the Russian biologist, Lysenko, and makes the sweeping and inaccurate assertion that Lysenko's theories are universally rejected by authorities outside Russia. The Russian controversy in biology came to a head only a few months ago, and there has not been sufficient time for Lysenko's views to have had any effect, good or bad, on the economy of the country. One of the basic principles of scientific work is the unity of theory and practice, and one of Lysenko's main criticisms of his biological opponents was that nothing practical had come out of their idealist theories, that their theories had not helped the Russian

farmers one little bit. No doubt Lysenko's views will require modification in detail in the light of experience and further knowledge. The proof of the pudding is in the eating.

Huby, near Leeds. P. J. WADDINGTON.

Parliament

QUESTION TIME

National Campaign against Crime

Sir WALDRON SMITHERS asked the Home Secretary what steps he was taking to deal with the present crime wave; and if he would consider calling a conference of religious and political leaders to advise on further steps.—Mr. CHUTER EDE replied: Following the debate in the House of Lords, I have had a preliminary and informal talk with the Archbishop of York, and I am considering in consultation with the Minister of Education and others what practicable means there are of arousing the public conscience in this matter. Mr. WILSON HARRIS: Is the Minister satisfied that something effective can be achieved along these lines to deal with this unhappy situation?—Mr. EDE: I should not like to prophesy at this stage, but I hope that all men of good will, whether they are in the churches or not, will take steps to bring home to their fellow citizens the effect of the permanent lowering of moral standards in this country.

National Health Service

Sir HENRY MORRIS-JONES asked the Minister of Health whether, in view of many anomalies and some injustice, both to sick persons and those who had to minister to them, in connexion with the National Health Service Act, he would soon issue an interim report on the working of the Act.—Mr. ANEURIN BEVAN replied: I cannot accept the implications in this question. I am, of course, always ready to supply the House with whatever available specific information may be requested. Sir HENRY MORRIS-JONES: Can the Minister say when he hopes to introduce his amending Bill, and whether that Bill will deal also with some of the anomalies which are patent to everybody in the country, even if they are not patent to the right hon. gentleman?—Mr. BEVAN: The hon. gentleman has addressed his supplementary to an entirely different question. This matter of an amending Bill has been under discussion with the representatives of the medical profession and when full agreement has been reached, or when full agreement has not been reached, then the Bill will be presented to the House.

Mr. SOMERVILLE HASTINGS: Is the Minister also aware of the many expressions of satisfaction which have been received from all sections of the community; and does he agree that the thanks of the nation are due to the many people who are working the scheme?—Mr. BEVAN: When the time comes for the report of the Ministry of Health to be presented to Parliament, I hope that it will give an objective review of what has happened. It is undoubtedly the case that very many millions of people have already benefited under the Act. It is also noticeable that certain hon. members belonging to the Opposition claim in the country credit for things at which they jeer in the House of Commons.

Amendment of Lunacy Act

Mr. E. McN. COOPER-KEY asked the Minister whether he was aware that under the provisions of the Lunacy Act, 1890, as amended by the National Health Service Act, 1946, a person could be seized and removed to a mental hospital against the wishes of the appropriate relative, but must be subsequently discharged on the direction of that relative, unless the patient was both dangerous and unfit to be at large; and what steps he was taking to correct this contradiction in the Act which is causing unnecessary distress.—Mr. BEVAN replied: The amendment effected by the National Health Service Act enlarged the powers of discharge. The operation of these provisions will be carefully observed with a view to obviating anomalies when amending legislation can be undertaken.

Mr. COOPER-KEY asked the Minister whether he was satisfied that the interests of the public and patients were sufficiently safeguarded by the provisions of section 74 of the Lunacy Act, 1890.—Mr. BEVAN replied: I am satisfied that, in general, the safeguards provided by the section in question are adequate. But in view of a recent case to which the hon. member has drawn attention, the point has been noted for consideration when amending legislation is undertaken.

Doctors' Remuneration

Sir ERNEST GRAHAM-LITTLE asked the Minister if he was aware of the severe hardships being suffered by doctors in all parts of the country as a consequence of inadequate remuneration under the National Health Service; and whether he would now fulfil the recommendations of the Spens Committee, which would partially remedy this position.—Mr. BEVAN replied: No, Sir. The remuneration of general medical practitioners in the National Health Service is based on the recommendations of the Spens Committee and was agreed with the profession. I am aware that the initial distribution of the total amount of money made available is giving rise to some temporary difficulties, which I am discussing with representatives of the profession.

Inducement Fund

Sir ERNEST GRAHAM-LITTLE asked the Minister if he was aware that his directive to executive councils to the effect that it was not his intention that payments from the Inducement Fund should be made in cases where difficulty could be met by a fixed annual payment would, in fact, result in a general lowering of the capitation grant; and whether he would now withdraw this directive, and allow such payments to be met from the Inducement Fund.—Mr. BEVAN replied: I see no reason to alter these arrangements.

Emergency Dentistry

Mr. A. L. SYMONDS asked the Minister if he would issue a circular to local executive councils in the National Health Service asking them to arrange for dentists in the service to keep a certain time each day free from appointments so as to be able to deal with emergency cases.—Mr. BEVAN replied: I am considering with the dental organisations what can be done on the lines of this suggestion.

Medical Certificates for Eye-testing

Dr. SANTO JEGER asked the Minister whether, in view of the pressure of work on doctors, the long waiting in doctors' waiting-rooms, and the formal nature of the certificates involved, he would remove the necessity for patients requiring to have their eyes tested by opticians to obtain doctors' certificates saying so.—Mr. BEVAN replied: This requirement was instituted in the light of advice received from the medical profession and I should not feel justified in abolishing it except on professional advice.

Priority Spectacles

Mr. F. J. ERROLL asked the Minister what steps he was taking to ensure priority of supply for urgent cases, in view of the great demand for spectacles under the National Health Service.—Mr. JOHN EDWARDS replied: The Minister is seeking to ensure that the supply of spectacles shall be equal to the demand. In the meantime he hopes opticians will distribute their available stocks in the best interests of their patients.

Doctors' Bags

Sir WALDRON SMITHERS asked the Chancellor of the Exchequer if in view of the extra pressure of work placed on doctors under the new Health Act he would exempt from purchase-tax articles necessary for the use of doctors in their professional duties, especially the doctor's bag.—Sir STAFFORD CRIPPS replied: No, Sir. It would not be possible to give doctors special privileges for the few chargeable articles they use professionally.

Employment of Disabled

Replying to a question Mr. G. A. ISAACS stated that 907,899 people were registered under the Disabled Persons (Employment) Act, 1944 at Oct. 1, 1948. Of these, 73,975 were unemployed, including about 20,000 who had been unemployed for 12 months or over. The number unemployed included 10,660 classified as unlikely, owing to the nature and severity of their disablement, to get employment except under sheltered conditions. Of the extremely disabled, 1685 had already been placed in 30 sheltered factories and 86 were working in their own homes. There were 90 other factories under construction or being planned which were expected to absorb the balance of the disabled.

Housing for the Tuberculous

Mr. JOHN RANKIN asked the Secretary of State for Scotland what steps were being taken to deal with the housing of tuberculosis patients in Glasgow.—Mr. ARTHUR WOODBURN

replied: I understand that the corporation allocate 90% of new houses to families from overcrowded dwellings, of which 10% are allocated to tuberculous families. In addition, 400 permanent aluminium houses have been allocated to Glasgow out of the special programme of 1000 for areas where the incidence of tuberculosis is high.

Advisory Council on Child Care

Replying to a question Mr. EDE stated he had now appointed the following to the advisory council provided for in section 43 of the Children Act: Prof. Alan Moncrieff, F.R.C.P. (chairman), Lady Allen of Hurtwood, Dr. Muriel Barton Hall, Mr. R. Beloe, Miss S. C. Bertie, Mrs. F. M. Brown, Mr. P. B. Dingle, Mrs. K. W. Jones-Roberts, Mr. P. T. Kirkpatrick, Mrs. G. R. Morrah, Miss L. M. Rendel, O.B.E., and the Hon. David Smith. Departmental representatives of the Home Office, and the Ministries of Education, Health, and Labour had also been appointed.

Deaths from Bovine Tuberculosis

Mr. A. E. MARPLES asked the Minister of Health how many children died each year from bovine tuberculosis; and what evidence had he as to the primary causes of this disease.—Mr. BEVAN replied: About 450 die in England and Wales each year, usually infected by consuming raw milk.

Private Patients and Drugs and Appliances

Sir WAVELL WAKEFIELD asked the Minister of Health why a person insured under the Act who elected to remain a private patient of a doctor who was taking part in the State service was debarred from receiving pharmaceutical drugs and appliances free of charge under the Act.—Mr. BEVAN replied: Such a doctor would have no responsibility for observing the general conditions which govern prescribing at public expense.

Animal Experiments

Mrs. LEAH MANNING asked the Home Secretary whether he would consider introducing a special certificate for experiments performed on monkeys under the Cruelty to Animals Act, 1876, as in the case of cats and dogs.—Mr. EDE replied: I have no power to require such a certificate.

Births, Marriages, and Deaths

BIRTHS

ASTON.—On Dec. 3, the wife of Dr. J. N. Aston—a son.
BATES.—On Dec. 3, in London, the wife of Dr. D. V. Bates—a daughter.
CHILD.—On Nov. 28, at Newcastle-on-Tyne, the wife of Dr. J. P. Child—a son.
COLBECK.—On Nov. 27, at Auckland, N.Z., the wife of Dr. S. C. Colbeck—a daughter.
GILMORE.—On Nov. 29, the wife of Dr. H. C. Gilmore—a son.
HOEY.—On Nov. 28, at Oxford, the wife of Dr. Trevor Hoey—a son.
ILIFF.—On Nov. 29, at Leamington Spa, the wife of Dr. Arthur Iliff—a daughter.
MCCARTER.—On Nov. 26, at Guildford, the wife of Dr. G. R. B. McCarter—a daughter.
MACKELLAR.—On Nov. 25, at Dewsbury, the wife of Dr. John MacKellar—a son.
MURRAY.—On Nov. 27, at Aberdeen, the wife of Dr. F. Murray—a daughter.
SLATER.—On Dec. 3, at Bushey, the wife of Mr. N. S. Slater, F.R.C.S.—a son.
TRUELOVE.—On Nov. 30, at Oxford, the wife of Dr. Leslie Truelove—a son.

MARRIAGES

HILL—HAMILTON.—On Nov. 24, at Croydon, Alan George Seymour Hill, M.R.C.P.E., to Hilary Frances Hoyte Hamilton, M.R.C.P.E.
STEELE—TELFER.—On Dec. 4, in London, Ludovic MacWhinnie Steele to Florence Lindsay Telfer, M.D.
WATERSTON—TANNER.—On Dec. 1, at Perth, Scotland, David James Waterston, F.R.C.S.E., to Anne Tanner.

DEATHS

BRADLEY.—On Dec. 3, in London, James Edmund Campbell Bradley, B.A., M.B. Camb., aged 84.
CALLENDER.—On Dec. 2, Constance Muriel Callender, O.B.E., L.R.C.P.E.
DAVIS.—On Dec. 2, at Sonning-on-Thames, John James Davis, M.R.C.S., aged 43.
DREW.—On Nov. 27, at Fleet, Charles Milligan Drew, D.S.O., M.A., M.B. Glasg., colonel, A.M.S. retd, aged 68.
DURBRIDGE.—On Dec. 3, at Newport Pagnell, Henry Durbridge, M.R.C.S., aged 77.
GROVE.—On Nov. 28, William Reginald Grove, M.D. Camb., aged 79.
HORSLEY.—On Dec. 2, in London, Lancelot Horsley, M.R.C.S.
MONCRIEFF.—On Dec. 1, in London, Agnes Moncrieff, M.B. Glasg.
PARSONS.—On Dec. 4, in London, Frank Bett Parsons, M.A., M.D. Camb. F.R.C.P., aged 46.
ROBINSON.—On Dec. 3, at Eastbourne, Arthur Robinson, M.D., LL.D. Edin., F.R.C.S., F.R.C.S.E., aged 86.
STEWART.—On Dec. 4, in London, Edward Stewart, K.B.E., M.D. Brux., M.R.C.P., aged 91.

Notes and News

PAYMENTS FROM THE INDUCEMENT FUND

No final decisions on the disposal of the Special Inducements Fund will be possible until the full extent of the demands on it are known. However, after consultation with the Medical Practices Committee the Minister of Health has decided that in the meantime provisional payments should be allowed in cases of special hardship, with particular consideration for claims from sparsely populated areas. Before the final allocation is determined all applications will be reviewed to decide what further payments should be made and whether those already made should be increased. Information submitted in support of claims has hitherto often been incomplete; and executive councils have now received a standard form of application, on which the applicant is required to supply details about his full professional income and other data on his practice. The executive council then has to state, after consultation with the local medical committee, whether the practice concerned is necessary for the provision of general medical services in the area.

TYPHOID FEVER: TYPE J

IT is believed that 3 patients with typhoid fever—1 at Plaistow, 1 at Romford, and 1 at Lyme Regis—contracted the infection while en route from Australia to the United Kingdom, where they arrived in the first week of November. The organism responsible appears to belong to Vi-phage type J, which is not indigenous in England and Wales. It can be fairly assumed that type-J infections appearing here at the present time come from a common source, and it is suggested that practitioners caring for patients suffering from typhoid should make a special effort to see that strains of the infecting organism reach the National Public Health Laboratory Service. Medical officers of health hearing of other patients who may be associated with the incident are asked to send details direct to S.M.O., Med. 3, Ministry of Health, Whitehall, London, S.W.1.

A CHILD-HEALTH GROUP

IMPRESSED by the need for closer coördination, doctors and others engaged in the West of England in the various aspects of health and disease in childhood last March formed a group. This meets monthly; and at the first meeting members took part in a discussion, opened by Prof. A. V. Neale and Prof. R. H. Parry, on the Integration of the Preventive and Curative Aspects of Child Health. As a result of the group's activities, a breakdown of departmental barriers, an increasing integration of divided functions, and a widening interest in every facet of well-being in childhood are said already to be apparent. The secretary, Dr. R. C. Wofinden, may be addressed at Kenwith Lodge, Westbury Park, Bristol, 6.

FILM ON MILK PRODUCTION

The Milky Way (35 min.), produced by United Dairies Ltd., is a documentary film made primarily for student nurses; but it will be useful also to doctors, especially those concerned with public health, and to the general public. Each stage is shown from the cow on the farm to delivery at the front door. There is a clear diagram of H.T.S.T. (high-temperature short-time) pasteurisation; and scenes showing the testing of samples, without being too technical, illustrate the care taken to safeguard our milk-supplies.

University of Cambridge

On Nov. 27 the following degrees were conferred:

M.D.—T. St. M. Norris,* D. S. Short.

* By proxy.

University of Liverpool

Dr. R. A. Gregory has been appointed to the Holt chair of physiology in succession to Prof. W. H. Newton.

Dr. Gregory was awarded a Bayliss-Starling scholarship at University College in 1935, and in 1936 he took his M.SC. Lond. During the next three years, while holding a Sharpey physiology scholarship, he completed his clinical training at University College Hospital and in 1936 he obtained the Conjoint qualification. The same year he was awarded a Rockefeller travelling fellowship, and while in America he took his PH.D. at the North Western University, Chicago. After he returned to England he again held a Sharpey scholarship until, in 1942, he was appointed lecturer in physiology at University College. In 1944 he took up his present post of senior lecturer in experimental physiology at Liverpool.

University of Durham

On Thursday, Jan. 20, at 5 P.M., at the Royal Victoria Infirmary, Newcastle-on-Tyne, Sir Henry Dale, O.M., F.R.S., will deliver the fourth Rutherford Morison lecture. He is to speak on Physiology and Surgery.

University of Edinburgh

Mr. Walter Mercer has been appointed to the newly established chair of orthopædic surgery. He will also be director of orthopædics for the South-Eastern region of Scotland.

Mr. Mercer, who is 58 years of age, was educated at George Watson's College and the University of Edinburgh where he graduated in 1912. After holding resident appointments at the Cumberland Infirmary, Carlisle, and the Edinburgh Royal Infirmary, he served during the 1914–18 war in France, Italy, and the Mediterranean, later becoming specialist in operative surgery at the Edinburgh War Hospital in Bangour. After he was demobilised he settled in consulting practice in Edinburgh, and at present he is surgeon to the Royal Infirmary and lecturer in clinical surgery in the university. He is also surgeon in surgical tuberculosis to the S.E. Counties of Scotland Joint Sanatorium Board Hospital and to the City of Edinburgh, consulting surgeon to the Clinic for Limbless Pensioners, and surgeon to the the thoracic unit of Bangour Base Hospital. In 1938 he delivered the Lady Jones lecture, at Liverpool, on anomalies of the fifth lumbar vertebra, and his recent papers include an article on the surgical treatment of patent ductus arteriosus (1946). His textbook on *Orthopædic Surgery* reached its 3rd edition in 1945.

University of Hong-Kong

Colonel L. T. Ride has been appointed vice-chancellor of the university.

As an Australian Rhodes Scholar, Dr. Ride graduated in medicine at Oxford in 1927. Two years earlier he had been awarded a senior scholarship at Guy's Hospital, and after qualification he became demonstrator in physiology and pharmacology there. In 1928 he was appointed to the chair of physiology at Hong-Kong. During the late war Professor Ride had an active military career in China, and since then he has been in command of the Hong-Kong Volunteer Defence Force.

Royal College of Physicians of Edinburgh

At a meeting of the college held on Dec. 2 Dr. W. D. D. Small was elected president, and Dr. W. A. Alexander, Dr. James Cameron, Dr. T. Douglas Inch, Dr. Ian Hill, Dr. James Hamilton, and Dr. A. P. C. Campbell were elected councillors for the ensuing year. Dr. Alexander was nominated vice-president.

Royal College of Surgeons in Ireland

The following have received the fellowship of the college:

D. V. Kneafsey, J. J. O'Shaughnessy, C. I. Wilkinson, W. H. de W. De Wytt.

Royal Air Force Appointment

Air Vice-Marshal F. J. Murphy has been appointed principal medical officer, R.A.F. Mediterranean and Middle East Command.

Air Vice-Marshal Murphy was until recently principal medical officer of R.A.F. Technical Training Command, to which he went in July, 1947, after having held a similar post at Bomber Command for nearly two years. He was formerly P.M.O., British Air Forces of Occupation, Germany, from July, 1945, and previously of the 2nd Tactical Air Force.

South-East Metropolitan Regional Tuberculosis Society

The inaugural meeting of this society was held on Nov. 13 with Dr. W. E. Roper-Saunders, assistant senior administrative medical officer to the regional hospital board, in the chair.

The following officers were elected: president, Brigadier H. L. Glyn-Hughes, S.A.M.O. to the board; vice-president, Dr. Roper-Saunders; chairman, Dr. F. Temple Clive; vice-chairman, Dr. R. Livingstone; treasurer, Dr. T. W. Lloyd; secretary, Dr. D. L. Pugh. Brigadier Glyn-Hughes said that the aims of the society were purely clinical; and he believed that the board would welcome the views of such a large body of informed opinion. The position of tuberculosis had deteriorated since the war, largely owing to shortage of staff. In the South-East Metropolitan region they were 3800 nurses short, and 8000 beds were unstaffed. With these shortages, he continued, careful assessment of cases for admission was needed. It was sometimes difficult for the tuberculosis officer to know for whom he was working, the board or the local health service, and the answer was to work as a team with the local health committees. The long and short term policy of the board was to give the chest physicians a number of beds under their own supervision.

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on Nov. 27, with Sir William Gilliatt, the president, in the chair, the following were admitted to the membership:

T. M. Abbas, Agnes U. Campbell, Margaret Fitzherbert, R. A. Irani, Mary S. Jolly, Premavathi Maddimsetti Naidu, C. G. Nairn, Mohammad Siddique Qureshi, Helen M. Russell, Saran Abdulkadir Siddiki, P. de S. Wijesekera.

The William Meredith Fletcher Shaw lectureship for 1949 was awarded to Prof. R. W. Johnstone. Leverhulme scholarships, tenable for one year, were awarded to Dr. Frank Reid (for research into X-ray diagnosis of placenta prævia) and to Dr. C. J. Mackinlay (for research into chronic infections of the vulva).

The following were granted the diploma in obstetrics of the college:

Tirath Ram Aggarwal, Patricia M. Aikman, Emma M. H. Albinson, Nicholas Alders, Beryl G. Anscombe, D. J. Atherton, Renu Kana Banerjee, A. S. Barling, J. W. Bartum, K. S. P. Blatchley, V. Y. Bockner, Mary M. M. Boyd, Mollie A. Brown, Joan M. Burrell, Michael Byrne, G. S. Caithness, Elspeth S. K. Campbell, Harriett A. Cawthorpe, Dorothy B. Charlton, G. R. Clare, M. H. Clark, Nancy G. Clegg, Shirley Clifton-Smith, G. R. Connolly, Margaret M. Coughlan, Vivienne A. Croxford, P. N. Cunliffe, R. G. Dewhurst, J. J. B. Dias, Mary Douglas, Aileen P. M. Dring, E. W. Duncan, Violet M. East, W. M. Edwards, Louise E. Elbert, Mary R. Ellis, W. I. Emslie, C. J. Farr, T. R. Farrimond, Mary E. G. Feetham, G. S. Foster, Frances M. Fountain, Maud M. Frankland, T. P. S. Frew, Shanta Galande, H.-J. B. Galbraith, P. D. Gange, H. L. Gardner, Joy M. Gardner, W. F. T. George, Maurice Gold, D. S. M. Graham, Jean A. Grant, F. G. Grant, Violet H. Gray, C. R. H. Green, A. G. Grossett, M. J. L. Hassall, J. K. Hawkey, Josephine M. R. Heber, F. W. Henderson, James Hendry, Mary M. Herley, J. T. Heron, S. R. Hewitt, Rachel M. Hickinbotham, H. F. Hills, J. D. Holdsworth, J. A. G. Holt, P. D. James, Robert Johnston, Daphne M. E. Kayton, R. G. M. Keeling, W. P. Kelly, R. F. S. Kirkham, Mary E. Larg, Helen M. J. Lawn, J. F. Leaver, Joyce R. Lewis, L. E. Lotimer, R. St. J. Lyburn, Ian Macdonald, A. M. Mackenzie, T. E. L. J. McNair, J. D. H. Mahony, Dorothy M. Marshall, Megat Khas bin Megat Omar, Rene M. Michelmore, J. L. Middlemiss, P. D. V. Moni, Valerie N. Nairn, W. L. Needham, L. P. A. Newborne, T. A. O'Donnell, Ann K. O'May, D. G. O'Sullivan, H. P. L. Ozorio, J. H. K. Parker, M. L. Paterson, L. J. Page, A. S. S. Playfair, P. K. Pybus, B. O. Reed, Dorothy M. Ridout, D. A. Road, Joan M. Robinson, Heather J. S. Ross, H. A. Rowley, J. L. D. Roy, A. O. Sankey, Eamon Sheehan, Pamela M. Smith, J. A. Sodipo, T. A. Solomon, F. V. Squires, P. J. Stack, Alexander Starritt, John. Stohlner, Doreen M. J. Stracey, A. S. Subramani, Elaine M. Sunderland, W. F. Sunderland, W. D. G. Tellam, Dorothy E. M. Thomas, S. W. Thomson, G. M. Turner, R. N. H. Vann, Lajjyavati Varma, A. S. Wallace, Alice M. Waters, Paul Watson, P. W. Wells, Philip, Wenchee Mao (Moore) D. B. B. Whitehouse, Edith J. Whitelaw, Alice R. E. Widdows, H. A. G. Winter, Ursula E. Zander, H. T. Zborowski.

Royal Society

The following have been elected officers and council for the ensuing year: president, Sir Robert Robinson; treasurer, Sir Thomas Merton; secretaries, Sir Edward Salisbury and Prof. David Brunt; foreign secretary, Prof. E. D. Adrian, O.M., M.D.; other members of council, Prof. J. D. Bernal, Prof. G. R. Cameron, F.R.C.P., Sir James Chadwick, Prof. S. Chapman, Prof. H. Davenport, Sir Frank Engledow, Prof. W. E. Garner, Prof. A. C. Hardy, Dr. C. H. Kellaway, F.R.C.P., Prof. G. F. Marrian, Sir William Stanier, Mr. H. G. Thornton, Prof. C. E. Tilley, Mr. A. E. Trueman, Prof. S. Zuckerman, M.D.

Oxford Graduates Medical Club

A dinner will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, on Friday, Feb. 18, at 7.30 P.M. All Oxford medical graduates who wish to attend should write to Mr. E. G. Tuckwell, the hon. secretary, 73, Harley Street, W.1.

Appeal Tribunals for Industrial Injuries

The Minister of National Insurance, under the National Insurance (Industrial Injuries) Act, 1946, has now set up medical appeal tribunals to deal with appeals from decisions of medical boards on the assessment of disablement resulting from industrial accidents and disease. A tribunal consists of a chairman, who is a lawyer, and two medical members drawn from a panel of consultants. The chairmen have been appointed by the Minister on the recommendation of the Lord Chancellor or the Lord Advocate, and the medical members on the recommendation of the heads of universities with medical faculties (in London, the presidents of the Royal Colleges of Physicians and Surgeons). These tribunals will meet as occasion demands in a number of towns throughout the country and notice of the meetings will be published locally. A tribunal sat in Birmingham on Dec. 7 and another will meet in Liverpool on Dec. 16. The proceedings will be in public, unless the tribunal directs otherwise.

A Welsh Society of Anæsthetists

A meeting will be held at Cardiff Royal Infirmary on Jan. 12, at 8 P.M., to discuss the formation of a society of anæsthetists in South Wales.

Medical Sickness Annuity & Life Assurance Society

From Nov. 17, 1948, no war-risk exclusion will be placed on new life-assurance policies made by this society. The war-risk clause on existing policies became inoperative from that date.

International Congress of Ophthalmology

The King and Queen have given their patronage to the 16th International Congress of Ophthalmology, which will be held in London, under the presidency of Sir Stewart Duke-Elder, from July 17 to 21, 1950. Those who wish to take part in the main discussions or to read papers should write to Mr. Keith Lyle, International Congress of Ophthalmology, 45, Lincoln's Inn Fields, London, W.C.2.

The New Social Legislation and the Family

A conference will be held at the Conway Hall, Red Lion Square, London, W.C.1, on Jan. 20 and 21, to discuss the working of the many new social measures now on the statute-book and to study their impact upon family life. There will be sessions on Children at School, the Children Act, the Family, and Old People. Speakers will include Dr. Margery Warren and Dr. A. Talbot Rogers. Further information may be had from the Town and Country Planning Association, The Planning Centre, 28, King Street, Covent Garden, W.C.2, or from the British Social Hygiene Council, Tavistock House North, Tavistock Square, W.C.1.

Care of Old People

At a conference held in London by the National Old People's Welfare Committee last month the 700 delegates from local authorities and voluntary organisations unanimously approved a resolution urging H.M. Government to grant priority for new building schemes to be started for the provision of accommodation and amenities for the old people under section 21 of the National Assistance Act. In the discussions Dr. T. Ruddock-West stressed the importance of coördination of statutory and voluntary services in the various fields of work which he described, and Dr. Trevor Howell explained the success of geriatric treatment of the aged sick and the dangers of an acceptance of the approach of senility.

Commonwealth and Empire Health and Tuberculosis Conference

The National Association for the Prevention of Tuberculosis will hold the second of these conferences at the Central Hall, Westminster, from July 5 to 8. The provisional programme includes discussions on Tuberculosis as a World Problem; Trends in Modern Treatment, including streptomycin and P.A.S.; Regional County Schemes; Comprehensive Schemes in a British Colony; Tuberculosis among Students and Nurses; Policy of B.C.G. Administration; Psychological and Social Readaptation in Industry; and Protection from Bovine Tuberculosis. Further particulars may be had from the secretary-general, N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.

Royal Dental Hospital

The 32nd annual clinical At Home of the school was held on Nov. 27, when the hospital was open for inspection. Practical demonstrations and lectures on the operative, orthodontic, and other aspects of dental surgery were given in the morning, and in the afternoon clinical cases of interest were shown.

In the evening there was a large gathering of old and present students at the dinner at the Savoy Hotel. Mr. S. A. Riddett, who was in the chair, proposed the health of The Hospital and School. Mr. H. L. Hardwick, the new dean, in his reply, spoke of the loss that the hospital had sustained through the death of his predecessor, Mr. Harry Stobie. He went on to discuss the policy of the future, and the new association between the Royal Dental Hospital and St. George's. Lord Webb-Johnson, Dr. E .W. Fish, and Mr. P. G. Capon responded to the toast of The Guests proposed by Mr. B. W. Fickling. Though fog prevented some guests and old students from attending, weather conditions did not manage to damp the enjoyment of a pleasant evening.

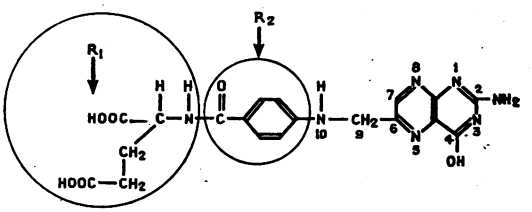
Florence Nightingale Hospital

This hospital for gentlewomen, which has now reopened, has occasional vacancies for acute cases. Fees are from 3 guineas for a cubicle and 6 to 8 guineas for a private room. The hospital has remained outside the National Health Service. Inquiries should be sent to the secretary at 19, Lisson Grove, London, N.W.1.

A memorial service for the late Dr. Louisa Hamilton will be held at St. Pancras Church this Saturday, at 11.30 A.M.

Mr. T. D. Haddow has been appointed an under-secretary in the Department of Health for Scotland. He was appointed to the department in 1935, and he was closely associated with the preparatory work for the National Health Service. He is at present visiting America under the auspices of the Commonwealth Fund, of New York, to study the administration of public health in that country.

CORRIGENDUM.—*Carcinogenic and Anticarcinogenic Substances:* In Professor Dodds's article of Nov. 27 the formula of folic acid (fig. 10) was given incorrectly. The formula is as follows:



Diary of the Week

DEC. 12 TO 18

Monday, 13th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. E. R. Boland: Silicosis.
ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. E. L. Patterson: Pelvic Floors and Walls.
5 P.M. Dr. J. Douglas Robertson: Disordered Metabolism in Thyrotoxicosis and Myxœdema.
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Dr. Paul Wood, Mr. A. Dickson Wright: Therapeutic Application of Anticoagulants.

Tuesday, 14th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Prof. D. M. Dunlop: Pharmacological Action of Anti-histamine Drugs.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Mr. S. Mottershead: Thoracic Operculum.
5 P.M. Dr. Robertson: Calcium Metabolism in Health and Disease.
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.
CHELSEA CLINICAL SOCIETY
7.30 P.M. (South Kensington Hotel, 47, Queen's Gate Terrace, S.W.7.) Mr. Sidney Gilliat: Films and their Influence.

Wednesday, 15th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. F. Avery Jones: Gastric and Duodenal Ulcer.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. C. McLaren West: Female Breast and its Development.
5 P.M. Dr. D. J. Bell: Carbohydrate Metabolism.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. C. W. McKenny: X-ray Technique.

Thursday, 16th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Professor Dunlop: Clinical Use of Anti-histamine Drugs.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. T. Nicol: Kidneys and Bladder.
5 P.M. Dr. Bell: Carbohydrate Metabolism.
INSTITUTE OF NEUROLOGY, Queen Square, W.C.1
5 P.M. Prof. M. Minkowski (Zürich): Cerebral Pathways of Vision.

Friday, 17th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Prof. L. J. Witts: Pathology of Pernicious Anæmia.
ROYAL COLLEGE OF SURGEONS
3.45 P.M. Mr. Clive Butler: Surgical Anatomy of the Rectum and Anal Canal.
5 P.M. Prof. A. C. Frazer: Fat Absorption and Metabolism.
MAIDA VALE HOSPITAL MEDICAL SCHOOL, W.9
5 P.M. Dr. E. A. Blake Pritchard: Case demonstration.
LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. Shirley Smith: Clinical and Cardiographic Methods in the Diagnosis of Coronary Syndromes.

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CONTENTS

METABOLISM IN EXPERIMENTAL DIABETES MELLITUS *

F. G. YOUNG
D.Sc., Ph.D. Lond.
PROFESSOR OF BIOCHEMISTRY IN THE UNIVERSITY OF LONDON, AT UNIVERSITY COLLEGE

UNDER the arresting title of Accident and Opportunism in Medical Research Sir Henry Dale delivered an address to the recent annual meeting of the British Medical Association in which he recalled, among other interesting examples of the importance of good fortune in research, the lucky accident which, in 1889, led von Mering and Minkowski to observe the existence of a condition resembling severe human diabetes mellitus in a dog from which the pancreas had been surgically removed. It was the intention of these investigators to examine the influence of pancreatectomy upon the absorption of fat from the gut, and the pronounced polyuria and glycosuria of the depancreatised animal was wholly unexpected.

Despite the many attempts which were subsequently made, in Minkowski's laboratory and elsewhere, to prepare from pancreatic tissue an extract whose administration would alleviate pancreatic diabetes, more than thirty years passed before the triumphant success of Banting and Best made insulin available to the world.

The term "epoch-making" is used and abused with equal facility these days; but never, in the whole history of medical art and science, could it be more appropriately applied than to the discovery of insulin by Banting and Best in 1921. There was nothing that could be described as accidental or opportunist in the methods by which was obtained the solution to a problem at which many experienced investigators had repeatedly failed. Even for those who did not know Banting himself it is not difficult to catch, from the published accounts, something of the tense determination and persevering optimism that was necessary to carry the two hardy investigators through the many difficulties of the hot Canadian summer of 1921. The experimental vindication of the views which Banting had developed on purely theoretical grounds provides the example *par excellence* of the wisdom of never scorning a frontal attack on a problem of apparent immense complexity.

DIABETES AS AN ENTITY

Although his true memorial lies in the benefits which he brought to his fellow men by his researches, it is not unfitting that Sir Frederick Banting should also be recalled each year in a discussion of research work in progress upon the subject of diabetes, since all such researches may be described, in a sense, as descendants of his own. The discovery of insulin provided a reasoned basis for the simplest view of the ætiology of diabetes mellitus (and we should always adopt the simplest view in the absence of concrete contrary evidence)—namely, that diabetes is caused by an absolute deficiency of insulin production in the body. When it was later found, as the result of the researches of Houssay and others, that a diabetic condition could be produced experimentally by means other than that of direct interference with the pancreas, and when, moreover, it was observed that experimental diabetes could be alleviated by means other than the administration of insulin, the problem assumed a greater degree of complexity. The possibility had to be envisaged that such complications might apply to clinical diabetes mellitus as well as to the experimental condition.

In a recent leading article in a medical journal occurs the statement: "There is no laboratory method of inducing diabetes . . . which is *exactly* comparable to the clinical condition. At best we can get only crude approximations." The writer presumably intends to compare with the clinical condition not the "laboratory method of inducing diabetes" but the laboratory-induced condition. We may therefore paraphrase his statement as follows: "there is no experimentally induced diabetes which is exactly comparable with the clinical condition. We can get only crude approximations." Does there exist, in fact, a single clinical entity called diabetes mellitus? Or are there numerous clinical conditions characterised by hyperglycæmia, glycosuria, &c., which are lumped together under the term diabetes mellitus? I am not competent to answer these questions myself, but I find among my many clinical friends a strong inclination to the view that there is no single clinical entity. Likewise, although the experimental diabetic condition induced by surgical removal of the pancreas may be a reasonably constant entity among similar animals of comparable nutritional status from one species (although here the geneticists may have something to say), pancreatic diabetes varies greatly in intensity and symptoms from one species to another, and the substantial differences between, for example, depancreatised carnivores and herbivores were recognised by the earliest investigators in this field. We appear to be leaving further and further behind the world of forms inhabited by such ancient Greek philosophers as Plato and are approaching a nominalist attitude in which every patient and every experimental animal is regarded as a research problem to be studied *ab initio*. Although the increasing complexity of advancing knowledge makes the development of such an attitude inevitable we owe much to Banting and Best for being in no way deflected by such considerations; and we also should be grateful to the dog for exhibiting so constantly, after complete removal of the pancreas, a severe but not immediately fatal diabetic condition.

INDUCTION AND ALLEVIATION

Since the early days of insulin there have been developed important new methods both of inducing and of alleviating experimental diabetes. They include the following:

Experimental induction of diabetes	*Relevant experimental method of alleviation of an existing diabetes*
Complete pancreatectomy / Partial pancreatectomy (Minkowski)	Treatment with insulin (Banting and Best)
Administration of anterior pituitary extracts (H.M. Evans, Houssay, Young)	Hypophysectomy (Houssay)
Administration of certain adrenal cortical steroids (Long, Ingle)	Induction of adrenal insufficiency (Long)
Administration of alloxan (Shaw Dunn)	
Administration of glucose (Dohan and Lukens)	
Hypothalamic lesions (?) (Ranson)	

In addition it has been shown that hypophysectomy—and to a somewhat less extent adrenal insufficiency—greatly exaggerate the sensitivity of many animal species to the hypoglycæmic action of administered insulin, while conversely the administration of suitable anterior-pituitary extracts or of certain adrenal steroids can greatly diminish sensitivity to the hypoglycæmic action of insulin without necessarily raising the blood-sugar level of the insulin-insensitive animal.

It should be emphasised that the diabetogenic action of anterior-pituitary extracts has been observed in relatively few species of animal. The intact adult dog and cat (but not the puppy—Young 1941, 1944a—or the kitten—Young, unpublished) both respond well; the ferret and the rabbit do respond but less consistently;

* The second Banting memorial lecture of the Diabetic Association, delivered in the Clinical Research Laboratories, University of Edinburgh, on Sept. 24, 1948.

while most other species of animal which have been tested without preliminary surgical interference with the pancreas respond infrequently or not at all. The intact rat is almost completely refractory to the diabetogenic action of our anterior-pituitary extracts (which are highly effective in the adult dog or cat), and in our department Dr. Gwen Toby and Mr. E. Reid have found that in some instances the partially depancreatised rat and the alloxan-diabetic rat, which are already excreting sugar, fail to exhibit even an acerbation of the diabetic condition when given large doses of our diabetogenic anterior-pituitary extracts. In the few unpublished cases investigated, human diabetic patients have also failed to exhibit an obvious response to similar diabetogenic extracts. Such results differ from those with adrenocorticotropic pituitary extracts in other laboratories, and such a difference supports the view that the diabetogenic action of our pituitary extracts is not necessarily mediated by the adrenal glands. In any case the dangers of arguing from one species to another, or even from one strain to another of the same species, are certainly not to be neglected.

Even within a given species of animal substantial variations may be encountered which are hard to account for, and we have met such an instance recently, in the behaviour of certain cats with metahypophyseal diabetes, which puzzles us greatly.

METAHYPOPHYSEAL DIABETES IN THE INTACT CAT

As was shown over ten years ago, a short period of the daily injection of a diabetogenic anterior-pituitary extract may induce the intact adult dog to become persistently diabetic (Young 1937), the islets of Langerhans exhibiting changes ranging from relatively mild degranulation to complete hyalinisation of the β cells (Richardson and Young 1938, Richardson 1940). Such a diabetic condition, persisting after the cessation of pituitary treatment (metahypophyseal diabetes), differs substantially from the condition found during the period of pituitary injections (which we may designate *idiohypophyseal* diabetes). For instance, substantial diminution in sensitivity to the hypoglycæmic action of insulin, a positive nitrogen balance, and an increase in body-weight may all be observed during the period of idiohypophyseal diabetes (Young 1945) but are not characteristic of the metahypophyseal condition (Marks and Young 1939, Young 1946). Indeed the simplest explanation of the existence of metahypophyseal diabetes is to attribute it to insulin deficiency resulting from the destruction of the insulin-secreting cells of the pancreatic islets; but, as I shall mention later, there are interesting differences between this condition and that resulting from pancreatectomy.

In the United States Dohan and Lukens (1939), having independently confirmed that metahypophyseal diabetes can be induced in the intact dog, extended their investigations to the partially depancreatised cat. Although these workers, unlike ourselves, were unable consistently to induce idiohypophyseal diabetes in the *intact* cat, they were successful with the cat from which had been surgically removed, at a preliminary operation, somewhat less pancreatic tissue than would have been required to induce glycosuria in the absence of further treatment. In such partially depancreatised cats it was relatively easy, by treatment with pituitary extract, to induce a diabetic condition which persisted after the treatment stopped. Such a persistently diabetic condition was associated with lesions of the pancreatic islets, which, however, differed from those observed in the dog with metahypophyseal diabetes in that the cat exhibited mainly hydropic vacuolation of the islet cells (cf. Lukens and Dohan 1942), in contrast to the total destruction often found in the dog. Working with partially depancreatised cats thus rendered persistently diabetic by pituitary treatment, Dohan and Lukens found that often animals which otherwise would have been expected to remain diabetic indefinitely became apparently cured of the condition if the blood-sugar was kept at a normal or subnormal level for more than a few days. Such diverse blood-sugar lowering procedures as reduction of the diet, treatment with insulin (Lukens and Dohan 1942), or the administration of phlorrhizin (Lukens et al. 1943) were all effective. In animals thus cured of an otherwise persisting diabetes the islet lesions were also healed and a good correlation was established between the cure of the diabetic condition and the restoration of the islet tissue (cf. Lukens and Dohan 1942).

Our diabetogenic anterior-pituitary extracts are so effective in the normal unoperated cat as to make it possible to employ the intact cat as a test animal for diabetogenic activity. In fact, before we were aware of the potency of our extracts in this respect, we killed a number of cats in diabetic coma by pituitary treatment. For the purpose of testing, and roughly assaying, the diabetogenic activity of our anterior-pituitary extracts we naturally try to avoid excessive treatment and aim to induce a condition which disappears within a few days of the cessation of pituitary injections; but, over a period of some years, we have unintentionally produced a diabetic condition which has persisted after the cessation of pituitary treatment (metahypophyseal diabetes) in eight of our intact cats. We observed these cats after cessation of treatment for a period averaging 12 weeks, during which they excreted, on an unlimited diet of meat, 7–10 g. of glucose per day per kg. body-weight, the corrected D/N ration being of the order of 3/1—i.e., the animals were excreting over 80% of the available carbohydrate. Some of these animals showed intermittent ketonuria.

Two of these cats (nos. 83 and 95) were killed at a time when the diabetic condition had persisted for 14 weeks after the cessation of pituitary treatment. Histological examination of the endocrine tissues of these (and other) cats was undertaken by Mr. K. C. Richardson, of the department of anatomy, University College, London, and the detailed results of his investigation will be published elsewhere (Richardson 1949). Mr. Richardson reported that the β cells of the islets of Langerhans of the pancreas of cats 83 and 95 were uniformly hydropic throughout, although the α cells appeared to be normal. Another cat (97) was treated with insulin after the metahypophyseal diabetes had persisted for 11 weeks, and was observed under insulin for 4 weeks before it was killed. This animal proved to require rather more insulin than was expected from day to day in order to control significantly the glycosuria (8–10 units protamine zinc insulin per day = about 3 units P.Z.I. per day per kg. body-weight). Mr. Richardson's report on the pancreas of this animal was that "nearly all the pancreatic islets had uniformly hydropic β cells but a few islets near the main duct had some intact β cells. Throughout this pancreas there were at least 12 microscopic foci of proliferation of duct epithelium leading to the formation of (presumably) new acini and new islet tissue, the latter also showing hydropic degeneration."

After the metahypophyseal diabetes had lasted for 9 weeks from the last injection of pituitary extract cat 98 was also treated with insulin. The insulin requirement was found to fall rapidly after 2 weeks of therapy; it became sugar-free at the end of 3 weeks and remained so despite the cessation of insulin administration. When it had been sugar-free for 9 days in the absence of insulin treatment it was killed, the terminal blood-sugar level (fasting overnight) being 71 mg. per 100 ml. According to Mr. Richardson, "the β cells of all the pancreatic islets of cat 98 were uniformly hydropic,

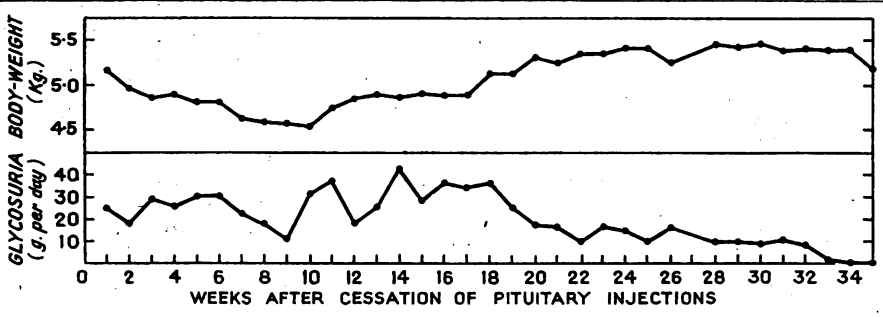

Fig. 1—Glycosuria and body-weight in cat 106 after cessation of pituitary injections. Final blood-sugar was 96 mg. per 100 ml.

the duct epithelium again showing foci of proliferative change."

In view of these results it was decided to keep cat 106 without insulin treatment for as long as it would last. After about 17 weeks of persistent and substantial glycosuria (circa 6–9 g. per day per kg.) subsequent to the cessation of pituitary treatment, the sugar excretion began slowly to fall, while the body-weight, which had initially declined, began to rise again (fig. 1). After 33 weeks of metahypophyseal diabetes the urine became sugar-free, and 11 days after the last appearance of sugar in the urine the animal was killed. Mr. Richardson reported that the islets exhibited uniform β cell hydropic degeneration, and after the most exhaustive study of the pancreas he was unable to find evidence for the existence of any β cell which had not undergone extreme hydropic degeneration. In these animals, therefore, unlike the pituitary-treated partially depancreatised cats of Dohan and Lukens, there appeared to be no correlation between the disappearance of the diabetic condition and the healing of the islet lesions.

Recently Dohan and Lukens (1948) have published an account of experiments in which a hyperglycæmia and glycosuria persisted after the cessation of a period of repeated intraperitoneal administration of glucose into one normal cat and two cats from which half the pancreas had been surgically removed at a preliminary operation. The glucose was given intraperitoneally in 20% solution, usually thrice daily, and the total daily dose varied from 10 to 90 g. The normal cat was killed 22 days after the cessation of glucose injections, by which time it "was obviously weak and depressed and showed clinical evidence of acidosis"; the islets of Langerhans showed severe hydropic degeneration. One of the two cats from which half the pancreas had first been removed died on the 9th day after the cessation of glucose treatment, and again hydropic lesions of the islets of Langerhans were found. The other surgically operated cat (G43) exhibited severe glycosuria for 7 weeks after the termination of glucose injections but during the period 7–12 weeks the glycosuria diminished and then disappeared. After 2 weeks' freedom from glycosuria the animal was killed and found to show abnormalities in the pancreatic islets. "These were diminished in number and the majority were very small with only a few hydropic β cells remaining" (Dohan and Lukens 1948).

In two of our cats with the pancreas intact, and in one of those of Dohan and Lukens with half of its pancreas removed, an induced diabetic condition has disappeared, after persistence for many weeks, in the presence of gross abnormalities of the β cells of the pancreatic islets. Mr. Richardson fixed the whole pancreas of our cat 106 (fig. 1) in over fifty blocks and examined many sections from each block without finding a single islet β cell that had failed to undergo gross hydropic degeneration. It seems very unlikely indeed that these grossly degenerate cells were capable of secreting much insulin. The disappearance of the diabetic condition is therefore hard to explain. Dohan and Lukens (1948) likewise comment that in their operated glucose-treated cat (G43) "the terminal disappearance of glycosuria is unexplained."

POSSIBLE EXPLANATIONS

We may consider the possible explanations of our results that might reasonably be entertained:

1. The degenerate pancreatic islet β cells were indeed secreting sufficient insulin for the needs of the animal.

2. Cells other than those of the pancreatic islets were providing sufficient insulin.

3. Hypoactivity of the anterior lobe of the pituitary gland accounted for the condition.

4. There had developed a depression in the rate of secretion of those adrenal cortical steroids which influence carbohydrate metabolism.

5. The enzyme systems concerned in the metabolism of carbohydrate had become adapted to conditions in which little or no insulin was available and were functioning adequately despite this lack.

For the third and fourth possibilites Mr. Richardson has found no histological evidence in any of our animals. The first possibility is difficult to preclude, but on a histological basis is perhaps unlikely.

The second possibility is an interesting one. The significance of the proliferative changes observed in the duct and acinar tissues of these animals is discussed elsewhere by Mr. Richardson (1949). It is clearly not possible to rule out with certainty that unrecognised embryo-like insulin-secreting cells were active in the pancreases of these animals. The existence of aberrant islet tissue in other organs is unlikely but also cannot safely be eliminated at this stage.

What has already been suggested with respect to the thyroid hormone (Young 1944b) may well be true for other endocrine secretions—namely, that the elaboration of the hormone is not entirely confined to one gland or to one recognisable type of cell but may be a widespread property of the tissues of the body—a property which, however, has been highly developed in the cells of one particular organ. There is nothing so chemically peculiar about the insulin molecule as to preclude the possibility that it is a product, in small amounts, of many different types of cell.

With regard to the fifth possibility envisaged above, I myself consider that the enzyme system is so much more fundamental than the hormonal mechanism, despite the fact that in some instances the latter may control the degree of activity of the enzyme system, that to me sometimes too much attention appears to be paid to the hormonal mechanism, at the expense of the enzyme system. At present there is no evidence to support a supposition such as no. 5 above, but it should certainly not be neglected.

The cat provides puzzling exceptions to the general relationship, established in the dog, between the severity of the condition of metahypophyseal diabetes and the extent of the islet damage. Such experience is not yet paralleled by clinical observations, where it is more common to find little or no evidence of islet lesions in cases of frank diabetes. It will be of great interest to know whether the human being is more dog-like or cat-like in this respect.

Species variations in physiological effects of hormones, variations in responsiveness to hormones with age

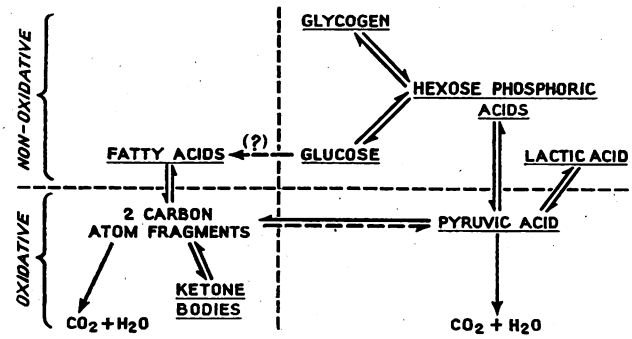

Fig. 2—Utilisation of glucose in the animal body.

within a given species (Young 1941, 1944a), and the important exceptions to the otherwise well-established correlationship between the persistence of diabetes and islet damage—all these phenomena lead the biochemist in particular to look for effects not on the animal as a whole (for these appear too often to be confusing), nor even on the organ as such (since here again species variations are sometimes met), but on the essential catalytic elements common to all living cells—the enzymes. Before, however, we consider the mechanism of action of insulin and of the pituitary diabetogenic factor in terms of their influence on enzyme systems I will say a few words about the state of our knowledge of the nature of these two substances, vast with respect to insulin, scanty with regard to the pituitary factor.

CHEMISTRY OF INSULIN

Probably more is known about the chemistry of insulin than about any other single protein, and the surprising fact has emerged that there is little very peculiar about it from the chemical point of view.

Evidence has accumulated during the past few years that many commercially available preparations of insulin contain a small proportion of an impurity which, in facilitating the conversion of glycogen to glucose in the liver may, in some degree, act antagonistically to insulin itself (cf. de Duve 1945, Sutherland and Cori 1947, Sutherland and de Duve 1948). Since, however, insulin is standardised on the rabbit or on the mouse with respect to its hypoglycæmic activity, the biological effectiveness of the different preparations should be constant, even though varying proportions of the impurity are present, unless the mouse and the rabbit differ substantially in the magnitude of their relative responses to insulin and to the glycogenolytic factor—a contingency which we may regard as unlikely in the absence of relevant evidence. The impurity has chemical properties very similar to those of insulin itself but is more chemically stable and so can survive treatments —e.g., with alkali—which destroy insulin.

At present it is not clear whether or not this substance is of physiological significance. If it is it may well be responsible for the significantly greater insulin requirement of the dog with metahypophyseal (Marks and Young 1939, Young 1946) or alloxan (Thorogood and Zimmerman 1945) diabetes as compared with the depancreatised dog. It might also account in some part for the other differences observed between depancreatised dogs and those exhibiting islet deficiency induced by treatment with pituitary extract or with alloxan. There is some evidence, which is not yet conclusive however, that the substance is produced by the α cells of the pancreatic islets; and if this is correct the chemical relations between insulin and its contaminant will be of interest to review in association with the morphological relation between the α and the β cells.

NATURE OF THE ANTERIOR-PITUITARY DIABETOGENIC SUBSTANCE

The fractionation of the anterior-pituitary diabetogenic factor has been pursued in our laboratory for some time past (Young 1939, Reid and Young 1948, Cotes et al. 1948) and the fact that all such fractions combine growth-promoting activity with diabetogenic activity emphasises once more the possible physiological significance of the identity of these two factors.

MECHANISM OF ACTION OF INSULIN

As we have seen above, the species variations encountered when the intact animal, or even the isolated organ, is examined leads one to look beyond the tissue to the enzyme system responsible for its metabolic activity. Fig. 2 outlines what we know about the metabolic fate of glucose in the animal body. Evidence is accumulating that the storage of glucose in the form of fatty acids is much more quantitatively important than its storage as glycogen (cf. Stetten 1946), but unfortunately we still know little about the mechanism of conversion of glucose to fatty acids in the body. It is quite probable that this process takes place mainly, if not entirely, via hexose phosphoric acids and pyruvic acid, but

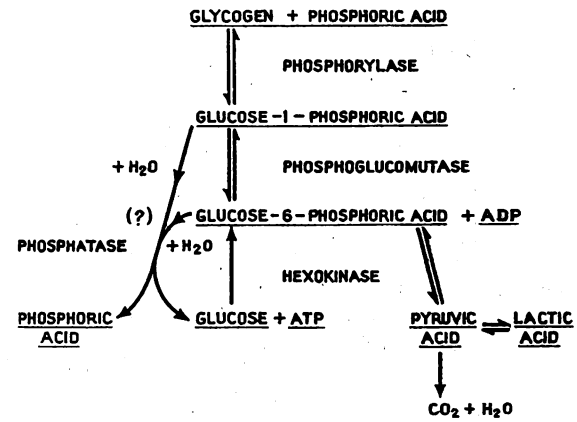

Fig. 3—Enzyme systems concerned in the formation of glycogen from glucose.

definite evidence on this point is lacking. Fig. 3 indicates the enzyme systems involved in the direct equilibrium between glucose and glycogen in the body. There is also good evidence that the conversion of glucose to glycogen also takes place by less direct pathways, involving fission of the glucose molecules into smaller fragments, part of which are later incorporated in the glycogen molecule.

When one considers that the structure of glycogen can be built up, on paper at least, by removal of the elements of water from suitable positions in a series of glucose molecules (fig. 4, equation 1) one may wonder why the direct biological conversion of glucose to glycogen appears to be a much more complicated process, and involves, as indicated in fig. 3, the intermediate formation of phosphoric acid derivatives of glucose. Although it is always unwise to attempt to answer the question "why" in relation to happenings in biology, it may be pointed out that any process in the body which involves the elimination of the elements of water is necessarily impeded by the fact that a cell is a dilute aqueous solution or suspension of the reactants; the high concentration of water in the system naturally assists a contrary reaction, that is, the addition of water to the products of the reaction. On the other hand the synthesis of glycogen from glucose-1-phosphoric acid, which involves the splitting out of the elements of phosphoric acid (equation 2), is subject to little impedance of this kind. Nevertheless, the direct synthesis of glucose-1-phosphoric acid from glucose and phosphoric acid does involve the elimination of a molecule of water (equation 3), and, moreover, under the conditions likely to obtain in biological systems the equilibrium position of this system (equation 3) involves such

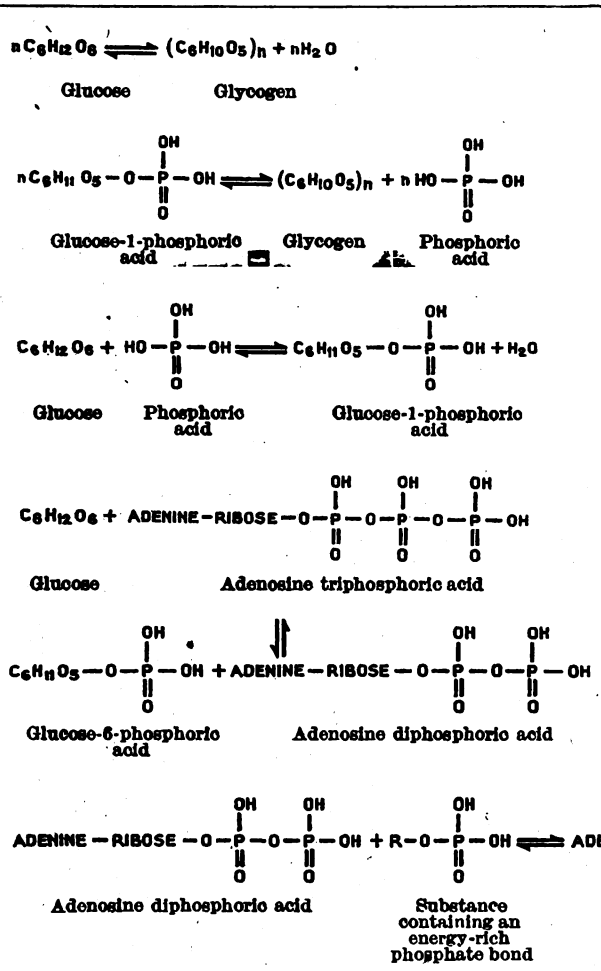

Fig. 4—Biological synthesis of glycogen.

a small mass of glucose-1-phosphoric acid as to render the reaction of little value in the biological synthesis of this derivative of glucose.

According to present views the phosphorylation of glucose in the animal body is largely, if not entirely, carried out by the passing over to it of a phosphoric acid grouping (radical ?

e.g., $-P(=O)(OH)OH$) from the important substance adenosine triphosphoric acid (A.T.P.) with the formation of glucose-6-phosphoric acid (equation 4). The glucose-6-phosphoric acid can then be converted into glucose-1-phosphoric acid under the influence of the enzyme phosphoglucomutase (cf. fig. 3). The formation of glucose-6-phosphoric acid by the interaction of glucose and A.T.P., a reaction catalysed by the important enzyme hexokinase, does not involve the elimination of a molecule of water between the glucose and the phosphoric acid residue emanating from the A.T.P. (cf. fig. 4). Furthermore, the reconstitution of the A.T.P. does not immediately depend upon a reaction in which the removal of the elements of water from the reactants occurs, since A.T.P. is replenished from adenosine diphosphoric acid (A.D.P.) at the expense of the so-called energy-rich phosphate bonds formed in metabolism; the replenishment involves the transfer of a phosphoric acid grouping rather than that of a molecule or ion of the acid (cf. equation 5).

If phosphoric acid groupings or radicals are to be available for the phosphorylation of — OH groups in the body it is clear that the removal of the elements of water from phosphoric acid or from its derivatives must occur at some stage of metabolism. For an example of this we may refer to the enzymic elimination of the elements of water from glyceric acid-2-phosphoric acid (containing a phosphoric acid grouping attached by a bond which is not energy-rich) to yield *enol* pyruvic acid-2-phosphoric acid (equation 6), a substance which possesses a high-energy phosphate bond and which can therefore transfer a phosphoric acid grouping to A.D.P. with the re-formation of A.T.P. The formation of *enol* pyruvic acid-2-phosphoric acid occurs intermediarily in the formation of pyruvic acid (and so of lactic acid) from glucose or glycogen and is therefore a reaction of some importance in carbohydrate economy. A perhaps even more important method whereby a phosphoric acid grouping may be made available from a molecule of phosphoric acid is the effective suppression of the elements of water under the guise of an oxidative reaction involving the retention of an oxygen atom accompanied by the elimination of two hydrogen atoms. For an example we may again turn to a reaction intermediate in the formation of pyruvic acid from glucose. Glyceric aldehyde-3-phosphoric acid may spontaneously add on a molecule of phosphoric acid with the formation of glyceric aldehyde-1 : 3-diphosphoric acid (equation 7a), a substance in which neither of the two phosphoric acid groupings is bound by an energy rich bond. Nevertheless, oxidative removal of two hydrogen atoms from the first carbon atom, produces glyceric acid-1 : 3-diphosphoric acid, the phosphate grouping attached to the first carbon atom becoming energy-rich and thus endowed to contribute to the resynthesis of A.T.P. from A.D.P. in a reaction of the type depicted in equation 5.

The over-all result of these reactions is that the elements of water have been removed between a molecule each of phosphoric acid and of A.D.P., the hydrogen being eliminated by oxidative removal while the oxygen atom, also involved in the oxidative conversion of the glyceric aldehyde derivative to the derivative of glyceric acid, becomes incorporated in the — COOH group of the latter, whence it will later emerge in a molecule of CO_2.

Whatever may be the reasons for the complexity of the reactions involved it is clear that the conversion of glucose to glucose-6-phosphoric acid, under the influence of the enzyme hexokinase and at the expense of adenosine triphosphoric acid (A.T.P.), is an indispensable preliminary

step in the utilisation of glucose for many metabolic purposes. Such a process of phosphorylation may be an essential step in the passage of glucose through many cell membranes, across which this sugar cannot freely diffuse in a physicochemical sense, and may thus mediate the utilisation of glucose within the cell for any metabolic purpose. Since the free energy available from glucose-6-phosphoric acid is much greater than that obtainable from glucose itself, it is clear that glucose will not be converted to glucose-6-phosphoric acid to any signfiicant extent unless a suitable source of free energy is available. Such a source is provided by the fission of A.T.P. to yield A.D.P. plus a high-energy phosphate grouping (radical ?). The formation of glucose-6-phosphoric acid may therefore be regarded as an energy barrier which must be surmounted, at the expense of A.T.P., before glucose can begin to release the free energy locked in itself.

The possible importance of the enzyme hexokinase in carbohydrate metabolism is therefore clear and the significance of the observations of Dr. and Mrs. C. F. Cori and their collaborators on the in-vitro influence of hormones on this enzyme system becomes apparent (see Cori 1945, Colowick et al. 1947).

Cori et al. have shown that certain freshly prepared anterior-pituitary extracts can depress the activity of hexokinase in vitro, this depression being reinforced by the addition of certain extracts of the adrenal cortex to the system. This depressive action of anterior-pituitary extract on hexokinase activity can be prevented by the in-vitro addition of insulin to the system. Thus, for the first time, a direct antagonism has been demonstrated on an enzyme system in vitro between insulin and anterior-pituitary extract. At University College the essential observations of Cori et al. in this respect have been confirmed (Reid et al. 1948), but we have found that many pituitary extracts which are highly diabetogenic in the intact adult cat are without insulin-reversible hexokinase-inhibitory action in vitro. The pituitary hexokinase-inhibitor is extremely labile and disappears within a few hours of its preparation even if the extract is stored at low temperature, but the pituitary diabetogenic substance is much more robust. Hexokinase-inhibiting pituitary extracts are diabetogenic under the condition of our test (Reid and Young 1948), though the converse situation is not necessarily true. Reid et al. (1948) have put forward the view that the pituitary hexokinase-inhibitor and the diabetogenic substances are indeed substantially the same but that when pituitary extracts are stored for a few hours the responsible substance undergoes a change which deprives it of its hexokinase-inhibiting activity in vitro, such a change being reversible in vivo. Although it has not yet been possible in our laboratory to reverse, in vitro, the supposed change in stored diabetogenic pituitary extract and thus to restore the ability to inhibit reversibly hexokinase activity in vitro, nevertheless, Mr. J. H. Ottaway and Mr. R. H. Smith have recently made an interesting observation which may well be relevant to this problem. These investigators have used the isolated rat diaphragm, an isolated muscle preparation on which insulin acts in vitro to bring about an enhanced uptake of glucose from the suspending medium (Gemmill and Hamman 1941). Ottaway and Smith (1948) have found that preliminary in-vitro treatment of the isolated diaphragm with diabetogenic anterior-pituitary extract abolishes the expected rise in glucose uptake when the diaphragm is subsequently incubated with fresh medium containing insulin. Adequate control experiments demonstrate that the effect is not associated with non-specific proteins.

It is tempting to assume that in this isolated muscle preparation insulin and the pituitary extract are both influencing hexokinase activity, although there is no direct evidence for such an assumption. If, nevertheless, this view is correct it may well be that, since an inhibitory effect is exerted by stored diabetogenic pituitary extract which has no insulin-reversible inhibitory action on cell-free hexokinase preparations in vitro, the intact cells of the muscle tissue are bringing about a reversal of that supposed change in stored diabetogenic pituitary extract which was referred to above. Direct proof of this is lacking, however, at the present time.

With the kind coöperation of Prof. H. P. Himsworth and Dr. M. E. Morgans of the medical unit, University College Hospital medical school, Mr. Smith has been able to test, for insulin reversible-hexokinase-inhibiting activity in vitro, samples of blood plasma from different types of clinical diabetes mellitus, but with completely negative results (Smith 1948).

If the pituitary diabetogenic factor inhibits hexokinase activity it inhibits a reaction which may be an obligatory step in the utilisation of glucose for many metabolic purposes. Such an activity could play an important part in the diabetogenic effect of our anterior-pituitary extract, although an alteration in the rate of insulin production in the pancreas may also be concerned. It is not so certain, however, that the main action of insulin in the body is the release of hexokinase from pituitary inhibition. Since the experiments of Houssay and Magenta (1924) it has been known that insulin exerts a greatly exaggerated hypoglycæmic action in hypophysectomised animals, and unless we assume that the hypophysectomised animal has some pituitary-like hexokinase-inhibitor available we must assume that insulin is here exerting some other action. Nevertheless, in view of the possibility discussed above that hormones are not necessarily and entirely specific for the endocrine glands that are their prime secretors, even in the hypophysectomised animal hexokinase activity may be under the antagonistic and balanced control of small amounts of (non-hypophyseal) pituitary factor and insulin. A small dose of exogenous insulin might then exert a greatly exaggerated effect. A similar argument could be applied to the metabolism of the hypophysectomised depancreatised animal.

Sutherland and Cori (1947) have recently stated in a short note that insulin promotes the formation of glycogen from glucose-1-phosphate in liver slices in vitro under certain conditions. This claim is as yet unconfirmed; but if it is correct it does not appear, a priori, that any effect of insulin on hexokinase is primarily concerned.

It is generally conceded that administration of insulin raises the rate of combustion of glucose provided that the blood-sugar of the treated animal does not fall to hypoglycæmic levels. Although insulin may play no direct part in accelerating the oxidation of glucose the influence of this hormone on the hexokinase system, leading to an enhancement of the phosphorylation of glucose, might be expected secondarily to bring about a rise in the combustion of glucose, and indeed also to promote the conversion of glucose to fatty acids, &c.

FURTHER RESEARCH

We thus see that many of the protean activities of insulin may be brought under one roof by the study of the influence of hormones on enzyme systems in vitro. It is clear that much awaits to be learned from the further pursuit of such investigations but danger may lie in the over-emphasis of in-vitro reactions, since the importance of the economy of the animal body as a whole may be neglected. The biochemist is interested in taking a cell to pieces in order to examine its constitution, and particularly its enzyme constitution, but since it is the body as a whole in health and disease which is the ultimate object of his interests, it is important that the fitting of the pieces into the economy of the animal as a whole should not be neglected.

In paying tribute to the memory of Frederick Banting we have a clear example before us of the paramount importance of courage in attempting the nearly impossible with the intact animal only as a guide. If we remember that the significance of Banting's work has lost nothing of its immensity with the passage of nearly thirty years, we are less likely to neglect the sort of research he carried out, albeit we are so much less successful at it than he was.

SUMMARY

Earlier work on experimental diabetes is briefly reviewed, and more recent observations on the influence of the pituitary gland are discussed.

A distinction is drawn between idiohypophyseal diabetes (found experimentally during the period of pituitary injections) and metahypophyseal diabetes (persisting after the injections cease). Unlike idiohypophyseal diabetes, metahypophyseal diabetes in the adult dog and cat is a condition not characterised by gross insulin insensitivity.

In the dog metahypophyseal diabetes usually increases in severity with the passage of time, but in two intact cats the condition, initially severe, disappeared after many weeks. In these two animals the pancreatic islets showed extensive β cell hydropic degeneration after the diabetes ceased.

The importance of phosphorylation in the utilisation of glucose for metabolic purposes is discussed, particularly with regard to the formation of glycogen from glucose-1-phosphoric acid by the elimination of the elements of phosphoric acid, as opposed to the direct formation from glucose involving the elimination of the elements of water.

The observations of Cori et al. on the inhibition by anterior pituitary extract of hexokinase activity in vitro, with reversal of this inhibition by the addition of insulin also in vitro, have been confirmed. Though no simple identity can at present be established between the diabetogenic pituitary substance and the insulin-reversible hexokinase-inhibiting factor, the responsible substances appear to be closely related.

I wish to express my gratitude to the Medical Research Council for their generous support of the researches on experimental diabetes carried out by myself and my colleagues over a period of many years. I wish also to thank the Diabetic Association not only for inviting me to give this lecture but also for their assistance on many occasions dating from the inception of the association. In this connexion the advice and interest of Dr. R. D. Lawrence have been invaluable.

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EARLY AMBULATION IN OBSTETRIC AND GYNÆCOLOGICAL CASES

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THERE is considerable variation in what is meant by early ambulation. In the United States it means getting out of bed in the first twenty-four hours after operation or delivery. In some parts of Europe the patient walks back from the theatre or delivery room. To me early ambulation means out of bed on the third postnatal or postoperative day, though occasionally I have followed Leithauser's (1946) technique of making the patient stand by the bedside and cough three or four times within eight hours of operation, particularly where pulmonary complications may be expected.

The results of a year's trial of such early ambulation is here compared with those of a previous year in a survey of 2735 admissions, with 1878 deliveries, including a large proportion of abnormal work, as follows:

OBSTETRICAL CASES

	1947	*1945*
No. of beds	80–103	70–80
No. of admissions	2735	1719
No. of deliveries	1878	966
No. of early risers	1611	Nil
Types of Case—	***1947***	***1945***
Spontaneous vertex delivery	1486	643
Forceps (all types)	204	201
Breech delivery	105	52
Cæsarean section (all types)	76	50
Episiotomy	293	178
Resutured	29	17
Second-degree tears	90	?
Resutured	2	—
Manual removal of placenta	82	8
Abortion	315	275
Thrombophlebitis (14 cases rose early)	24	10
Early Risers in 1947—		***No. of cases***
Spontaneous vertex deliveries		1308
Forceps (all types)		162
Breech deliveries		91
Cæsarean section (all types)		50
Average Days in Hospital after Delivery—	***1947***	***1945***
Spontaneous vertex deliveries	9·5	11·3
Forceps (all types)	11·2	16·8
Breech deliveries	11·8	13·2
Cæsarean sections	15·4	23·8
Thrombophlebitis (14 cases)	13·4	27·4

Obstetric patients normally lie in bed without putting a foot to the floor for 7 days at least in maternity hospitals and 10–12 days in nursing-homes. Owing to the shortage of hospital beds it has been impossible in maternity hospitals to keep patients for 12 days, and at times of stress they have had to be sent home on their fifth and sixth days. I felt it would be fairer to patients who had to go home at this early stage if they could at least go to the lavatory and perform simple duties for their babies on their arrival home. It is a serious hardship on a woman who has spent 7, 8, or 9 days in bed and lost a considerable amount of muscle tone to have to perform arduous household duties immediately on discharge from hospital.

RÉGIME FOR MATERNITY CASES

It is essential to have one's régime as simple as possible; nothing puts a patient off more than complicated exercises. This is particularly so with British women, with their self-consciousness and fear of seeming ridiculous. Fitzgibbon (1946), who has always been a keen protagonist of early activity, is very strong on this. My patients are allowed to lie or sit as they desire. If the baby is born in the morning, in the afternoon the

mother sits on the edge of her bed and swings her legs; and if the baby arrives in the afternoon, the patient swings her legs next morning. The women are allowed to sit on the bedpan in bed or on a chair. A physiotherapist gives the patient simple abdominal breathing, foot circling, and knee exercises. All this takes place with the patient in bed. On the day after delivery, while dangling, they do more simple leg and foot exercises, and on the second day they are once more encouraged to sit in bed and swing their legs, and are given exercises for the contraction of the abdominal muscles; this never lasts for more than 10 min.

Either in the evening of the second or at the beginning of the third day after delivery they are encouraged to stand, walk round the foot of the bed, and sit in a chair; unless there is any contra-indication they are allowed to use the lavatory with the assistance of the nurses, who accompany them there and wait outside in case the patient may feel frightened or faint; so far this has not happened. After this the patients are allowed to move about at their own discretion in the wards and rooms, and go to the lavatory on their own. On the recommendation of a patient I had a simple broad platform with a railing and two steps made, so that patients could get accustomed to going up and down stairs, since many of them have to do so as soon as they get home.

This régime is applied to all normal vaginal deliveries with or without tears and episiotomies. In 1947 the proportion of episiotomies requiring resuture was 9·9%. In 1945, before early ambulation was introduced, the proportion was 9·6%, so early rising does not seem to have interfered with the rate of healing after episiotomy. Out of 90 second-degree tears in 1947 only 2 required resuture. Cæsarean sections and other abdominal operations are treated on the same régime. Baths are allowed after the fourth day.

Some patients are not permitted to rise early. These include cases of severe pre-eclamptic toxæmia where the blood-pressure has been over 160/100 mm. Hg; these patients are allowed to stay in bed until the blood-pressure shows signs of settling with their other symptoms. Simple cases of essential hypertension, however high the blood-pressure, will not benefit by 7 days in bed, so those are treated like normal deliveries. For example, a case of malignant hypertension with systolic blood-pressure of 280 mm. Hg had a hysterotomy done at the 26th week, her only therapeutic treatment being the extraction of a pint of blood, and she left the hospital after 12 days, on her feet and feeling very well. It is unlikely that anything will affect this woman's prognosis, and certainly not the lack of 10 days in bed. Eclamptic patients are treated with the usual amount of rest in bed whether they have had normal vaginal deliveries or not. If a patient's hæmoglobin is below 45%, she is not encouraged to walk until she has had a transfusion of packed cells and until her hæmoglobin has risen above 50%. Patients with heart trouble are kept at rest in bed as long as there are signs of decompensation.

RÉGIME FOR GYNÆCOLOGICAL CASES

The treatment of gynæcological cases by early post-operative rising has been popular in continental clinics for many years. In 1899 Ries cited a large series of surgical and gynæcological cases, and since then many doctors have used this method. Leithauser (1946) has summarised the procedure, but his cases were mainly general surgical ones.

My series is small; and, since this unit was only started in 1946, with 3–5 beds, comparison with the past is difficult.

GYNÆCOLOGICAL CASES

Beds available for first	3 months	..	3
,, ,, ,, second	3 ,,	..	9
,, ,, ,, last	6 ,,	..	14 (never completely filled)

Abdominal Operations—	
Total hysterectomy	27
Subtotal hysterectomy	7
Myomectomy	4
Gilliam suspension	7
Laparotomy	6
Oöphorectomy	10
Presacral neurectomy	4
Salpingectomy	2
Ectopic gestation	2
Total	69
Vaginal Operations—	
Vaginal hysterectomy	12
Fothergill-type repair	17
Aldridge sling	3
Other pelvic-floor and vaginal operations	28
Complete tears	3
Total	61
Miscellaneous non-operative	21
Dilatation and curettage	61
Total cases dealt with	212

Complications of Gynæcological Cases

Urinary

Two cases of cystitis: (1) after Fothergill-type repair (post-operative days 15); and (2) after vaginal hysterectomy (post-operative days 17). Both patients rose early.

Chest

Three cases: (1) bronchitis after repair of cystocele and pelvic floor (postoperative days 19); (2) small area of consolidation after repair of cystocele and pelvic floor (postoperative days 13); and (3) partial collapse of lung after abdominal operation (postoperative days 13). All these patients rose early.

Thrombophlebitis

Two cases: (1) after repair of cystocele and pelvic floor (post-operative days 12); and (2) after dilatation and curettage (post-operative days 11). Both patients were elderly women with varicose veins.

Wound Infection

Abdominal wound sepsis	7
Wound hæmatomata	2
Pelvic hæmatomata	3
Perineal wound sepsis	6
Total	18

Among early risers in this group were 5 women who had had abdominal operations (postoperative days 16, 14, 24, 18, 16) and 2 who had had vaginal operations (postoperative days 26, 18).

Average postoperative days in early rising cases of this group 18·8.

Among non-early risers there were 4 women who had had abdominal operations (postoperative days 24, 28, 19, 31) and 7 who had had vaginal operations (postoperative days 17, 27, 24, 12, 22, 33, 19).

Average postoperative days in non-early rising cases in this group 23·4.

Early ambulation was introduced because of lack of beds and nurses; but I would stress the point that it does not mean that the number of nursing staff in a ward is cut down. During the first three months of 1947 there were only 3 beds available. The number gradually grew until in the last six months of the year 14 beds were used. A long waiting-list made a quick turnover necessary. The procedure is almost the same as that followed in the maternity hospital for operation cases and need not be repeated here.

My operative technique is as simple as possible. Only double no. 0, double no. 1, and medium hard catgut is used with Mayo needles and a needle-holder, and for the skin continuous silk or clips. All suturing, whether in the abdomen or on the pelvic floor, is continuous. No interrupted sutures are used. Uterine pedicles &c. are ligated with double no. 1, and small skin vessels with no. 0. The patients are in hospital for two nights before operation, during which time they are examined and have simple preoperative treatment. They are all examined by the anæsthetist on the day before operation, and a general anæsthetic is always given. In the pelvic work no silkworm gut is used, the perineum being sutured with a continuous subcuticular catgut stitch.

Vaginal operations are followed by the same post-operative régime, the bowels being opened with mild purgatives and oil and soap-and-water enemas on the fourth day. The wounds are kept dry and are swabbed after the patient has used a bedpan. A male rubber catheter is put into the bladder and drained into a bottle for 3–5 days. If patients wish to sit up they are allowed

to; otherwise they find the most comfortable position in bed. When they get up, the catheter is clamped and fixed to the skin with sticking plaster. Sedatives are used as required, and most of these patients go home 10–12 days after operation.

If home conditions were satisfactory I have no doubt that these patients could go home within a week, but I would not go so far as some and send them home within 2–3 days of their operation. This would be a tremendous saving in bed days and in money, both from the hospital's and the patients' points of view, but with present housing conditions and servant problems most of the patients have insufficient help at home to warrant their early return. In hospital, after the first week, the time is spent in progressing further in their ambulation and becoming more able to look after themselves.

RESULTS

It is in cases of cæsarean section, myomectomy, and other operations that the psychological response to early rising is most pronounced, particularly in cases of repeat cæsarean section in women who previously had been 14 days in bed. The patients appear to be impressed by their rapid return to normality, even when allowance is made for the loyalty that patients have for those that treat them (*Lancet*, 1947). I am convinced that they are better in every way than those kept in bed for a fortnight. Early rising is particularly valuable after an abdominal operation because the loss of muscular tone is more rapid, and the interference with respiration more complete, than in any other type of case, and recumbency reduces the vital capacity (McMichael and McGibbon 1939).

Many articles have been written to show that long recumbency is especially dangerous in increasing the liability to pulmonary embolism, and Dock (1944) cited a large series of middle-aged and elderly women in whom, after days or weeks in bed, thrombosis in the dorsal part of the legs and feet was demonstrable in from a quarter to a half of the cases. Another type of case where there is a threat of embolus is myomectomy, and early rising routine has been successfully adopted in cæsarean myomectomy, and in myomectomy where the fœtus has not yet been viable. There has been no death from pulmonary embolism or respiratory complication in either the obstetric or the gynæcological unit in 1947, in spite of the fact that there were 24 cases of thrombophlebitis in the obstetric side and 2 in the gynæcological side. In the obstetric unit most of these cases were women with old varicose veins in the legs; and, though early ambulation does not prevent these patients getting thrombophlebitis, they give the surgeon less anxiety, and their convalescence is not delayed more than 3–4 days. When thrombophlebitis develops they are kept in bed, but the leg is not immobilised, and the condition quickly settles down; during the last six months of 1947 heparin was used in these cases.

Other concrete advantages of early rising are the reduction in the incidence and duration of respiratory complications; the very minor amount of discomfort experienced in passing urine after total hysterectomy; and, in operative obstetric deliveries, the reduced need of catheterisation for residual urine.

A fact noted among the gynæcological cases is the high incidence of wound infection. This has never been serious but has lengthened the patient's stay in hospital. That the incidence of these infections is not due to early rising is shown by the fact that of the 18 wound infections, 7 rose early and 11 were kept non-ambulatory. The number of wound infections in obstetric cases is not given, because these have mainly occurred after lower-segment operations done in the presence of potentially infected wounds; the number was very small, and all the patients recovered rapidly.

I suppose every surgeon embarking on early rising imagines the wound gaping open, the intestines falling out on the abdominal wall, or the viscera dropping through a gap in the perineum. So far the only case in which there has been a dehiscence of the abdominal wound was one of tuberculosis of the uterus, for which the patient had a total hysterectomy and stayed in bed for 3 weeks. After a secondary suture she made an excellent recovery. The causes of burst abdominal wounds are rapid autolysis of the catgut and distension. In 90% of cases of postoperative hernia in abdominal wound scars there is a history of peritonitis and tube drainage; in these cases in the past the patients have been confined to bed.

Newburger (1943) found in experiments on rats that the tensile strength of wound scars after the third day was the same in animals kept at rest as in those left free to move about. In surgery on animals there is no simple method for keeping them at rest, yet their wounds usually heal without trouble. Markowitz (1937), in animals, emphasises the importance of careful closure and uses a technique very similar to that which I have outlined.

VERDICTS OF OTHERS

A Patient's View.—Recently a girl was delivered here who had been trained as a nurse at St. Mary's and Queen Charlotte's Hospitals, London. Asked to describe her experiences with early rising, she said that at first there was a feeling of heaviness in the vulva, perineum, anal region, and the bottom of the back, and some stiffness of the thigh muscles. These feelings gradually wore off by the seventh day. She was most comfortable walking properly with a straight back, with abdomen and buttocks well in. Getting up helped her to forget the confinement and prevented her from brooding over whether she could bear to have another baby or not; it also made her feel that her figure was getting a chance of a speedier return to normal.

The Sister's View.—Sisters in charge of postnatal wards are enthusiastic about early ambulation. One of them says that early rising is appreciated by the patients; involution appears to be no different, though the lochia are more profuse perhaps on the eighth day. There is no appreciable difference in the amount of linen soiled or the amount of work for the nurses, but the ward is apt to be untidier because the patients move about.

General Practitioners' Opinion.—I sent a questionnaire to all general practitioners in Ayrshire, and of the 55% who answered, 69% were in favour of early ambulation, 11% had no opinion either way, and 20% were against it. In gynæcological cases most practitioners were wholeheartedly for early ambulation, emphasising its excellent emotional effect on the patients on their return home, and their more rapid return to normal. With regard to obstetric cases the practitioners were more cautious. In some districts the wise women condemn early ambulation out of hand, and they are still a power in the land. The idea that a woman who has a child is entitled to 14 days' prostration afterwards is still current from Victorian days, when the middle-class had servants and the working-class had a daughter who stayed at home. The woman who rises after 10–14 days in bed takes another 10 days to get on her feet. The object of early ambulation is to avoid this, and it does so. There is, however, one thing which has to be guarded against and is important from the practitioners' point of view. A woman who has risen early under hospital discipline cannot go straight home and carry out her full household and social duties as she did before she was pregnant. Some women do this and consequently get over-tired.

CONCLUSIONS

I am convinced that early ambulation does no immediate harm either to obstetric or to gynæcological

patients, and it certainly allows a much bigger turnover of patients in hospital. It is hard perhaps on the staff, and for really efficient working a full ward staff is necessary as well as a physiotherapist, who saves the nurses much work by encouraging patients in their exercises.

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SOME ASPECTS OF THE ACTION OF HISTAMINE ANTAGONISTS

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THE reaction to an intradermal injection of histamine is modified if the injection is repeated at an interval after the oral administration of an adequate dose of a histamine antagonist. (Warembourg et al. 1944, Friedlaender and Feinberg 1946, Halpern et al. 1946a and b, Leavitt and Code 1947.) We present here the results of some preliminary observations in which the modification of the intradermal histamine reaction has been used to study the variation in effective dosage, duration of action, and other properties of various anti-histamine agents: 2-dimethylaminoethyl benzhydryl ether hydrochloride, introduced by Loew et al. (1945) and marketed as 'Benadryl' (Parke Davis); N(2-dimethylaminoethyl) N(*p*-methoxybenzyl) 2-aminopyridine, introduced by Bovet and Walthert (1944) as '2786 R.P.,' known in France and the U.S.A. as 'Neoantergan,' and now obtainable in this country under the name of 'Anthisan' (May & Baker); and N(dimethylamino-2-propyl) phenothiazine, first described by Halpern et al. (1946a and b) and known as '3277 R.P.' Administration of equal quantities of the different drugs was precluded by the wide differences in the ratio between the therapeutic and the toxic doses; ordinary clinical doses were therefore used.

TABLE I—EFFECTS OF SINGLE DOSES OF BENADRYL 100 MG. BY MOUTH ON INTRADERMAL HISTAMINE REACTION

Subject	Average diameters before benadryl (cm.)		Average diameters after benadryl (cm.)					
			1 hour		3 hours		10 hours	
	Flares	Weals	Flares	Weals	Flares	Weals	Flares	Weals
A	3·1	1·25	2·1	1·1	2·4	1·05	2·7	1·15
B	2·6	1·15	2·4	1·2	2·1	1·1	2·4	1·15
C	3·1	1·3	2·0	1·2	2·1	1·1	2·4	1·15
D	3·7	1·3	3·9	1·25	4·3	1·3	4·6	1·3
E	3·6	1·2	3·6	1·25	3·1	1·2	3·6	1·2
F	3·6	1·4	3·6	1·25	4·1	1·25	4·6	1·25
G	4·1	1·3	3·1	1·1	3·6	1·2	4·6	1·25
H	3·6	1·2	3·8	1·25	4·0	1·25	4·7	1·25
I	4·3	1·25	4·6	1·3	4·1	1·2	3·9	1·3
J	4·0	1·2	4·1	1·1	3·8	1·1	4·1	1·1
K	3·6	1·2	3·8	1·15	3·4	1·2	3·8	1·25
Mean	3·57	1·25	3·36	1·19	3·36	1·18	3·76	1·21
$m_1 - m_2$	..	..	−0·21	−0·06	−0·21	−0·07	+0·19	−0·03
*E*m	0·147	0·024	0·259	0·027	0·250	0·024	0·268	0·024
*E*d	..	..	0·298	0·036	0·290	0·034	0·305	0·034
t	..	..	1·18	1·82	1·24	2·04	0·97	1·53

The histamine reactions were produced on the volar surface of the forearm by the intradermal injection of 0·05 ml. of a solution of histamine acid phosphate 0·01% *w/v* in saline solution. Each injection thus contained 5·0 μg. of the acid phosphate, equivalent to 1·81 μg. of histamine base.

Whereas the flare component of the histamine response is clearly an area, the weal is three-dimensional and would be properly measured as a volume; but it was not found feasible to do this, and so both flares and weals were treated as areas. These can be determined by inking the outlines of the reactions on the skin, transcribing them to thin tracing-paper, and computing directly. With the dose of histamine used, however, the reactions were such that the areas as directly determined were virtually identical with those calculated from the mean radius of each reaction, as obtained from the average of two diameters, measured at right angles, in each instance. The labour involved in measuring the diameters was much less than in computing areas directly; so all the measurements on patients were made in this way, the average diameters of the weal and of the flare being determined 5–10 min. after the injection of each dose of histamine. It is these measurements which are given in tables I–IV and figs. 4–9, but in figs. 1–3 the areas calculated from these diameters are used. All the injections and measurements on patients were carried out by the same observer (R. P. W.).

In eleven men intradermal histamine reactions were measured before, and at intervals after, a single dose of benadryl 100 mg. by mouth. After a week's rest the observations were repeated with anthisan 200 mg. and, after a further week, with 3277 R.P. 50 mg. Other observations were made on twenty patients with chronic urticaria in whom the effect of anthisan on the modification of the intradermal histamine reaction and of the urticaria was compared.

RESULTS

Modification of Normal Histamine Reaction by Single Doses of Histamine Antagonists

Tables I–III give the results of these observations, together with their means, the differences in the means ($m_1 - m_2$), and the standard errors of the means (*E*m) and of their differences (*E*d) calculated in the ordinary way. The paired t-test (Fisher 1944) has been applied to the estimate of t given in the lowest row of the tables. A diagrammatic representation of the mean results is given in fig. 1.

Judged from the mean maximal reduction of both weals and flares, the effects of anthisan 200 mg. and of 3277 R.P. 50 mg. were considerable and did not differ significantly, but the effects of benadryl 100 mg. were barely significant, and in the weal response alone, at three hours.

The differences in duration of action of each of the three drugs are also shown. Thus, though there was only a questionably significant reduction of the weal response 3 hours after administration of benadryl 100 mg., the effect of anthisan 200 mg. was still significant, both in weal and flare responses, at 27 hours, and of 3277 R.P. 50 mg. at 32 hours.

The frequency of our observations was not sufficient to enable us to get accurate information about any differences in the rate of establishment of the effect with each of the drugs, but it seems that anthisan and 3277 R.P. have some effect within an hour, and that the maximal effect is likely to be reached in 3–4 hours. The maximal effect persists longest with 3277 R.P.

TABLE II—EFFECTS OF SINGLE DOSES OF ANTHISAN 200 MG. BY MOUTH ON INTRADERMAL HISTAMINE REACTION

Subject	Average diameters before anthisan (cm.)		Average diameters after anthisan (cm.)							
			2 hours		4 hours		11 hours		27 hours	
	Flares	Weals	Flares	Weals	Flares	Weals	Flares	Weals	Flares	Weals
A	3·5	1·3	3·5	1·3	1·0	0·5	2·0	0·6	2·0	1·0
B	3·0	1·3	2·5	1·3	1·0	0·6	1·5	0·6	1·5	0·9
C	3·0	1·3	2·5	1·0	1·0	0·5	1·4	0·6	1·5	1·0
D	3·6	1·3	2·5	0·75	2·4	0·7	3·5	0·6	3·5	1·0
E	3·5	1·0	1·5	0·55	1·0	0·5	1·8	0·6	3·0	0·9
F	3·5	1·6	3·0	0·8	2·5	0·7	2·5	0·8	3·5	1·05
G	4·0	1·3	2·5	1·0	1·0	0·5	2·0	0·55	3·0	1·05
H	4·5	1·2	3·5	1·2	1·5	0·6	2·9	1·0	4·0	1·2
I	4·5	1·2	3·5	1·1	2·7	1·1	2·5	0·8	3·5	1·0
J	3·8	1·2	3·5	1·0	2·0	0·55	2·8	0·8	4·0	1·0
K	3·1	1·0	2·0	0·8	2·0	0·6	2·1	0·8	3·0	0·8
Mean	3·63	1·25	2·77	0·98	1·63	0·62	2·27	0·70	2·91	0·99
$m_1 - m_2$	..	..	−0·86	−0·27	−2·00	−0·63	−1·36	−0·55	−0·71	−0·26
Em	0·160	0·051	0·206	0·069	0·208	0·054	0·19	0·042	0·274	0·033
Ed	..	..	0·261	0·086	0·262	0·074	0·248	0·066	0·317	0·061
t	..	..	2·66	2·38	3·01	3·02	2·94	3·98	2·47	2·83

Variation in Response to Histamine Antagonists

The response of different people to the anti-histamine drugs varied in the degree of maximal reduction of the erythema and wealing. When the maximal response of a person was poor with one of the drugs it was usually poor with the others also. Of the eleven persons studied, the degree of response in five (A, B, C, E, and G) was good; in three (D, F, and I) poor; and in the remaining three (H, J, and K) intermediate. Examples of good and poor responses taken from tables I–III are shown in fig. 2.

This variation in response did not seem to depend on the extent of the initial reaction to intradermal histamine; nor was there any obvious correlation between the degree of specific response to the drugs, the toxic side-effects, and the weight or build of the person.

It would be expected, on general pharmacological grounds, that people who responded poorly to an ordinary dose of an anti-histamine drug would respond well if the dose were raised sufficiently. This was found to be so, and is demonstrated in fig. 3, where the effect of raising the dose in subjects D, I, and J is shown.

Apart from the differences already noted respecting the mean duration of action of each of the different anti-histamine drugs there is considerable variation from one person to another in this respect. But, as with the maximal effects, a person who showed a long duration of action with one of the agents showed, in most instances, a long duration of action with the other two. This is illustrated in subjects A, B, C, E, and G, all of whom showed a good maximal response (tables I–III), and it suggests a close correlation between these two aspects of the action.

Side-effects of Histamine Antagonists

In comparing the clinical value of anti-histamine drugs an important consideration is the ratio between the therapeutically effective dose and that which gives rise to side-effects. The assessment of the incidence and importance of the various side-effects is, however, complicated. The commonest symptoms are drowsiness and lassitude, and the reaction to these depends considerably on the sensitivity and type of the patient. Again, toxic symptoms are more common in ambulant persons than in those resting in bed. Thus seven ambulant medical workers on a single dose of anthisan 200 mg. all experienced mild symptoms, whereas of eleven men resting in bed on the same dose only one complained of a little drowsiness. When large clinical doses of the drugs were given, nearly all patients complained of some unpleasant side-effects. Such effects have occurred

TABLE III—EFFECTS OF SINGLE DOSES OF 3277 R.P. 50 MG. BY MOUTH ON INTRADERMAL HISTAMINE REACTION

Subject	Average diameter before 3277 R.P. (cm.)		Average diameter after 3277 R.P. (cm.)									
			1 hour		3½ hours		7½ hours		24 hours		32 hours	
	Flares	Weals	Flares	Weals	Flares	Weals	Flares	Weals	Flares	Weals	Flares	Weals
A	3·0	1·3	1·8	0·95	1·5	0·8	1·2	0·75	1·2	0·65	1·4	0·9
B	3·4	1·3	1·4	1·0	1·6	0·7	1·0	0·75	1·0	0·85	2·2	0·95
C	2·6	1·35	1·6	0·95	1·1	0·7	1·2	0·7	1·4	0·7	1·2	0·9
D	3·4	1·15	2·1	0·85	2·4	0·75	1·8	0·85	3·6	0·95	3·2	1·1
E	3·9	1·3	1·65	0·95	0·15	0·7	1·1	0·65	1·4	0·7	1·4	0·8
F	3·6	1·2	3·2	0·95	2·4	0·9	2·2	0·7	2·6	0·9	2·9	0·9
G	4·2	1·4	2·9	0·85	0·9	0·75	1·7	0·7	1·6	0·8	1·9	0·95
H	4·5	1·4	3·7	1·0	2·1	0·9	2·2	0·9	3·2	1·1	3·9	0·95
I	3·2	1·1	3·4	0·9	1·9	0·8	2·2	0·65	2·9	0·9	2·9	0·8
J	4·0	1·0	2·2	0·8	1·5	0·6	1·7	0·6	3·2	0·9	3·0	0·8
K	4·2	1·2	1·6	0·75	1·1	0·55	1·4	0·85	1·7	1·2	2·4	0·8
Mean	3·64	1·25	2·32	0·90	1·63	0·74	1·61	0·74	2·16	0·88	2·4	0·89
$m_1 - m_2$	..	..	−1·32	−0·35	−2·01	−0·51	−2·03	−0·51	−1·48	−0·37	−1·24	−0·36
Em	0·175	0·042	0·247	0·024	0·154	0·036	0·138	0·136	0·283	0·048	0·259	0·030
Ed	..	..	0·303	0·087	0·233	0·055	0·223	0·055	0·333	0·064	0·312	0·051
t	..	..	2·73	3·22	2·897	3·09	3·04	3·08	2·64	2·72	2·73	3·06

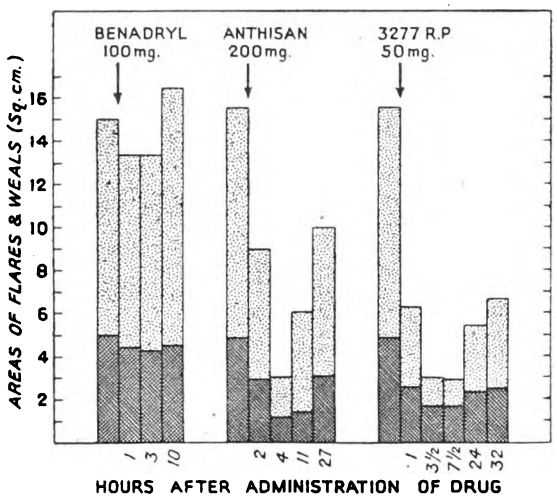

Fig. 1—Modification of intradermal histamine reaction by single doses of anti-histamine drugs (mean results from eleven people): stippled area 1½ times area of flares; hatched areas 4 times area of weals.

with low doses in a few people, and in some people have been pronounced before an effective anti-histamine dosage could be reached.

Of our eleven subjects benadryl 100 mg. caused drowsiness and lassitude in four, anthisan 200 mg. in one, and 3277 R.P. 50 mg. in five. The results in this small series are in accord with observations on other people, though experience with 3277 R.P. has been limited. Anthisan certainly has a considerably higher therapeutic ratio than has benadryl, but we have insufficient information to reach any definite conclusion about 3277 R.P. in this respect. Vallery-Radot et al. (1947), however, agree that side-effects are commonly experienced with 3277 R.P., but state that, when the therapy is continued for a few days, they tend to pass off.

Dryness of the mouth has been noted with benadryl and 3277 R.P. but was commoner with anthisan, developing in about 20% of patients on an average dose. It was noted about 2 hours after ingestion of the drug and lasted 1½–2 hours but did not cause serious discomfort or complaint. Average doses of anthisan in some patients caused mild colic, diarrhœa, nausea, and vomiting, which began about 1½ hours after ingestion and cleared after 1–1½ hours. Since the precaution of administering the drug in the middle of meals was introduced we have had very little trouble from these effects.

Light-headedness, aching limbs, and ataxia have been experienced with 3277 R.P.

Observations on Patients with Chronic Urticaria

Similar observations to the foregoing have been carried out on twenty patients with chronic urticaria, the intradermal histamine reactions being noted at various times before, during, and after treatment with anthisan.

The weals were suppressed or considerably modified in all patients. Variation from one person to another in the response to the anti-histamine drug was shown as in the foregoing observations, and in three patients who required large doses of anthisan the side-effects outweighed the value of continuing the suppressive therapy.

In all cases the dosage necessary to reduce adequately, or to suppress, the urticaria was that necessary to modify appreciably the intradermal histamine reaction.

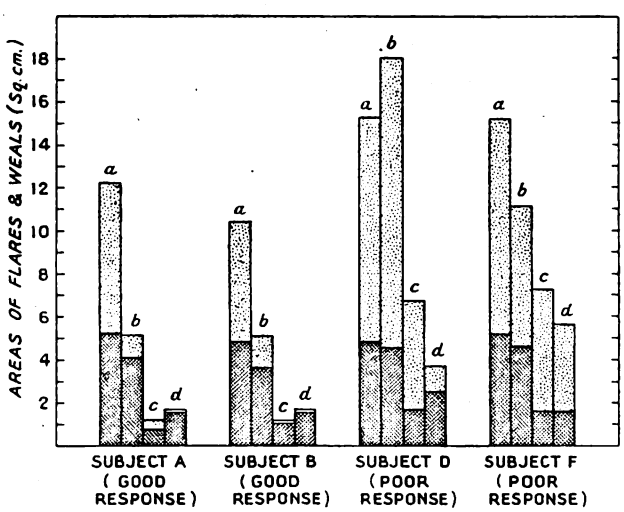

Fig. 2—Modification of intradermal histamine reaction by single doses of anti-histamine drugs in different people (A, B, D, and F): *a*, before administration of anti-histamine drug; *b*, after benadryl 100 mg.; *c*, after anthisan 200 mg.; *d*, after 3277 R.P. 50 mg.; stippled and hatched areas as in fig. 1.

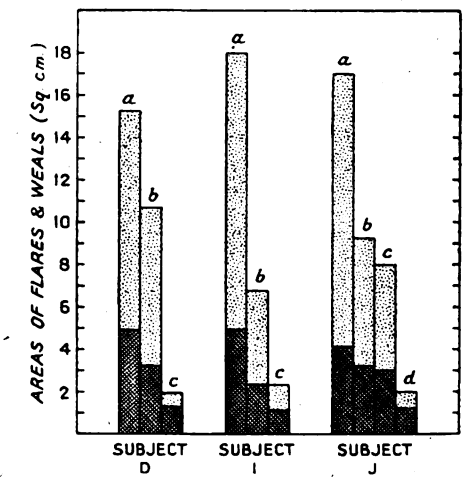

Fig. 3—Effect of increasing dose of anti-histamine drug in different people (D, I, and J) giving poor response to ordinary dose: *a*, before administration of anthisan; *b*, after anthisan 300 mg. daily for three days; *c*, after anthisan 600 mg. daily for three days; *d*, after anthisan 900 mg. daily for three days; stippled and hatched areas as in fig. 1.

Five of the patients had various degrees of factitious wealing. Measurements of the size of the weal and erythema provoked by different stimuli were made before, during, and after therapy. The stimuli used were weak and firm pressure with the stroke of a pin-point, and weak and firm pressure with the end of a cylindrical stick 2 mm. in diameter. The degree of reduction of weal and erythema by anthisan paralleled the reduction of the intradermal histamine reaction.

When the drug was stopped, urticaria recurred in most patients; two complained that it was more severe than before treatment, but in these, as in the others, the intradermal histamine reaction was about the same as before therapy. In the five patients who showed factitious wealing the measurements of the weal and erythema, when the drug was stopped, were about the same as they were before therapy.

The action of anthisan in these patients followed in all respects the course to be expected from the results of the observations recorded above. Various points are illustrated by examples from the case-records. Figs. 4–8 illustrate variation of the effective dose of anthisan from one person to another. The following are examples of variation of duration of action of anthisan from one person to another.

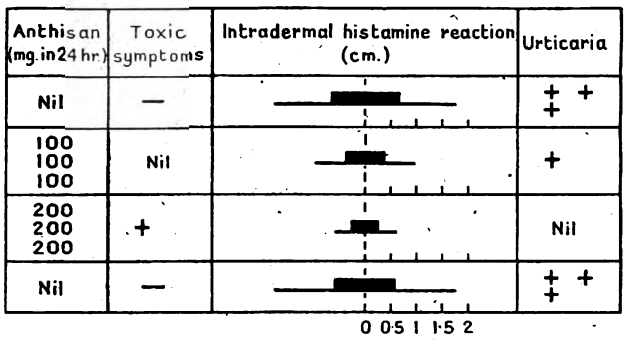

Fig. 4—Average effective dose of anthisan in a man, aged 69, weight 78 kg., with urticaria present for 3 months.

Short Duration.—In a woman, aged 38, weight 50·5 kg., with urticaria present for 6 months, the intradermal histamine reaction was modified by anthisan 200 mg. t.d.s. Coincidentally the urticaria was suppressed during the day but reappeared about 2 A.M. (the doses of anthisan were given at 7 A.M., 1 P.M., and 6 P.M.). Thus, in this patient an effective level of anthisan was maintained for only 8 hours after ingestion. A further dose at 11 P.M. relieved this early morning urticaria.

Long Duration.—In a woman, aged 23, weight 63·5 kg., with urticaria present for 4 months, who provided an example of a low effective dose (fig. 7), anthisan 100 mg. modified the intradermal histamine reaction, and, given as a single dose at 8 A.M., suppressed the urticaria for 24 hours. If anthisan was discontinued, urticaria reappeared only 36 hours after the last dose. The intradermal histamine reaction remained modified 24 hours after the dose.

An example of side-effects associated with a low effective dose is given in fig. 9. Drowsiness and lassitude were too severe for the patient to derive benefit from continued therapy. On the other hand, in a case cited as providing an example of a high effective dose of anthisan (fig. 5) toxic symptoms were not experienced until a dosage of 1200 mg. in 24 hours had been reached. Even then the symptoms were so mild that therapy was continued.

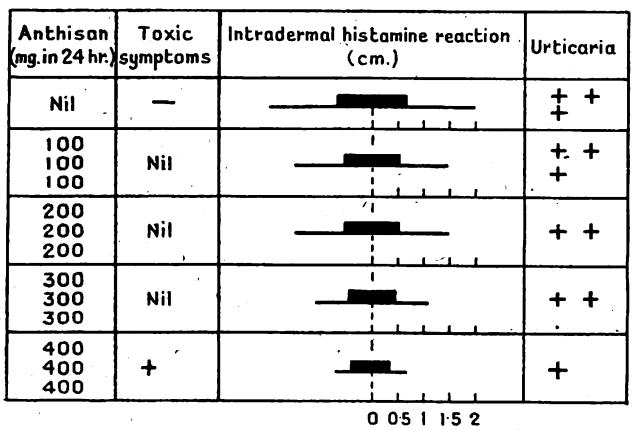

Fig. 5—High effective dose in a woman, aged 49, weight 55·5 kg., with urticaria present for 2½ years.

DISCUSSION

The intradermal histamine response shows clearly that there are well-marked differences not only in potency but also in the mean duration of action of the different anti-histamine drugs. Benadryl is short-acting, anthisan and 3277 R.P. are long-acting, and the action of 3277 R.P. lasts longer than that of anthisan.

This factor of duration of action for a single dose merits more attention than it has received in the clinical assessment of anti-histamine drugs. Indeed, next to the therapeutic ratio it may be the most important feature in any new drug of this class.

The question immediately arises: what mechanisms determine duration of action in the different drugs? Are the anti-histamine drugs, for example, analogous to the long-acting and the short-acting barbiturates, where duration of action depends simply on the rate of breakdown by the liver, or excretion by the kidneys, or both?

From preliminary experiments made by one of us (W. A. B.) in collaboration with P. B. Dews, it seems that the explanation is not so simple, and that one of the main factors may be variation in the degree and duration of fixation of the different drugs by the tissues on which they act. The subjects of these observations were medical students of either sex. In the first experiment it was intended to show the relative potencies of the three drugs by local administration to the skin. Each of thirty people had four intradermal injections, one of

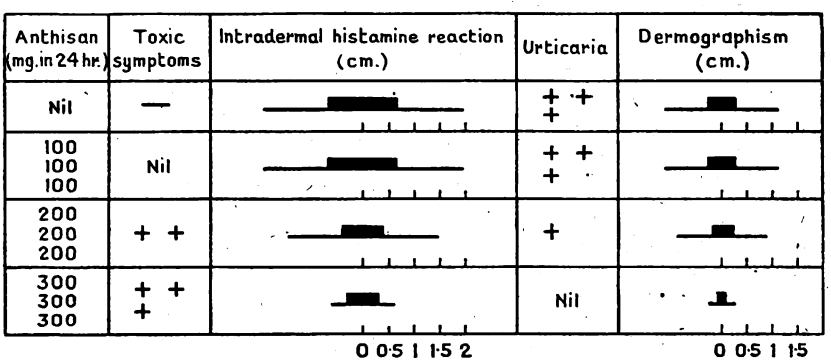

Fig. 6—High effective dose in a man, aged 23, weight 65 kg., with urticaria present for 2 years associated with dermographism (mean of four measurements after use of different traumatising stimuli).

which contained 10 μg. of histamine base as control, and each of the others 10 μg. of histamine plus 100 μg. of the anti-histamine drug. The area of each weal was outlined in ink 5–10 min. after the injection, and the area determined from a tracing of the weal outline. Flares were disregarded because of the known local anæsthetic properties of the drugs. For convenience of presentation the results are expressed for each drug as the mean percentage reductions of the weal area below that of the control. The effects of simultaneous administration of histamine and the three anti-histamine drugs are shown in the first row of table IV. Benadryl and anthisan both gave significant reductions in the response, but, very surprisingly, 3277 R.P. did not.

In view of these results we made further observations, in which areas of the skin were infiltrated with the anti-histamine drugs (0·2 ml. of 0·1% *w/v*) and the histamine was injected in different groups of people at different intervals thereafter. The control injection of histamine was made to an area of skin infiltrated with saline solution. The anti-histamine drugs in the concentration used caused a characteristic red reaction. The limits of the reaction were readily visible, and the subsequent histamine injection was given into this area. The results are given in the second and subsequent rows of table IV. The effect of benadryl was maximal at zero time (complete immediate fixation with maximal exclusion

Key to figs. 4-9: (1) toxic symptoms: +, slight symptoms on questioning; ++, complaint of mild symptoms; +++, complaint of moderate symptoms; ++++, severe incapacitating symptoms; (2) urticaria: +, occasional weal; ++, a few weals; +++, moderate number of weals; ++++, profuse weals.

Intradermal histamine reaction from 0·05 ml. of 0·01% histamine acid phosphate. Mean diameters of flare (thin line) and weal (thick line) are recorded in cm.

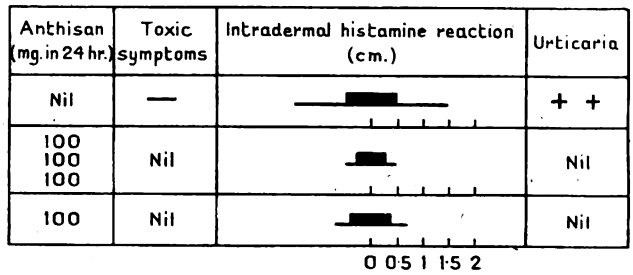

Fig. 7—Low effective dose in a woman, aged 23, weight 63·5 kg., with urticaria present for 4 months.

of histamine), began to pass off almost immediately, and was only questionably significant at 30 min. (light and short-lasting fixation). With anthisan the effect at zero time was not maximal (incomplete immediate fixation) but became so in a few minutes; there was still a significant effect at 100 min. (firm and lasting fixation). With 3277 R.P. there was no significant effect at zero time (slight immediate fixation), but the effect was maximal by 10–15 min. and was still at this level at 100 min. (firm and lasting fixation). In some subsequent observations on other subjects, but using a 1·5 μg. test dose of histamine, significant effects have persisted with anthisan to about 1000 min. and with 3277 R.P. to 3000 min. The standard errors of the observations in table IV give some idea of the variation from one person to another in both degree and duration of effect with the different anti-histamine drugs when administered locally to the skin.

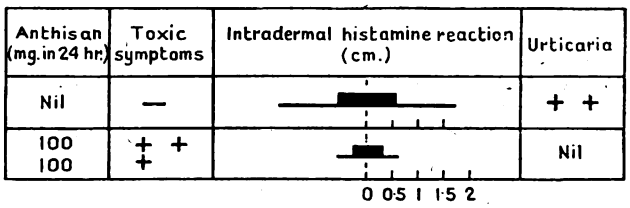

Fig. 9—Low effective dose associated with side-effects in a woman, aged 42, weight 58 kg., with urticaria present for 3 months.

It is thus evident that the differences in duration of action of the three anti-histamine drugs given by mouth have features analogous to those shown after their local application to tissues. It cannot therefore be supposed that the different durations of action observed clinically are due simply to differences in the rate of excretion or detoxication of the drugs, but are probably due, in part at least, to differences in the "firmness of fixation" of each drug by the tissues.

Besides these differences in the duration of action characteristic of each of the anti-histamine drugs, it was to be expected that there would be considerable variation from one person to another in the response to the drugs as indicated by the intradermal histamine reaction or by the modification of an urticaria. This is amply shown by our results, as is the further point that the response in any person is comparable for all three drugs, with the result that a person who is, for example, resistant to anthisan is also resistant to 3277 R.P.

It was to be expected, however, again on general grounds, that in people resistant to any anti-histamine drug (and in whom therefore the response to a given dose was less in degree and duration than the mean response), the degree and duration of the response could be made to approximate to the mean response for the particular drug by a suitable increase of the dose. This, in fact, is what happens. Thus, whereas the average daily dose of anthisan is 300 mg., people resistant to it

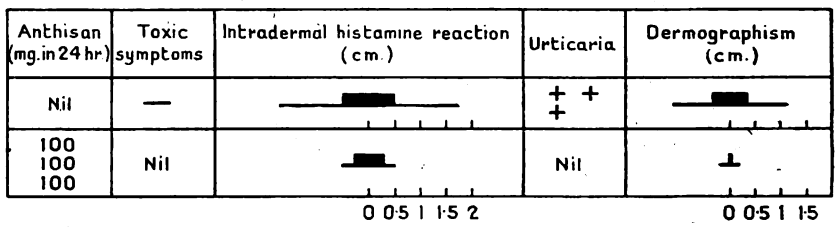

Fig. 8—Low effective dose in a woman, aged 20, weight 64 kg., with urticaria present for 2 years associated with dermographism.

and those who show a small and short response to such a dose, may give an adequate response after 600, 900, or even 1200 mg. in 24 hours. On the other hand, though in our 20 patients treatment with anthisan suppressed or considerably modified the urticaria in all, in three of these who were resistant to the drug, and to whom therefore large doses had to be administered, therapy was discontinued because toxic symptoms outweighed the value of suppressing the urticaria. Therefore, though adequate anti-histamine effects can be obtained with the present anti-histamine drugs, in resistant people by a suitable increase of dose, the toxic effects which may derive from such a dosage are an important limiting factor in their usefulness.

In some people who are only moderately resistant to these anti-histamine drugs adequate clinical effects may be obtained with normal dosage during the day; but, the duration of effective action being shorter than normal, a subeffective level is reached between the last dose on one day and the first on the next. Three of our patients on anthisan t.d.s. had recurrences of the urticaria in the early hours of the morning, some 8–12 hours after the last dose. This was completely controlled by giving an extra dose, with a little food, last thing at night.

Nearly all the reports published on the clinical use of anti-histamine drugs in chronic urticaria have shown that some patients were not improved. This number has varied from one worker to another as follows:

Reference	*Drug*	*No. of cases treated*	*No. not improved*
Friedlaender and Feinberg (1946)	Benadryl	14	4
Friedlaender (1946)	Benadryl	11	2
Goldberg (1946)	Benadryl	15	3
Shaffer et al. (1945)	Benadryl	8	1
O'Leary and Farber (1947)	Benadryl	75	10
McGavack et al. (1947)	Benadryl	36	3
Curtis and Owens (1945)	Benadryl	17	4
Levin (1946)	Benadryl	9	3
Waldbott (1946)	Benadryl	20	4
Osborne et al. (1947)	Pyribenzamine	15	6
Arbesman et al. (1946)	Pyribenzamine	107	23
American Academy of Allergy (1946)	Pyribenzamine	97	21
Britton (1947)	Antistin	11	6
Hunter (1947)	Anthisan	8	—
Vallery-Radot et al. (1947)	3277 R.P.	47	1
Total		490	91

TABLE IV—ACTIONS OF ANTI-HISTAMINE DRUGS ADMINISTERED LOCALLY TO SKIN

Time between giving anti-histamine drug and histamine (min.)	No. of people	Mean % reduction in area of weal response, ± standard error of mean		
		Benadryl	Anthisan	3277 R.P.
0	30	25·5 ± 5·7	32·6 ± 5·8	9·9 ± 7·3
10	10	24·3 ± 8·0	46·6 ± 6·3	46·6 ± 9·1
30	10	16·8 ± 8·4	33·1 ± 6·0	41·1 ± 5·6
100	10	7·7 ± 12·2	26·8 ± 7·9	43·3 ± 5·2

On the basis of our observations it is difficult to escape the conclusion that many of these failures were in people resistant to the drug, and that, if the dose had been suitably increased or a change made to a more powerful drug, the response in these people would have been satisfactory, as it was in our cases. In any event it is probable that, in previous work on anti-histamine drugs, even where attention was paid to differences in the potency and duration of action of the different drugs, there was little appreciation of the variation in response from one person to another to any one of them. It is clear, however, that this variation is important, and the methods described here are readily applicable to its assessment for clinical purposes.

SUMMARY

The quantitative modification of the intradermal histamine reaction by the oral administration of the anti-histamine drugs 'Benadryl,' 'Anthisan' ('Neoantergan'), and 3277 R.P. is described.

These drugs differ in their weight-for-weight effectiveness and in their duration of action, benadryl being classed as relatively weak and short-acting, and anthisan and 3277 R.P. as potent and long-acting.

There was considerable variation from one person to another in the degree and duration of the specific anti-histamine response to the drugs and in the incidence of side-effects. If the specific response to one drug was poor it was usually poor to the others also.

In people resistant to any of the anti-histamine drugs a "normal" response could be obtained by a suitable increase in the dose, the chief limiting factor being the incidence of unpleasant side-effects.

In 20 patients with chronic urticaria treated with anthisan, in all of whom the weals were suppressed or greatly modified, intradermal histamine reactions were recorded before and throughout treatment, and the modification of the reaction was found to parallel closely the response of the urticaria.

There was considerable variation from one person to another in the dose required to suppress the urticaria, and it is suggested that many of the reported failures in the treatment of urticaria with anti-histamine drugs were in patients resistant to the drugs, and that higher doses or more potent drugs might have produced satisfactory effects.

The results are discussed, with special reference to the importance of the differences in potency and duration of action of the different drugs and to the variation from one person to another in the response to any one. A possible factor in determining differences in duration of action is noted, and the significance of the variation in response from one person to another is emphasised.

Our thanks are due to Dr. J. T. Ingram for access to, and help with, the cases; Dr. B. N. Halpern for a supply of 3277 R.P.; Dr. W. R. Thrower for a supply of anthisan; and the Medical Research Council for an expenses grant to one of us (W. A. B.) to defray the cost of the work.

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DIMETHYLSULPHANILAMIDO-ISOXAZOLE (NU-445) IN URINARY INFECTIONS

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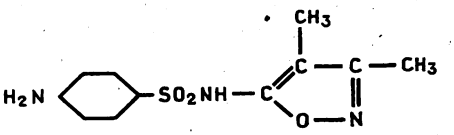
THE properties of a new sulphonamide, 'NU-445' (3-4 dimethyl-5-sulphanilamido-isoxazole),



make it suitable for the treatment of urinary infections, particularly those caused by gram-negative organisms. The drug is considerably more soluble than other sulphonamides (Gilligan and Plummer 1943), so that the risk of crystalluria is minimal, and high concentrations are easily obtainable in the urine, where it exhibits satisfactory antibacterial activity over a wide pH range (Schnitzer et al. 1946). The rate of absorption is high, and an adequate blood-level may be maintained with eight-hourly doses by mouth, while the incidence of toxic reactions is reported to be extremely low (Sarnoff 1948).

In the last eighteen months the drug has been submitted to clinical trial in urinary infection. It was thought that the value of the drug could be effectively assessed only by comparing the results with those in a control series treated with another optimally active sulphonamide ('Sulphamezathine'). Furthermore, it seemed desirable to avoid extraneous conditions which might influence the course of the infection in an irregular manner, such as operative procedures, continuous catheterisation, and suprapubic intubation, so that the trial should be restricted to well-defined cases apparently not needing auxiliary treatment. It was therefore decided to treat a consecutive series of female patients admitted to the Central Middlesex Hospital with a provisional diagnosis of pyelitis or cystopyelitis, alternate cases being treated with NU-445 and with sulphamezathine. In all, 60 cases were treated in this way.

METHOD OF TRIAL

All patients received uniform treatment except for the sulphonamide prescribed. NU-445 or sulphamezathine was administered in an initial dose of 3 g. followed by 2 g. at eight-hourly intervals until 31 g. had been given over five days. An adequate fluid intake was maintained, and small doses of alkali (potassium citrate gr. 60 daily) were given in all cases, though its omission in cases receiving NU-445 would have been warranted by the high solubility of this sulphonamide in acid urine.*

* Some evidence has been adduced from a recent clinical trial that, despite its high solubility in acid urine, NU-445 may exert a greater bacteriostatic effect in slightly alkaline urine (Rodgers and Colby 1948).

PROFESSOR BAIN AND OTHERS: REFERENCES—*continued*

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Catheter specimens of urine were obtained immediately before treatment began and thereafter daily at 6 A.M. when the patient was awoken. Every precaution was taken to avoid contamination, and patients were urged not to micturate immediately before catheterisation, so that the samples of urine obtained might be as uniform as possible. All urines were examined for pus and organisms, and cultures were prepared from the early morning specimens to demonstrate the approximate number of bacterial colonies developing per ml. The urinary pH was also recorded.

Clearance of infection was assumed when there had been three successive negative cultures, cells had disappeared from the urine, and all symptoms had subsided. Subsequent follow-up examinations were conducted at intervals to assess the liability to recurrence.

Whenever infection persisted after the initial treatment, and in patients with recurrent infections, intravenous pyelography and a leucocyte-count were carried out before instituting a further course.

RESULTS

In 8 patients it was found that, owing to treatment before admission, the infection was already subsiding and urinary cultures were sterile. These 8 patients were therefore excluded from the study.

Of the remaining 52 patients, half of whom received NU-445 and half sulphamezathine, all showed unequivocal evidence of urinary-tract infection, with pus in the urine and positive bacterial cultures of coliform organisms (except in 1 instance, complicated by renal calculus, where staphylococci were isolated). As was to be expected, a small proportion of the cases (6) proved to be complicated by conditions necessitating surgical treatment. In addition, 4 patients were found to be diabetic, and 17 were pregnant.

TABLE I—RESPONSE TO SINGLE COURSE OF NU-445 OR SULPHAMEZATHINE

GROUP A: 26 CASES TREATED WITH NU-445

	No. of cases		
INFECTION CLEARED	19		
Uncomplicated cystopyelitis	12	Average period before urinary cultures sterile: 3·3 days.	Average period before pyuria disappeared: 5·4 days
Pyelitis of pregnancy	6		
Cystopyelitis and diabetes	1		
NO RESPONSE	7		
Pyelitis of pregnancy	5	Temporary remission followed by recurrences till term (3 cases). No further sulphonamide given. Temporary diminution of infection (2 cases). Subsequent courses of sulphamezathine ineffective.	
Congenital megalo-ureter	1	No response before surgical treatment.	
Calculous pyonephrosis	1		

GROUP B: 26 CASES TREATED WITH SULPHAMEZATHINE

	No. of cases		
INFECTION CLEARED	15		
Uncomplicated cystopyelitis	11	Average period before urinary cultures sterile: 4 days.	Average period before pyuria disappeared: 5·7 days.
Pyelitis of pregnancy	3		
Cystopyelitis and diabetes	1		
NO RESPONSE	11		
Uncomplicated cystopyelitis	4	No response. In all 4 cases infection subsequently cleared after course of NU-445.	
Pyelitis of pregnancy	1	Temporary remission followed by recurrences till term. Subsequent course of NU-445 ineffective.	
Cystopyelitis and diabetes	2	In 1 case infection subsequently cleared after course of NU-445. In 1 case infection persisted after course of NU-445.	
Pyelitis complicating: Renal calculus	2	No response before surgical treatment.	
Renal calculus and pregnancy	1		
Renal tuberculosis and pregnancy	1		

TABLE II—BACTERIOSTATIC EFFECT OF A SINGLE COURSE OF NU-445 OR SULPHAMEZATHINE IN 23 UNCOMPLICATED CASES OF CYSTOPYELITIS.

GROUP A: 12 CASES TREATED WITH NU-445

Days for urine to become sterile	No. of cases	Colonies of *Bact. coli* per ml. urine (daily estimation)
2	6	>1,000,000; —; —; — 10,000; —; —; — >1,000,000; —; —; — 50,000; —; —; — >1,000,000; —; —; — >1,000,000; —; —; —
3	3	>1,000,000; 100,000; —; —; — >1,000,000; 300; —; —; — >1,000,000; 1,000,000; —; —; —
4	1	100,000; 6000; 50,000; —; —; —
5	2	7,000,000; 1,000,000; —; 50,000; —; —; — >1,000,000; >1,000,000; 1,000,000; 10,000; —; —; —

GROUP B: 11 CASES TREATED WITH SULPHAMEZATHINE

2	2	1,000,000; —; —; — 1,000,000; —; —; —
3	3	31,000; 1000; —; —; — >1,000,000; 6000; —; —; — >1,000,000; 1,000,000; —; —; —
4	5	500,000; 13,000; 5000; —; —; — >1,000,000; —; 1,000,000; —; —; — 6000; 1000; 10,000; —; —; — >1,000,000; 1500; 2000; —; —; — >1,000,000; 25,000; 5000; —; —; —
7	1	>1,000,000; 10,000; 3000; 50,000; 2000; —; —; —

— = Sterile culture. Three successive sterile cultures, with no pus in the urine and abatement of symptoms, were taken as indicating clearance of infection.

The results after a single course of treatment are summarised in table I.

Allowing for some variation in the acuteness of the infection and the stage at which treatment was begun, it appears from this table that the merits of the two sulphonamides are closely similar; but it is unfortunate, in such a small series, that the group receiving NU-445 was handicapped by an unduly high proportion of cases associated with pregnancy. Most cases started treatment within two or three days of the beginning of symptoms, and in all but 9 instances the initial urinary cultures yielded over a million colonies of coliform organisms per ml. (In the remaining 9, figures between 6000 and 100,000 were obtained.) Symptomatically the cases corresponded closely in type, being mainly women of child-bearing age with well-marked urinary frequency, dysuria, and moderate fever; only 2 patients had the classical form of acute pyelitis with severe loin pain and high pyrexia.

Progress during treatment in the cases which responded favourably to either sulphonamide was characterised by a remission of symptoms, diminution of the amount of pus in the urine, decline in the number of colonies of coliform organisms cultured per ml., and an increase in the urinary pH. Taking these points in order, it appeared clinically that the symptomatic response was slightly more rapid with NU-445. This impression was later substantiated by the subjective evidence of those patients who had not responded completely to a single course of one drug, and were subsequently treated with the other. There was no well-defined difference, however, in the over-all rate of disappearance of pus from the urine, nor in the diminution of bacterial colonies cultured; but on selective analysis of the 23 cases uncomplicated by pregnancy or diabetes, there was some indication that NU-445 exerted a more immediate bacteriostatic effect. Such an analysis may well be considered a more accurate indication of the value of NU-445, since it is well known

that structural and functional changes in the urinary tract during pregnancy, and reduction of the general resistance in diabetes, may both affect the course of the infection in varying degree. The results obtained are listed in table II.

Despite the use of alkalis the urinary pH in most cases showed a decidedly acid reaction (average pH 5·6) during the first two or three days, rising thereafter to 6·5–7 in both groups uniformly as the infection subsided.

The 18 cases in which infection did not clear with a single course of sulphonamides (table I) may be grouped in two categories. 6 were found to be associated with a gross anatomical defect, tuberculous infection, or urinary calculus of sufficient significance to preclude any chance of the infection abating without operative measures. The other 12 cases were comparable in type with those which responded. It will be noted that 4 of these, though apparently uncomplicated, did not clear with a single course of sulphamezathine; symptoms and pyuria persisted, and cultures of urine on the fifth day of treatment still showed over a million colonies of coliform organisms per ml.; but a subsequent course of NU-445 ended the infection in an average of four days. Of the remaining 8 cases, all associated with either pregnancy (6) or diabetes (2), some abatement of infection took place during the initial course of sulphonamide in all except 1 diabetic.

In 3 of the pregnant patients treated with NU-445 temporary bacteriostasis and relief of symptoms were obtained, but recurrent infection was noted at the follow-up examination; no further sulphonamide was given. Of 3 other pregnant cases, 1 responded temporarily to sulphamezathine, but a subsequent recurrence of infection proved resistant to NU-445, and 2, though partially relieved, did not clear completely either with NU-445 or later with sulphamezathine. Of the 2 diabetic patients treated initially with sulphamezathine, 1 showed some reduction of the infection (as indicated by the bacterial-colony count) and finally cleared with a course of NU-445, whereas the other remained unchanged despite similar treatment.

In addition to the above series of cases, NU-445 has also been given to a small number of other patients, but without control. In cases of prostatic obstruction with infected urine the clinical results did not appear to differ from those obtained with other sulphonamides, and similar findings were obtained in the prophylaxis of urinary infection during indwelling catheter drainage for retention.

After suprapubic drainage of the bladder, instillation through the cystotomy tube of the lithium salt † in 10% solution, in place of the usual irrigating fluid, was not found to have any beneficial effect—in fact, in 1 case it seemed slightly irritating. The local growth of *Ps. pyocyanea* in 2 cases was not demonstrably inhibited by this method of application, and a single case of *Proteus* infection was not affected by a combination of local and oral therapy. In a recent report (Lazarus 1948), however, the instillation of a 20% solution of the lithium salt into the renal pelvis via a nephrostomy tube has proved successful in eliminating persistent infection, which suggests that there may be some scope for treatment by local application.

No toxic reactions, crystalluria, or other side-effects were observed in any of the controls or other patients to whom NU-445 was given.

SUMMARY

The new sulphonamide, NU-445, has been used to treat a controlled series of cases of coliform infection of the urinary tract. The advantages claimed for the preparation which led to the trial being undertaken were high solubility in urine (minimising the risk of crystalluria), effective antibacterial activity against gram-negative organisms, and extremely low toxicity.

Sixty cases of cystopyelitis in women were treated, alternate cases receiving NU-445 and sulphamezathine in similar dosage. The findings indicate that NU-445 falls into the class of optimally active sulphonamides, and that it compares favourably with sulphamezathine in its effect on gram-negative urinary infections. Although, for purposes of control, the dosage of NU-445 was lower than its solubility warranted, NU-445 achieved more rapid bacteriostasis than sulphamezathine in uncomplicated cases of cystopyelitis. In a small number of cases which proved resistant to sulphamezathine the infection cleared rapidly with NU-445. No toxic effects were observed in any case treated with NU-445, and it seems probable that the preparation may safely be given in much higher dosage to the more resistant cases of urinary-tract infection.

We wish to thank Dr. J. D. A. Gray for conducting the bacteriological investigations, Miss B. J. Smith for her painstaking work in organising the collection of specimens, and Roche Products Ltd. for supplies of NU-445.

† This is the soluble form of the drug, prepared for intramuscular injection. It corresponds to the sodium salt of other sulphonamides.

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DETERMINATION OF HÆMOGLOBIN

VI. TEST OF THE M.R.C. GREY-WEDGE PHOTOMETER

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PREVIOUS papers in this series (Macfarlane et al. 1948, King et al. 1948a) have given the results obtained with a grey-wedge photometer described by King (1947). This is a modification and improvement of previous grey-wedge photometric instruments described by King et al. (1937) and King and Delory (1944). An instrument operating on a somewhat similar principle has been described by Duffie (1942, 1944, 1945). These results were so promising that the instrument is now being produced commercially as the "M.R.C. grey-wedge photometer." * In its manufactured form it has been subjected to test, the results of which are presented here.

PROCEDURES

A blood sample was taken from each of ten healthy adults. Alternate donors were male and female.

Base-line Methods.—Iron and gas analyses were done at the Postgraduate Medical School of London. Iron was determined by the titanous-chloride method of Wootton and King (1948), oxygen capacities by the Van Slyke manometric apparatus (Peters and Van Slyke 1930).

Preparation of Solutions.—Calibrated glass apparatus was used throughout. Oxyhæmoglobin solutions were prepared by diluting the blood samples 1 in 200 with $N/150$ NH_4OH. To prepare carboxyhæmoglobin solutions, the samples were diluted 1 in 200 with $N/15$ NH_4OH, shaken for several minutes in an

* This instrument can now be obtained from Keeler Optical Products Ltd., 39, Wigmore Street, London, W.1.

atmosphere of coal gas, and allowed to stand for at least 30 min. to make sure of complete saturation.

Spectrophotometric measurements were made at the National Physical Laboratory as described by King et al. (1948a).

Colour Comparator.—The carboxyhæmoglobin solutions were compared in the National Physical Laboratory (N.P.L.) colour comparator with the B.S.S. Haldane standard.

M.R.C. Grey-wedge Photometer.—This is an instrument designed to measure the optical density of coloured

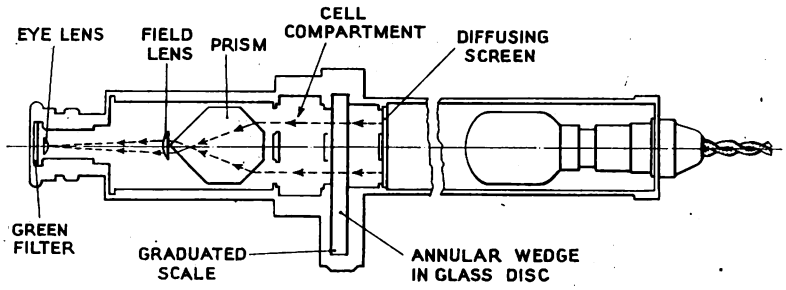

Fig. 1—Optical system of the M.R.C. photometer.

liquids. It may be used in daylight by holding it squarely before an evenly illuminated window, or by artificial light, in which case a specially designed lamp-housing is attached to the front of the wedge-housing (fig. 1). The light falls on a diffusing screen and next passes through two apertures into the body of the photometer. In one light-path is placed a glass cell, 1 cm. deep, containing the coloured solution. The other light-path passes through a segment of an annular grey wedge and next through a compensating cell, filled with an appropriate solvent, to balance losses due to reflection and absorption. Light travelling along these symmetrical paths illuminates the two halves of an optical field viewed through the eyepiece of the instrument. In use, the light absorbed by the coloured liquid is balanced by rotating the annular grey wedge until equal brightness is obtained on both halves of the field. To make this match possible a monochromatic light filter is fitted over the eyepiece. The choice of filter is governed by three considerations: it must pass light of a colour strongly absorbed by the liquid; it must be of sufficiently high transmission to give a well-lit field; and, most important of all, the colour difference, if any, in the field, should be small enough not to disturb the accuracy of the matching. For solutions of oxyhæmoglobin the most suitable filter in the commercial range was found to be Ilford bright spectrum yellow-green no. 625.

Calibration.—The experiment described here compares results on the calibrated M.R.C. photometer with results obtained by the standard base-line methods, measurement of iron and oxygen capacity. A brief outline of the calibration should suffice to show the principle that has been followed. First, the method of calibration is necessarily an easy practical one which can be used both by the manufacturer and by a standardising laboratory such as the N.P.L. It consists of preparing neutral glasses having absorptions corresponding to 50%, 100%, and 150% on the Haldane scale, and using these in the instrument to fix the 100% point and to indicate the spacing of the scale graduations. When this is done, the instrument reads directly in terms of percentage on B.S.S. Haldane scale, 100% ≡ 14·8 g. of Hb per 100 ml. (King et al. 1947). The preparation of the neutral standards is based on the absorption curve of oxyhæmoglobin in the visible spectrum. A mean curve for 21 bloods was obtained in a previous experiment (King et al. 1948a). If the photometer had been designed to use light that was strictly monochromatic, the absorption curve alone would have given all the data required to make a neutral standard. The wave-length band transmitted by filter no. 625, however, is too broad for the filter to be assumed monochromatic. Fig. 2 shows the transmission curves of oxyhæmoglobin, the filter, and the combination of both. It can be seen that the distribution of the light transmitted by the filter is altered considerably by the oxyhæmoglobin. In using a broad-band filter it is still possible to calculate the required optical density of oxyhæmoglobin to the same accuracy as with monochromatic light, provided the transmission curve of the filter is known. This was done for oxyhæmoglobin with filter no. 625, and neutral standards were made in accordance. We hope to publish more about this type of calculation and its application to photo-electric hæmoglobinometers.

The calibration of the photometer is thus done in a roundabout way, starting from iron analysis and proceeding via optical absorption, calculation, and neutral standards. In this experiment results with the calibrated photometer are checked directly against determinations of iron and oxygen.

Two instruments were used and twelve observers, six at the Postgraduate Medical School of London and six at the National Physical Laboratory. The instruments were loaded with the oxyhæmoglobin solutions mentioned above; on each solution each observer took five readings in daylight and five in artificial light.

RESULTS

All results are given in percentage of the B.S.S. Haldane scale. The following factors were used for interconversion:

(1) Hæmoglobin contains 0·334% Fe } (Hüffner 1894)
(2) 1 g. of hæmoglobin ≡ 1·34 ml. of O_2 }
(3) 100% Haldane ≡ 14·8 g. of Hb per 100 ml. (King et al. 1947).

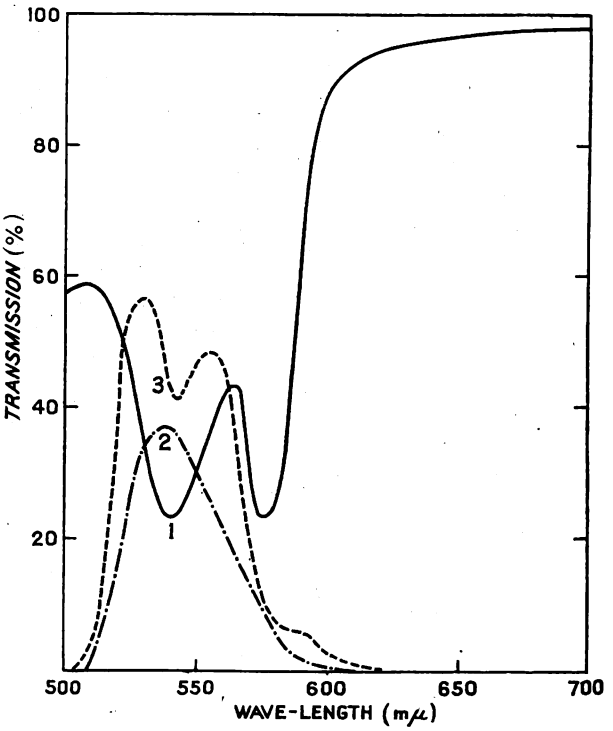

Fig. 2—Spectral transmission curves of oxyhæmoglobin solution (1), Ilford bright spectrum yellow-green filter no. 625 (2), and combination of oxyhæmoglobin and filter (3). Curve 3 is plotted on a scale five times as large—i.e., the ordinates for this curve run from 0 to 20% transmission.

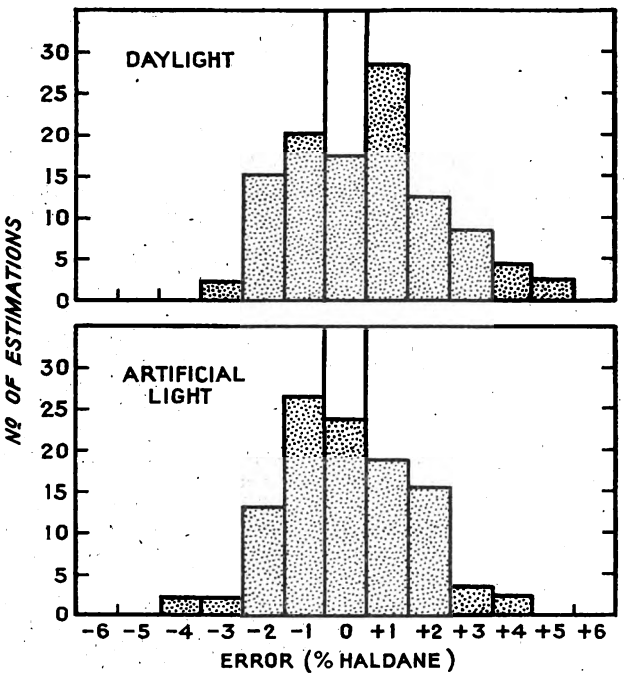

Fig. 3—Histogram showing the relationship between individual estimates and error.

The " base-line " results are given in the accompanying table. Column 1 is the iron analysis, column 2 the Van Slyke oxygen capacity. In column 3 the result is obtained from spectrophotometric absorption measurements at 540 and 560 mμ on the oxyhæmoglobin solutions. The complete spectral curve of these solutions in the visible range was obtained at 10 mμ intervals, and the colour calculated from these curves in terms of hæmoglobin. Results are given in column 4. The data on which these last two methods depend will be presented elsewhere. The results of the Haldane colour comparator are shown in column 5.

Since it was desired to test the performance of the instrument so far as possible under clinical conditions, each observer's five readings were averaged and constituted that observer's estimation of the hæmoglobin value. For each blood sample a grand average was struck of the twelve observers' estimates both by daylight and by artificial light. These grand averages are compared in column 6 with the mean of columns 1, 3, and 4—i.e., the iron determination and the absorption measurements on the same oxyhæmoglobin solutions.

Except for the oxygen capacity results, the agreement is excellent. As shown by King et al. (1948b), oxygen capacity gives results which are a few per cent. lower than those given by the other methods.

It is convenient to present the individual estimates as a histogram. For either daylight or artificial light there are twelve estimates on each of the blood samples. The total 120 estimates are given in fig. 3. It will be seen that in no case is an estimate more than 5% Haldane from the "true" value.

In fig. 4 the comparison of eight observers who remained unchanged throughout the experiment is presented. Each line represents the range within which 90% of the observers' estimates would be expected to fall, and shows that there is no very great individual bias towards high or low results.

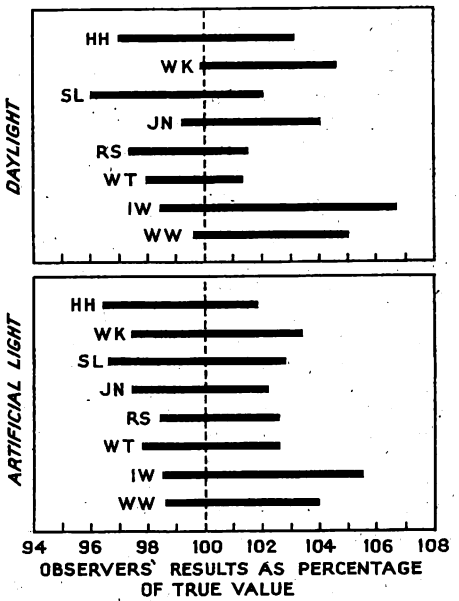

Fig. 4—The estimated 90% ranges of eight of the observers.

DISCUSSION

The foregoing experiment has confirmed previous findings that the neutral grey-wedge photometer gives results of satisfactory reliability even in the hands of several different observers. It demonstrates also that the commercial version of the experimental instrument, developed during the previous trials, is at least as good in performance as its prototypes, and it therefore seems that it can be recommended for routine use with some confidence.

COMPARISON OF HÆMOGLOBIN RESULTS BY DIFFERENT METHODS

(All values are in % Haldane)

Blood sample	(1) Iron analysis	(2) Van Slyke oxygen capacity	(3) Absorption measured at 540 and 560 mμ	(4) Calculated from total spectrum	(5) Haldane colour comparator	Mean of 1, 3, and 4	(6) M.R.C. photometer (grand average)
1	104·6	100·3	102·2	102·5	101·5	103·1	103·5
2	89·4	86·1	89·5	89·5	89·9	88·8	91·2
3	108·7	104·0	108·3	108·0	108·9	108·3	109·2
4	78·2	75·9	78·5	78·5	78·3	78·4	78·0
5	103·0	98·6	104·5	104·0	104·1	103·7	103·2
6	88·3	86·1	88·5	88·4	87·8	88·4	88·4
7	97·4	94·5	98·2	98·7	97·3	98·1	97·3
8	97·9	95·5	98·7	99·4	97·5	98·7	98·2
9	82·0	78·6	82·0	81·4	81·7	81·8	81·6
10	68·8	67·2	70·0	70·1	68·9	69·6	70·0
Quotient against iron as a percentage — Mean	100·0 %	96·6 %	100·3 %	100·3 %	99·7 %	100·1 %	100·3 %
Quotient against iron as a percentage — S.D.	..	0·81	1·10	1·17	1·06	0·78	0·93

Certain reservations must, however, be made with regard to these instrumental trials as a whole. They have been designed to assess instrumental errors in the estimation of hæmoglobin and the effect of personal differences between observers on the magnitude of such errors. The neutral grey-wedge photometer has been shown to give small variations in the hands of different observers, as compared with other instruments, under the conditions of the trials. This does not mean, however, that in actual clinical practice errors will be restricted to the limits reported here and previously. For instance, venous blood carefully collected and mixed was used throughout in the trials, so that the sampling errors inherent in the collection of successive samples of capillary blood from patients in clinical practice were eliminated. The present experiments had no concern with such errors, but they will inevitably be included in the over-all error of clinical hæmoglobinometry, irrespective of the type of instrument used. Probably, also, during the trials the care and accuracy with which pipetting and other measurements were carried out exceeded the usual clinical standard, and considerable care was taken to see that the glass cells and windows of the various instruments were clean and the solutions used were clear. Relative neglect of such basic precautions in clinical practice will adversely affect any method of estimation, but in particular the high precision instruments will lose much of their advantage over cruder methods if carelessly used.

We therefore feel that, though we have done our best to produce a simple and easily used instrument, reasonable care is essential if this instrument is to give good results.

SUMMARY

Two examples of the commercially produced M.R.C. grey-wedge photometer have been tested for accuracy in hæmoglobin estimations.

In an experiment involving 240 separate estimates no estimate was more than 5% Haldane from the true value.

The eight observers who went through the whole experiment showed no pronounced bias in favour of estimates higher or lower than the true value.

This investigation has been made for the Medical Research Council's subcommittee on analytical methods. The expenses were partially defrayed by a grant from the Medical Research Council, to whom grateful acknowledgment is made. Our thanks are due to Sir Charles Harington, chairman of the subcommittee on analytical methods, for much valuable advice, and to the patient and willing observers. Colour and absorption measurements were carried out at the National Physical Laboratory on behalf of the Medical Research Council.

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. . . We are told that the population of the earth is increasing by 50,000 a day, and that land capable of cultivation is shrinking. . . . On the other hand, we are thwarted in our efforts by shortage of man-power. . . . There are too many to feed and too few to work. So we have those clamouring for higher family allowances and amenities with the hope of increasing the birth-rate, and others calling for contraceptives in order to diminish it.—*Medical Officer*, Nov. 27, p. 235.

DIAGNOSTIC FLUOROSCOPY AT A CHEST CLINIC

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THE fluoroscopic diagnosis of pulmonary tuberculosis is looked on askance by many experienced physicians. The fundamental objections are threefold: (1) risk of X-ray injury to the observer; (2) lack of a permanent record; and (3) the perceptive limitations of the human eye in dim light.

Bacon and Leddy (1945) found that the risks of irradiation were greater among doctors who used fluoroscopy occasionally than among radiologists specialised in handling X rays. These writers conclude: "Training, common sense, and experience are the most important protective devices, and carelessness and ignorance the commonest cause of injury from irradiation." The proper precautions to be taken are now well known, and arrangements can easily be made with the National Physical Laboratory to test quantitatively an operator's degree of exposure to irradiation.

The value of an initial X-ray film showing the extent of disease at diagnosis is obvious when disease is present, but this argument does not apply when the findings are normal.

Licht (1936), Bromley (1944), Wright (1944), and Chamberlain (1942) have shown convincingly that the perceptive accuracy of the human eye is diminished in conditions of diminished illumination such as fluoroscopy necessitates, but this does not necessarily mean that perceptive accuracy is so reduced as to affect diagnostic accuracy.

Published opinions of the value of fluoroscopy in the diagnosis of pulmonary disease vary considerably. Reid (1934) emphasised its superiority to physical examination for case-finding. Fellows and Ordway (1937), in a survey of 2300 cases, only detected 87% of the clinically significant lesions which were revealed by X-ray film. Israel and Hetherington (1941) concluded that an observer with moderate experience should be able to detect almost all tuberculous lesions of immediate clinical significance, and they contended that failure to wait for dark-adaptation is the chief factor responsible for poor results. Stiehm (1941), in a series of 423 cases, found 4% more by fluoroscopy than by film. He described a meticulous routine of fluoroscopic examination, and urged the importance of dark-adaptation. Garland (1942) reviewed previous reports rather sceptically, emphasising the varied accuracy experienced by different observers. Hall (1942), in two surveys of factories, screened 1370 workers, mainly women. He found an incidence of 3·5 previously unknown cases per thousand, a figure which closely approaches the results of mass-radiography surveys of civilian populations, and he suggested that in skilled hands fluoroscopy can attain a high degree of diagnostic accuracy. Stauffer (1945) used fluoroscopy to survey 1038 civilian employees in an advanced naval base, and found the technique a useful "sieve" to reduce the number of films taken.

THE READING SCHEME

Every properly equipped chest clinic nowadays has its screening apparatus, even if this is only used for the control of pneumothorax refills. At the Reading clinic the apparatus is a Solus-Schall (design S.S.II.). This has a Levy West fluorescent screen and gives an output of 80 kV from its transformer (used voltage).

Since fluoroscopy possesses two major advantages—cheapness and rapidity of use—it was decided in

September, 1946, to offer Reading practitioners a rapid fluoroscopy service. They were invited to refer any patient for examination and were promised a report by return of post. A simple "request letter" was designed carrying full instructions for the patient, and this is given to him by his own doctor, who writes in the name and address of the patient. A space on the letter is completed by dictation during the examination, and the letter is then posted back to the doctor.

RESULTS

The scheme has proved so successful that it is perhaps of general interest to report the results of the first two years of its operation during which 2908 patients have been screened. This number compares with 723 new cases referred in the usual way in 1945, 875 in 1946, and 750 in 1947. There has therefore been hardly any falling off of patients in this respect because of the additional facility for examination. Of the 2908 patients screened, 90% were discharged forthwith. (Patients found to have non-pulmonary abnormalities were discharged and their further investigation left to their own doctor.) No patient who was passed as normal has subsequently been found to have tuberculosis (any notifications of tuberculosis would come to the notice of the tuberculosis officer). Altogether 314 patients were selected for fuller examination, including appropriate X-ray films. Perhaps this is a high proportion, but every case that was in the slightest degree doubtful was investigated. Of these 314 cases, 83 (26%) were found to have pulmonary tuberculosis, making an incidence of 3% of the total number sent for fluoroscopy. Of the 83 cases with definite parenchymatous tuberculosis, only 32 (39%) had a positive sputum. Thus a substantial proportion of relatively early cases have been discovered in this way.

Since this fluoroscopy service was instituted in the autumn of 1946, 20% of the cases of pulmonary tuberculosis in Reading have been found in this way, and with increasing confidence in the method the number of sessions has been increased to four each week. It is found that about 20 people can be examined in half an hour, a great deal of time is saved, both for doctor and patient, and films are not wasted on normal persons. Thorough visual accommodation is essential, and the writer wears extra-dark glasses for half an hour or so before each session.

SUMMARY

The value of diagnostic fluoroscopy is considered, together with its risks and its accuracy.

A scheme is described in which 2908 people were referred for examination during the past two years by the general practitioners in a town of 100,000.

Pulmonary tuberculosis was found in 3% of cases.

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New Inventions

CALIBRATED ELECTRICAL AID TO FACIAL-NERVE DISSECTION

IN REMOVING PAROTID TUMOURS

THE bold approach to the parotid gland by Hamilton Bailey [1] has led to a new interest in dissection of the facial nerve in cases of parotid tumour. The pattern of the facial nerve is fairly constant, but there are always individual variations brought about through displacement by the tumour itself. Nerve filaments are not always visible, but mechanical stimulation by pinching with forceps may give warning of their presence by producing facial contraction. Unfortunately the injury to the nerve from pinching often prevents further response at the time, and the nerve may be divided without additional warning. Mild electrical stimulation does not impair the function of the nerve and can be repeated indefinitely.

An experimental apparatus was made to give an intermittent direct current variable from 0–9 volts and measurable by a sensitive meter reading from 0–300 microamperes. Interruptions of about 40 per sec. were obtained by using an electric-bell mechanism. This type of current gives a tetanic response in the muscle and is fast enough to give a steady reading on the meter. One electrode was coupled to the patient by a zinc sheet placed under the buttocks, the other by a sterilised lead to a pair of fine-tooth dissecting forceps. A current of 100 μA caused muscular contraction when the forceps were in contact with tissue up to 2–3 mm. distant from a nerve filament.

With this accurately measured current dissection can be carried out speedily, the tissues being picked up gently in the forceps before division, and ample warning is given of approach to any nerve filament by tetanic contraction of the corresponding part of the face.

Such an apparatus has been used in 12 cases of parotid tumour in the last year with conspicuous success. Even the finest filaments can now be easily found and preserved, and the whole pattern can be confidently laid bare with certainty.

In practice the negative lead is coupled to the patient before the operation is begun. When the full skin

1. Bailey, H. *Brit. med. J.* 1947, 1, 404.

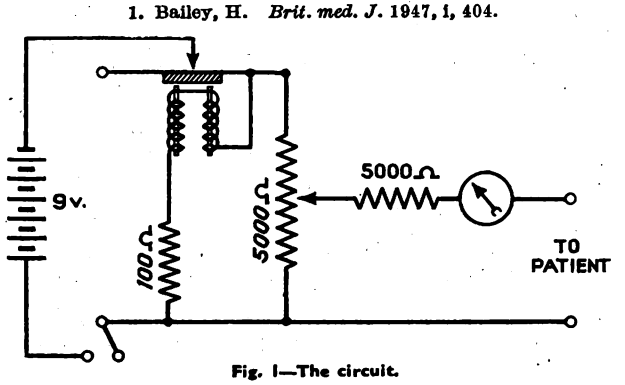

Fig. 1—The circuit.

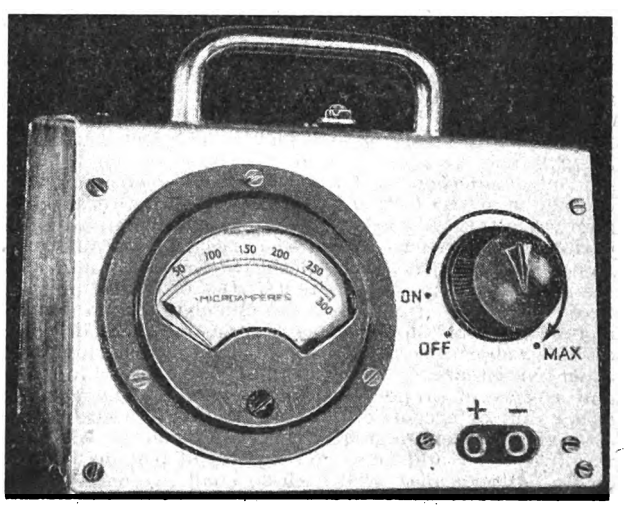

Fig. 2—The apparatus.

exposure has been made, the positive lead is coupled to the dissecting forceps. An unselected portion of parotid tissue is taken in the tip of the forceps and the current adjusted to exactly 100 μA (owing to polarisation the amount of current flowing diminishes somewhat if the same portion of tissue is held for long). It is essential to make this adjustment at the beginning of each operation owing to variations in resistance of the human part of the circuit. The deflection of the needle on the meter each time the forceps touch tissue indicates that the apparatus is working satisfactorily, and it can be relied on completely.

The apparatus can be made easily by any technician. A good-quality electric-bell mechanism makes a satisfactory interrupter. The power is derived from a standard radio 9-volt grid-bias battery. A 5000 ohm resistance is incorporated in the circuit (fig. 1) to safeguard the meter and the potentiometer, which is also of 5000 ohm resistance. The specially sensitive meter was made by the Weir Electrical Instrument Co., of Bradford-on-Avon. The instrument (fig. 2) is self-contained and compact. The battery can be expected to last for at least twelve months with normal use.

I am grateful to Mr. S. J. Lloyd, a medical student, for making the final model, and to Mr. G. M. FitzGibbon and Mr. R. G. Paul for encouraging me to develop the apparatus and for allowing me to operate on some of their cases.

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Reviews of Books

The Skin Diseases

A Manual for Practitioners and Students. JAMES MARSHALL, M.D., consulting dermatologist, Central Middlesex County Hospital; director of venereal diseases clinic, Royal Northern Hospital, London. London: Macmillan. 1948. Pp. 363. 30*s*.

THIS students' manual has been produced as a companion to the same author's work on venereal disease. It nevertheless includes a good section on syphilis; and rightly, for cutaneous manifestations in syphilis are so varied that the dermatologist must have a wide knowledge of the disease, just as the venereologist must be expert on its rashes. There is a small but useful section on the increasingly important subject of industrial dermatitis, as well as sections on eruptions caused by sensitisation to the sulphonamides and penicillin, and on the psychological aspects of skin diseases. The book is well illustrated and the colour plates are fairly accurate. It will be valuable to students and those practitioners who want to have a working knowledge of the subject without going into it too deeply.

Intracranial Tumours

PERCIVAL BAILEY (2nd ed.), professor of neurology and neurological surgery, University of Illinois. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 478. 55*s*.

THE reappearance of this book is welcome. It is a highly individual account, intended for students but rich enough to be interesting to postgraduates and teachers. Professor Bailey's plan is to select a tumour, to give one or more actual case-histories as told to students, and then to discuss what is known about the behaviour of the tumour, and the prospects of surgical removal. It is a good method; and the emphasis on pathology is such as might be expected from one who has contributed so much to the real understanding of the natures and growth characteristics of brain tumours. Professor Bailey is an observant clinician and an experimental neurophysiologist, as well as a neurosurgeon: on this subject he is probably better armed than any other living teacher. Moreover, he has a sense of humour and a sense of proportion that prevent him from being either dull or eccentric. He writes vividly, sure of his own views, even dogmatic, knowing exactly what he wants to say; and he is no respecter of persons alive or dead. Experts may well wish to challenge some of his statements, or to supplement descriptions; but they can be sure that Professor Bailey has good reasons for his views and selections.

This lively and authoritative book is well illustrated in an original fashion, though some of the drawings are too dark and fussy. Like all Thomas books it is attractive to handle and read.

Functional Cardiovascular Disease

M. FRIEDMAN, M.D., director, Harold Brunn Institute for Cardiovascular Research, Mount Zion Hospital, San Francisco. London: Baillière. 1948. Pp. 266. 16*s*. 6*d*.

THIS book deals with Da Costa's syndrome, or effort syndrome, which is now generally regarded as an expression of psychological disturbance. Colonel Friedman, after marshalling the evidence, including his own, suggests that it is the result of a corticohypothalamic imbalance. It therefore seems a mistake to use the words "cardiovascular disease" in any description of this syndrome, even when qualified by the adjective, "functional"; for an essential part of the treatment is to convince the patient that there is no disease of the heart or blood-vessels themselves. Though rather discursive, the book gives a comprehensive account of the symptoms, diagnosis, and treatment of the condition, with many original observations of particular interest to the psychiatrist and cardiologist.

Management in Obstetrics

ANDREW M. CLAYE, M.D., F.R.C.S., F.R.C.O.G., professor of obstetrics and gynæcology, University of Leeds. London: Oxford University Press. 1948. Pp. 186. 12*s*. 6*d*.

IN this short book Professor Claye describes what he himself has found to be the best and omits much that is generally accepted. It seems a pity then that he should waste a page on external pelvimetry, which he himself often finds misleading. The figure (28%) given for the infant mortality in breech birth is too high; and too little emphasis is laid on the value of intravenous ergometrine in the treatment of postpartum hæmorrhage, though the use of the extract of the posterior part of the pituitary gland is repeatedly advocated. Such objections, however, are less important than the good and sound help given throughout the work. The sections on the retroverted gravid uterus, fibroids in pregnancy, and the management of antepartum hæmorrhage, of the first stage of labour, and of the occipitoposterior position, are particularly good; and the delightful chapter headings are not only amusing but instructive.

General Cytology

E. D. P. DE ROBERTIS, department of biology, Massachusetts Institute of Technology; W. W. NOWINSKI, department of anatomy; FRANCISCO A. SAEZ. Philadelphia and London: W. B. Saunders. 1948. Pp. 345. 27*s*. 6*d*.

THIS book was first written in Spanish for Latin America, and Dr. Warren Andrew has now translated it into English. The final result is praiseworthy; both writing and arrangement are clear. The text describes both the principles and the practice of modern techniques such as electron microscopy, X-ray diffraction analysis, and ultramicrorespirometry, instead of assuming that the reader has an intuitive understanding of how these things work. Contrary to British convention, nuclear cytology and chromosome mechanics have been included as well; there is no reason why they should not be there, except that the goings-on of chromosomes do not really make functional sense without a fuller background of Mendelian theory than the authors have been able to provide. The book can be strongly recommended.

The Medical Annual (Bristol: J. Wright. 1948. Pp. 368. 25*s*.) has reached its sixty-sixth year in good style. Sir Henry Tidy and Prof. A. Rendle Short, the editors, again review in their introduction some topics of special interest, such as the poliomyelitis epidemic, the use of B.C.G. vaccine, seasickness, streptomycin, and advances in surgical techniques. The main text is again provided by a body of distinguished contributors.

THE LANCET

LONDON: SATURDAY, DEC. 18, 1948

No Room at the Hospital

IN the early months of next year the general practitioner is going to find it very hard to get any elderly patient into hospital. Though the winter has hardly begun, it is already difficult to secure a bed for anyone who is likely to occupy it for a long time. The fact that the patient cannot be satisfactorily nursed at home makes little difference to the prospect of admission; for resident medical officers of general hospitals, remembering the need to keep room for acute cases, are obliged to deafen their ears to appeals on behalf of those who cannot be expected to recover quickly, while the wards for the chronic sick seldom have vacancies. There are too few beds in commission, usually because nurses cannot be spared to serve them. And unfortunately some local authorities have so far been unable to organise the kind of home nursing that would enable many of the patients to be treated decently in their own beds.

What is to be done? We know that pioneers in this field such as Dr. MARJORIE WARREN and Dr. L. Z. COSIN get good results by treating acutely ill old patients vigorously in short-stay wards. Their long-stay wards are reserved for those who cannot be made fit enough to go home; and these are surprisingly few. Such thorough treatment not only spares hospital beds but also saves lives and reduces chronic illness. We have to admit, however, that lack of trained staff, and building difficulties, make it unlikely that this system will be widely adopted in the very near future. Another line of approach is that of Dr. E. B. BROOKE, at St. Helier Hospital, Carshalton. When lack of a bed obliges him to refuse an old person admission he sends a geriatric social worker to visit the home and assess the circumstances. Sometimes it then proves possible to arrange active treatment—often in the form of physiotherapy—from the hospital, and to send the equipment needed to make the old person more comfortable. This recalls the former arrangement by which district medical officers, attached for the purpose to certain general hospitals, undertook the same kind of out-door treatment. When a general practitioner applied for the admission of an old person, the district medical officer would visit the patient in his home, with authority to provide what was necessary; and for this he could call on the hospital resources, including if necessary such items as oxygen cylinders and air mattresses. Often the old person could thus be tided over the acute phase of an illness, while at the same time the hospital's beds were kept free for short-term cases. It has been suggested that the virtual disappearance of district medical officers under the National Health Service Act has deprived many old people of the only type of hospital care—albeit given outside the hospital precincts—which they could count on getting. The new authorities would do well to consider the possibilities of reviving this type of service, in a form acceptable to the practitioner responsible for the patient's care. Where his remuneration is based purely on capitation, the practitioner's financial interest lies in transferring the patient to hospital rather than in giving him continual attention at home; and this is an element in the situation that should not be overlooked, especially at a time when the strain on general practice is great. But where it is clear that admission is out of the question, practitioners in general would welcome an arrangement whereby some of the resources of the hospital were brought to the patient. Such resources exceed those at the disposal either of the family doctor or of the district nurse; for example, physiotherapy must generally be undertaken by the hospital or not at all. The fact remains that often the chief need of the patient, or that of his family, is for more domestic aid; and we are glad to know that the home-help service is beginning to make progress—at any rate in London, where it is already four times as busy as it was in July. The secret of success in this department is to appoint a keen and able organiser who will get to know the team of workers in her district and see that they find their conditions of work satisfactory; they then act as recruiting sergeants among their friends.

The question also arises whether it would not be possible, during the coming danger period, to reopen some of the closed wards of hospitals, staffing them, on a temporary basis, with part-time nurses and helpers. It is usual nowadays to say that the part-time scheme is played out in London, and that the response, for various reasons, has never been as enthusiastic as, for instance, in Gloucestershire. But comments reaching us from qualified nurses who have tried to do part-time work in London suggest an important and remediable reason for this failure: the part-timers have not as a rule been made to feel that *they were the staff*; they have been regarded from the outset as supernumeraries. The success of the Gloucestershire scheme is largely due to the sense of responsibility that the part-timers have been encouraged to develop. They have known that they were the actual staff of the hospitals, and they have responded as people do to positions of responsibility and trust. We believe that special appeals, in each area, inviting women to give temporary care to the old—until, say, the end of April—might meet with a generous response, especially if it was made clear that the wards opened for this purpose would be staffed and managed entirely by part-timers—some of whom of course would have to be State-registered nurses. As a short-term policy this is certainly worth trying; for its success would prevent a great deal of misery.

Twenty Years of Pregnancy Tests

TWENTY years have passed since Aschheim and Zondek[1] revolutionised pregnancy diagnosis by devising an early and reliable test; and in that time at least twenty other methods have been evolved. They fall into two groups—those performed on the patient herself, and those in which her blood or urine is investigated.

Ideally a test for pregnancy should be reliable, convenient, simple, and speedy; and those involving the patient's participation fall short of the ideal if they are irksome or require her to visit anyone but her own doctor. Some of the seven "direct" tests depend on novel and ingenious principles. For

1. Aschheim, S., Zondek, B. *Klin. Wschr.* 1928, 7, 8.

instance, the Bercovitz test [2] consists in instilling into the patient's conjunctival sac 5–6 drops of her blood diluted with 1 drop of normal saline; if she is pregnant the pupil will either dilate or contract, and its size may be compared with that of the other pupil. Unfortunately it seems to be by no means specific, for some workers have reported an error of over 50%. The 'Antuitrin-S' test was introduced by Gilfillen and Gregg [3]: in pregnant women the intradermal injection of this gonadotrophic hormone does not produce the customary flare. This too has been found to be uncertain. Smith and Brunner,[4] making use of the histological changes in the vaginal mucosa during pregnancy, used vaginal biopsy as a method of early diagnosis. This has the disadvantage of being unsuitable for a busy surgery; paraffin sections have to be examined by a morbid anatomist; and any pathological modification of the vaginal mucosa, as in chronic vaginitis, may vitiate the end-point. All these tests certainly have the merit of speed, for both the Bercovitz and the antuitrin-S reactions may be obtained in the course of a consultation, and it should be possible to have the histologist's report on the vaginal biopsy on the following day. More time is needed for tests in which the production of uterine bleeding indicates that the patient is not pregnant. The first of these was the 'Prostigmin' reaction.[5] With delayed menstruation not due to pregnancy, injection of 1 mg. of prostigmin on 3 successive days leads to uterine hæmorrhage within 72 hours. Cases have to be carefully selected, however, for the bleeding response may be absent at the menopause or in women with a history of menstrual or endocrine disorder; and even so the test is only 90–95% accurate in the absence of pregnancy. A test recently described by Garrett [6] depends on inducing withdrawal bleeding in non-pregnant women after three injections of 1 mg. of œstrone in oil on alternate days. Use of an œstrogen that is active when given by mouth would make the procedure more convenient; but unless the cases are very carefully chosen false positive results are likely. Gediz [7] gives progesterone 10 mg. daily for 5 days, which in the non-pregnant causes withdrawal bleeding within a week of the last injection. A different principle is involved in the use of basal temperature records to indicate the onset of pregnancy. If the postovular rise in temperature, due to the action of progesterone, is maintained for more than three weeks, pregnancy is almost certain. This method is simple and less irksome, but is applicable only when pregnancy has been planned and the patient has kept temperature records since the beginning of the previous period.

In the second group, tests are made on the patient's urine or blood. Blood tests are obviously the less popular, and the one we shall mention is of academic rather than practical interest. In pregnancy it is possible by the seventh week after the last period to demonstrate—by assay on strips of guineapig intestine—an increase in the histaminolytic power of the patient's plasma.[8] The rise can be directly related to the stage of pregnancy, and Ahlmark claims that the commencement of pregnancy can be dated to within about 6 days, especially at the third month. Urinary tests depend on either chemical or biological methods. None of the chemical reactions is as accurate as the better-established biological tests. The bromine test of Voge,[9] based on the presence of histidine in the urine of pregnant women, was simple, cheap, and rapid, but unfortunately gave 25% false negative and 13% false positive results. This test, the first of the chemical tests in the post-Aschheim-Zondek period, was modified by Kappeller-Adler,[10] but still did not reach the necessary degree of accuracy. Another reaction of similar nature was that of Visscher and Bowman,[11] but this showed a 10% error. Chemical tests depending on the rapid increase in concentration of œstrogens in the urine during pregnancy have also been devised. Typical of these was the method of Schmulovitz and Wylie,[12] which involved the collection of inconveniently large quantities of urine and a complicated laboratory technique; the colour reaction was, however, not specific for œstrogens. Patterson's technique [13] was founded on the Kober phenolsulphone colour reaction for œstrogens, œstriol being liberated from its glycuronide by means of bacterial hydrolysis, the products of which did not mask the Kober colour reaction as happens when the glycuronide is hydrolysed by strong acid. The method is laborious, and the reaction is dangerously weak in the earliest stages of pregnancy. The principle of the Guterman test [14] is the excretion of pregnanediol in increased quantities during pregnancy, but Guterman himself claimed only 93% accuracy, and Reinhart and Barnes [15] found a 25% error. Much seems to depend on the level of pregnanediol excretion chosen as the diagnostic base-line.

Thus no satisfactory physical or chemical test has yet been devised for the early, simple, and efficient diagnosis of pregnancy; and it therefore becomes necessary to resort to biological responses to administration of urine. Here the choice of animal and the speed and simplicity of technique are important considerations. For instance the method of Konsuloff,[16] based on expansion of the melanophores and consequent darkening of the skin, has the disadvantage that the test animals are hypophysectomised frogs. Brouha's reaction,[17] depending on enlargement of the seminal vesicles of male mice or rats, was laborious in that ten daily injections were necessary; nor did it prove as accurate as the classical Aschheim-Zondek, Friedman,[18] and xenopus [19] tests, which reach an accuracy of 99% in skilled hands. The last-named has the advantage that the result, if positive, can be obtained in a few hours and, if negative, within 30 hours. Xenopus, however, is not indigenous to this country; the toads must either be imported from South Africa or bred here—a lengthy and

2. Bercovitz, Z. *Amer. J. Obstet. Gynec.* 1933, **25**, 882.
3. Gilfillen, G. C., Gregg, W. K. *Ibid*, 1936, **32**, 498.
4. Smith, B. G., Brunner, E. K. *Ibid*, 1937, **33**, 404.
5. Soskin, S., Wachtel, H., Hechter, O. *J. Amer. med. Ass.* 1940, **114**, 2090.
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16. Konsuloff, S. *Klin. Wschr.* 1934, **13**, 776.
17. Brouha, L., Simmonet, H. *C.R. Soc. Biol.* 1929, **101**, 368.
18. Friedman, M. H. *Amer. J. Physiol.* 1929, **90**, 617.
19. Bellerby, C. W. *Nature, Lond.* 1934, **133**, 494.

specialised task. In the Friedman test the result is known in 2 days, but the rabbits needed for it are expensive; they have to be bought from a reliable dealer to ensure that they are neither too young nor too multiparous to respond. The Aschheim-Zondek test calls for multiple injections of mice, which are easily bred in suitable animal houses; but the result is not known in less than 5 days. The Galli Mainini test,[20] on which Dr. Haines reported last week,[21] employs male toads and has the advantages of fairly simple laboratory technique and rapid reading of results with a high degree of accuracy. The disadvantage is that the male toads he used are indigenous to America, and must be imported—though they appear simple to keep, feed, and handle. Hinglais and Hinglais,[22] however, have used one of the frogs commonly found in France (*Rana esculenta*) with equally good results. Another rapid method is the ovarian hyperæmia reaction;[23] within 6 hours of subcutaneous injection of pregnancy urine the ovaries of the immature rat become conspicuously hyperæmic. Salmon and his associates have claimed 99% correct results at 6 hours; and a modification has yielded equally good results in the hands of Zondek, Sulman, and Black,[24] though only after 24 hours.

Thus at present biological tests hold the field; and these involve animal housing and Home Office licences, as well as the careful technique essential for close on 100% accuracy. The day has not yet arrived when the doctor can tell his patient that she is pregnant by pouring her urine into a tank of fish and watching their bellies become red; though this was the great expectation which the male bitterling at one time held out.

Criteria for Hospitals

Too little is known in this country about the influence on hospitals exerted for the past thirty years by the American College of Surgeons. To qualify for inclusion on the college's approved list, the hospitals have to reach certain standards; and the desire to qualify has greatly improved their organisation, equipment, and performance. Indeed Dr. E. H. L. CORWIN is probably right in saying that the college's programme "more than any other single influence has been responsible for salutary results in the efficiency of hospital work in the United States." When this programme was started in 1918, the college found that only about 13% of 692 large hospitals met all its requirements. But regular inspection continued, and the hospitals accepted it because of the benefit they could gain. The approved list is published annually by the college in the local press of the community concerned, and the hospitals on the list automatically gain public recognition. By 1932, Dr. RICHARD H. SHYROCK writes, "the percentage of hospitals either wholly or conditionally approved was quite high for all save the smallest type." The official survey is undertaken by doctors, paid by the college, who visit hospitals at intervals and also maintain contact through returns and correspondence. The many people in Great Britain who now find themselves visiting hospitals on behalf of boards and committees will be particularly interested in the new point rating system[1] which the college has introduced as a further incentive to the hospitals on its list. This system will be used by the assessors, and it is also suggested that hospitals should themselves use the form as a means of judging their own progress. No departure is intended from the standards laid down in the *Manual of Hospital Standardisation*, but the new method is intended to enable hospitals to take a more active part in meeting the college's requirements.

The report to be made by the assessors falls into two main sections—essential divisions, and adjunct and service divisions. The maximum points obtainable are:

Physical plant, 20; administration, 35; medical staff organisation, 250; medical record department, 150; clinical laboratory, 95; X-ray department, 50; nursing service, 35; dietary department, 20.

Total for essential divisions	655
Medical department, 50; surgical department, 125; obstetrical department, 75; anæsthetic department, 30; physical-therapy department, 15; school of nursing, 15; outpatient department, 10; pharmacy, 10; medical social-service department, 10; occupational-therapy department, 5.	
Total adjunct and service divisions ..	345
Grand total	1000

The high rating for the medical staff organisation and the medical record department (as contrasted, for example, with the nursing service and the school of nursing) reflect the special interests of the college. Reference to the detailed headings under medical staff organisation shows that the greatest emphasis is placed on the following questions:

Are medical staff meetings held at least monthly? (12 meetings a year required.) (*a*) Number of meetings? Average percentage attendance? (75% average attendance is minimum requirement for full score). (*b*) Average duration of medical staff meetings? (2 hours should be considered minimum to cover clinical review).

Are minutes of the medical staff meetings recorded in sufficient detail and do they show a thorough review and analysis of the clinical work as under by (*a*) Discussion of medical administrative problems? (*b*) Review of selected patients in the hospital at the time of the meeting? (*c*) Review of selected cases discharged since the last meeting? (Here should be included consideration of selected deaths, unimproved cases, infections, complications, errors in diagnosis, and results of treatment.) (*d*) Analysis of clinical reports from each department? (*e*) Reports of committees? (*f*) Discussion and recommendations for the improvement of the professional work in the hospital?

Are major clinical departmental meetings held regularly, weekly, bi-weekly, or monthly throughout the year?

The emphasis on the medical record department is also strong, and includes searching queries:

Do the medical records contain the following information: identification data; complaint; present illness; past history; family history; physical examination; consultations; clinical laboratory; X-ray reports; provisional diagnosis; tissue report, (1) gross, (2)

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22. Hinglais, H., Hinglais, M. *C.R. Acad Sci., Paris*, 1948, **226**, 1041.
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1. Hospital Standardisation Scoring Report. Obtainable from the Physicians' Record Company, 161, West Harrison Street, Chicago 5, Illinois. Pp. 17. 50 cents. Reduced prices for larger quantities.

microscopic; treatment (medical and surgical); final diagnosis; progress notes; condition on discharge; autopsy findings?

Who is head of the medical record department? Is the head (*a*) Registered? (*b*) Trained but not registered? (*c*) Provided with sufficient assistants?

Are records written promptly after admission of the patient and are they signed? (24–48 hours is considered limit of promptness.)

Is there an active record committee of the medical staff? (*a*) If active, does it control the calibre of the records? (*b*) Are all records examined by the committee before filing?

It is tempting to go on picking out questions which here as in America touch some sensitive spots:

X-ray department.—Are the reports of interpretations in writing or dictated; and signed by the radiologist? Are requisitions for X-ray examinations in writing?

Medical department.—Do the records justify the diagnosis and treatment (*a*) By a sufficiently complete history and physical examination? (*b*) By sufficient laboratory and other diagnostic tests?

Are consultations required, under the medical staff rules and regulations, in all serious cases; and are they always recorded?

Has the department (*a*) An electrocardiograph, with a member of the medical staff qualified to interpret electrocardiograms? Name? Qualifications? (*b*) Equipment for the estimation of basal metabolic rates?

Surgical department.—Is sterilisation of surgical supplies and water adequately tested by any of the following methods?: (*a*) recording thermometer on the discharge line; (*b*) fusion tubes, such as Diack controls; (*c*) colour indicators, such as sterilometer; (*d*) periodic cultures: how often? (Diack controls in each batch plus frequent culture checks at least monthly, should be made. Recording thermometer, either lag or clock, is considered the best check.)

Do the surgical records justify the diagnosis and operation by (*a*) Sufficient recorded evidence of preoperative study? (*b*) Record of surgeon's preoperative diagnosis? (*c*) An operation report, signed by the operating surgeon, of the findings and technique, written or dictated immediately following the operation?

Are all infections of clean surgical cases routinely: Recorded and reported to administration? Listed? Where? Investigated? By whom?

Enough has perhaps been quoted to show that a systematic review of this kind by an independent authority can be a real stimulus to progress, and that members and officers of the regional boards would find it useful to have a copy of this scoring sheet in their pocket as they are going round the regions. Indeed they might go further, and themselves compile a modified list of questions more directly applicable to conditions in hospitals in this country. In the United States the attention concentrated by the American College of Surgeons on a definite medical staff organisation for each hospital, on the keeping of accurate clinical records, and on the provision of diagnostic facilities, has done nothing but good. But the merits of the system should not blind us to its limitations, and it might be improved so as to cover better those aspects of hospital life that are of less immediate concern to the medical profession. Note has been taken of the slight emphasis placed by the system on the nursing services; and it is surprising to see that such a question as

Is the general atmosphere of the hospital (*a*) Pleasant with cheerful wards? (*b*) Suggestive of a reasonable amount of interest in the patient?

is awarded only 5 points in a total of 1000.

The system of hospital visiting introduced in London by King Edward's Hospital Fund, with its emphasis primarily on the lay and administrative aspects (not forgetting the amenities for the patients and for the staff) has been a potent factor in raising standards not only in London but indirectly throughout the country. Among the subjects to which the King's Fund has given attention in recent years are several which have led to widespread changes. Its well-known reports on hospital catering were initiated by inquiries made to visitors, as also were the report on the supervision of nurses' health, and the health record forms now used by many hospitals for their staff. Among the latest examples is a movement for the provision of a modern type of interior-spring or rubber mattress for the comfort of patients; and "comfort of patients" is a heading that has appeared repeatedly in the handbooks used by the Fund's visitors. In these and similar respects the American system is deficient. But a combination of the two systems might well give us an entirely satisfactory scheme of approach for all those now responsible for maintaining or improving hospital services. Furthermore, periodic surveys of the hospitals on these lines—possibly conducted by some non-official body sponsored by the Royal Colleges—might provide material for comprehensive reports to the Central Health Services Council and to the public. These reports would show how far the hospitals are able to realise current ideas of what they ought to be.

Annotations

NUFFIELD COLLEGE OF SURGICAL SCIENCES

Lord Nuffield's gift of £250,000 to the Royal College of Surgeons, which was announced last week, has been made "for the promotion of research and education in the surgical sciences, and in order to increase facilities for young surgeons from the Dominions, the United States, and other countries, who come to Britain for advanced studies." These general terms Lord Nuffield has translated into more concrete suggestions for a residential college to be attached to the Royal College, where students will have easy access to museums, library, and laboratories, and in their collegiate life opportunities to meet their teachers and seniors outside the operating-theatre and the lecture-room. Here, too, distinguished visitors from abroad will find a congenial centre. Though the foundations of the new Nuffield College have yet to be laid, it will soon have at least a partial existence, for the scheme is an extension of the experiment which the college are making in the New Year of providing in an adjacent house residential accommodation and common-rooms for 20 postgraduate students. Through the Sims travelling professor the college have already made fresh contacts among their colleagues abroad, and this gift will enable them to receive hospitably their new and old friends who come to pay a return visit. In welcoming Lord Nuffield to their honorary fellowship the college have recognised his many stimulating services to medicine, of which this latest gift is yet another example.

HYPNAGOGIC HALLUCINATIONS

SINCE the Pharaohs, and especially since Freud, dreams have been studied by soothsayers and psychiatrists. The similarity between dreaming and madness has often been pointed out; less attention has been paid to the peculiar states that characterise the transition between sleeping and waking. Familiar as they are to a majority of people, the "hallucinations" of the hypnagogic state, and the other normal disturbances of thinking and sensation which occur in falling asleep or in waking

up, are sometimes misconstrued by doctors, who mistake them for symptoms. They are also, as a letter from a correspondent elsewhere in this issue shows, sometimes alarming to the patient.

Hypnagogic hallucinations have been pretty widely recognised and investigated since Maury's report of 1861. Disturbances of the body image, however, during the hypnagogic or hypnopompic transition, have seldom been studied. They occur fairly often, and as good a description as any was provided by Paul Federn, the psychoanalyst. The body, he pointed out, seems to become flat and two-dimensional, and its surface may be distorted in many directions. The distance between symmetrical parts can appear enormously increased, as can many other bodily proportions. Parts of the body may seem normal while the rest becomes a vague mass, either much diminished or much enlarged. Sometimes the body seems to end at the bottom of the trunk, or at the knees; on the other hand, parts of the middle of the body may disappear. The borderline of the body in one direction may become blurred, and may seem to move in this direction. The face and head are usually spared from any distortion, as are also those parts of the body which are fully supported on the bed. Paul Schilder likewise described such phenomena; for example, one of his patients felt, as she was falling asleep, that she became smaller and smaller, until she was only a few centimetres long. Schilder drew attention to the similarity of this experience to those which may occur in dreams and in the first stages of hypnosis. The similarity to certain intoxications from mescaline is also striking. Not everyone would be disposed to go as far as Schilder in interpreting these phenomena in psychoanalytical terms, and relating them to the libidinal structure of the body image. Few, however, would contest their relevance to the problems of self-perception which are of such interest to neurologists and psychiatrists alike.

INCIDENCE OF DIPHTHERIA

IN his report for 1947 on the Seacroft Hospital, Leeds, Dr. E. C. Benn records that of 121 patients admitted with a notified diagnosis of diphtheria only 42 had clinical attacks (36 faucial and 6 simple nasal infections), while another 10 proved to be healthy carriers. In the 17 confirmed cases (including carriers) with a history of immunisation recovery was rapid and uncomplicated.

Ten years ago the medical superintendent of a large fever hospital could not have reported such modest figures. Without doubt the main agent in the decline has been mass immunisation, though even now the success achieved years ago in many American and Canadian cities is not paralleled here. Martin [1] points out that diphtheria mortality began to fall at the beginning of this century. This was due mainly to improved hygiene and treatment, and particularly to the introduction, in 1895, of antitoxin—which has since been improved and is now administered more intensively. Nevertheless, considering that the ætiology of the disease had long been known, the downward trend was disappointingly slight until 1940 when, with the start of mass immunisation the fall quickened; in 1946 mortality was less than a fifth of what might have been expected with the previous slower decline. The number of cases notified each year has fallen from an average of 60,000 (uncorrected) in the pre-immunisation years to 10,500 (corrected) in 1947. The decline in mortality has been still more rapid, partly owing, as Martin says, to the better chance of survival of the previously protected when they contract clinical diphtheria. As a cause of death the disease has fallen from third to sixth place in the 1–5 years age-group, and from first to third place in the 5–10 age-group.

1. Martin, W. J. *Mon. Bull. Min. Hlth P.H.L.S.* 1947, **7**, 232.

Improvement, however, is not uniformly good; during the last year or two there have been small localised outbreaks in the North and in Wales, due either to local variations in the extent of immunisation or to real regional differences of the sort that was recognised in pre-war years. The decline in the attack-rate has been most rapid in London; whereas in 1937–38 the rate here was 28% above the rate for the whole country, in 1946–47 it was 12% below the general rate. In nearly all "density areas" incidence was considerably lower in 1947 than in 1946. Martin observes that, as might be expected, the preschool child and the adult were relatively more often attacked in 1947 than in 1944; the greatest fall in the attack-rate has been in children aged 10–15, among whom the rate in 1947 was only a fifth of that in 1944. This is a reversal of the previous pattern throughout this century. As to sex incidence, the attack-rate is still much higher in adult females, but the difference is now less than it was, especially at age 25 or over.

The aim is to increase the percentage of immunised children to at least 75, and efforts should be concentrated particularly on the protection of infants under one year. With a larger initial dose of the prophylactic (0·5 ml. A.P.T.) and reinforcing doses (0·2 ml. A.P.T. or 1 ml. T.A.F.) midway between infancy and school age and again at school entry, diphtheria is likely to become still more rare.

BLOOD-PRESSURE AND THE SUPRARENAL CORTEX

MANY years ago, when it first became clear that the suprarenal had some part in the production of hypertension, the association seemed fairly straightforward. French workers, for instance, claimed that hypertension was accompanied by hypertrophy of the gland. This was not confirmed, and attention shifted to adrenaline itself. Then it emerged that the simplicity of the problem was illusory; for some twenty years ago the reports of Rogoff and Stewart [1] and of Hartman and his colleagues [2] revealed the vital rôle of the cortex, and within ten years the brilliant research of American [3] and Swiss [4] workers culminated in the isolation and synthesis of a series of cortical hormones. Of these the most important was desoxycorticosterone with its specific action in raising the blood-pressure.[5] The intensive work on Addison's disease prompted by observation of the potent action of cortical extracts in this previously fatal condition, brought to light the prime importance of the sodium and potassium ions; and it was immediately asked whether the blood-pressure changes in Addison's disease were due directly to lack of cortical hormones or to disturbance in the electrolyte pattern of the tissues. This question was almost immediately overshadowed by the experimental observations of Goldblatt and his associates on the effect of renal ischæmia in producing hypertension.

Probably what we vaguely describe as essential hypertension is a collection of conditions. Four factors clearly take leading parts—adrenaline; one or more of the hormones of the suprarenal cortex; the sodium and potassium ions; and renin—but how these factors combine in any one case no-one can tell. Perera and his colleagues [6] have reported the development of hypertension in 8 out of 24 patients with Addison's disease under protracted treatment with desoxycorticosterone

1. Rogoff, J. M., Stewart, G. N. *Science*, 1927, **66**, 327.
2. Hartman, F. A., MacArthur, C. G., Hartman, W. E. *Proc. Soc. exp. Biol., N.Y.* 1927, **25**, 69.
3. Mason, H. L., Myers, C. S., Kendall, E. C. *J. biol. Chem.* 1936, **116**, 267.
4. Steiger, M., Reichstein, T. *Helvet. chem. Acta*, 1937, **29**, 1164.
5. Soffer, L. J. Diseases of the Adrenals. London, 1946; p. 215.
6. Perera, G. A., Knowlton, A. I., Lowell, A., Loeb, R. F. *J. Amer. med. Ass.* 1944, **125**, 1030.

acetate. As an interesting corollary, Perera [7] has recorded the case of a hypertensive patient who developed Addison's disease; with desoxycorticosterone therapy the hypertension continued, but when the condition was treated with salt alone the blood-pressure fell to normal, even though with both treatments a normal serum-sodium was maintained. He has also shown: (1) that while the subcutaneous administration of desoxycorticosterone acetate for a week to normotensive patients had no effect upon the blood-pressure, its administration to hypertensive subjects for 1–4 days raised the pressure[8]; and (2) that this pressor action in hypertensive subjects was prevented by the rigid restriction of sodium-chloride intake, which also caused a slight decrease in "resting" blood-pressure.[9] The pressor action of desoxycorticosterone acetate in hypertensive patients has been confirmed by Goldman and Schroeder,[10] who gave this substance intravenously. They also found that in normotensive subjects it had no effect upon blood-pressure. Selye [11] noted in desoxycorticosterone-treated animals an increase in the serum sodium/chloride ratio; he later observed this increase in some hypertensive but never in normotensives. Arising from this he recorded apparent benefit from the treatment of hypertension with ammonium chloride 6 g. daily, particularly where the serum sodium/chloride ratio was raised. Finally Grollman [12] has reported that in 4 out of 6 hypertensives a severely restricted salt intake causes a fall in blood-pressure.

NEW PROSPECTS IN THE YOUTH MOVEMENT

> "... youth work is properly regarded as a form of preventive and constructive social medicine providing a cultural health service. It is one part among many parts of the systematic effort which our society makes to stop the transmission to the new generation of the cultural disorders of the old ...."

In *The Outlook for Youth Work*,[13] Mr. L. J. Barnes develops his theme with vision and passion. Young people in our uneasy day need to learn to carry freedom, and freedom he conceives as something other than the absence of formal restraints: man can develop himself only by helping to develop the human community, he believes, and many of our difficulties and disasters can be traced to "our forbears' absurd identification of individual freedom with absence of agreed social purpose." The young are faced with a society in which three trends are discernible: social groups may advance beyond freedom in its negative form (absence of restraint) to freedom in a positive form; or, by blind submission to a leader, they may be released from the alarming isolation which negative freedom begets; or they may conform compulsively to accepted patterns—a sort of automatism which some, he says, find typical of Western democracy. In this country we are groping towards more positive forms of freedom, as witnessed by measures of social security and economic planning; and in the task of helping young people to grow towards the ideal of positive freedom the youth organisations have a great chance, and a great responsibility.

Mr. Barnes has some free and positive ideas on the way they should set about it. He suggests that the voluntary organisations should now combine to form a Central Research Council for Youth Welfare to study the best means of providing the young with an opportunity to grow fully, as nature intends them to do, into people whose behaviour is "whole-hearted or whole-natured, as proceeding from a personality not divided against itself and not disorganised by feelings of guilt, inferiority, isolation, or fear." He calls such behaviour "spontaneous" because it is "immune alike from the anxieties of automatism and the obsessions of fascism, and is neither hysterical nor compulsive." Youth workers, he thinks, must learn that preaching does not pay, and that it is better to start from the belief that, given appropriate conditions, people can achieve the spontaneity and integrity which enable them to find the good life. But we need to know much more about the conditions which favour such personality growth, and hence the need for research.

He is perhaps asking rather much of the harassed—and voluntary—youth workers, as Dr. J. Macalister Brew points out in *Social Service*.[14] They are not numerous, and they already work exceedingly hard. Their anxiety has also been roused by Mr. Barnes's encouragement to them to forget some of the old destruction between official and voluntary agencies. Nevertheless, Mr. Barnes is surely right in saying we must find out about these things; and the youth service "already possesses the research material and the laboratory space, namely the young people in clubs and units." One practical experiment could be tried immediately: the youth service, though it always favours fresh air and exercise, has never paid much attention to the diet of its members. He proposes that clubs might join together, in scientific farming enterprise, to produce whole-wheat flour, milk from tuberculin-tested and attested herds, and fruit and vegetables. It would mean a business alliance between urban clubs, and bring them into collaboration with Young Farmers' Clubs and other rural organisations. On the long view, he suggests that the youth service should be extended to cover all ages between 7 and 25, the young people being grouped as juniors from 7 to 16 (or 14) and seniors from 16 (or 14) to 25. Like barristers taking silk, they would be at liberty to choose when they were ready to move up.

THE KING'S HEALTH

LAST Monday the following bulletin was issued from Buckingham Palace:

> Repetition of tests to measure the degree of arterial obstruction has given the following information:
>
> In the left leg and foot the process of restoration of circulation has reached a stage which would be sufficient to permit some activity. In the right leg and foot re-establishment of circulation, while progressive, has been less rapid, and it is still of a degree which allows only strictly limited activity indoors. The nutrition of the right foot is satisfactory.
>
> With the passage of time and continuing care, further improvement in the circulation of both legs and both feet may be anticipated. We have advised His Majesty to remain in London for the time being, but hope that early in the New Year it will be possible for him to continue his convalescence in the country.
>
> The improvements in the King's health, which we are happy to record, are in no small measure the result of His Majesty's willing submission to certain irksome restrictions and of his complete coöperation in all measures of treatment.
>
> MAURICE CASSIDY
> THOMAS DUNHILL
> J. R. LEARMONTH
> J. PATERSON ROSS
> MORTON SMART
> JOHN WEIR.

7. Perera, G. A. *Ibid*, 1945, **129**, 537.
8. Perera, G. A., Blood, D. W. *J. clin. Invest.* 1947, **26**, 1193.
9. Perera, G. A., Blood, D. W. *Ibid*, p. 1109.
10. Goldman, M. L., Schroeder, H. A. *Science*, 1948, **107**, 272.
11. Selye, F. L. *Canad. med. Ass. J.* 1947, **57**, 325.
12. Grollman, A., Harrison, T. R., Mason, M. F., Baxter, J., Crampton, J., Reischman, F. *J. Amer. med. Ass.* 1945, **129**, 533.
13. Report prepared for King George's Jubilee Trust Fund, 166, Piccadilly, London, W.1. Pp. 143. 3*s*. 6*d*.
14. December, 1948–February, 1949, p. 101.

Special Articles

A TEACHING MUSEUM IN MINIATURE

SLICES MOUNTED IN PORTFOLIOS

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IN the teaching of pathology no doubt the fresh, or wet preserved, specimen in the student's hands is the most informative, but this is not always readily available, and some form of mounted specimen becomes essential. The difficulty of getting specimen-jars and their prohibitive cost force one to seek alternative methods of mounting and first directed our attention to the value of sliced preparations. For large solid organs and tumours the method is ideal, and it is surprising how often very instructive preparations can be made from the most unlikely specimens. In solid tissues consecutive slices mounted in sequence in one frame (fig. 1) make visual reconstruction of a whole disease process quite easy. Hollow viscera mounted as such are usually unsuitable.

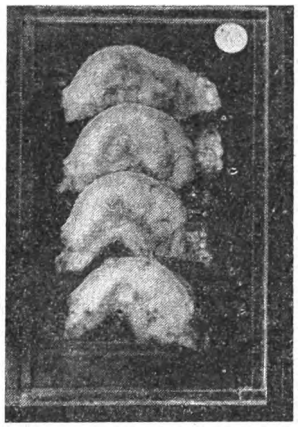

Fig. 1—Serial sections mounted in one folio to illustrate chronic mastitis and carcinoma.

The framed slices are fairly light and can be taken in the hand and examined with a lens. Optical problems are are reduced to a minimum, for the specimen is in a transparent solid medium and almost touching the 'Perspex' on both sides. The framed specimen forms one folio of a set which may include a tracing of the specimen on a transparent overlying sheet with explanatory notes, one or two photomicrographs in a coloured transparency, possibly a photograph or a drawing of the original tumour, a history of the case and the findings at necropsy or at operation, perhaps some remarks on the condition in general, and a list of references for further reading (fig. 2). The whole set of folios is in an opaque portfolio bound with ring clips and can be stored on the shelves like a book. There can be very little doubt that many of the large pallid monsters that we see floating on our museum shelves are suffering from an excess of exposure to light, and that a small part of them, properly mounted and with the colours adequately preserved, would give a far better picture of the pathological processes meant to be illustrated.

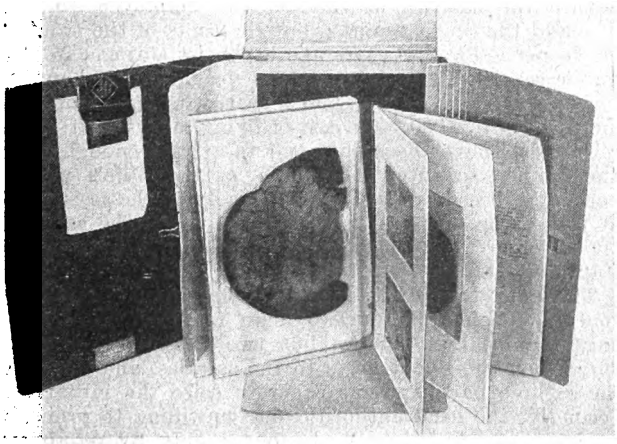

Fig. 2—Portfolio containing a slice of carcinomatous liver, 2 photomicrographs, a photograph of the uncut liver, a history of the case, a description of the specimen and its histological features, and a lantern slide.

There is no claim for originality in the mounting of a flat slice in a narrow cell, but one may emphasise the way in which a very large part of the material required to give an intimate knowledge of pathological processes can be presented in a very small compass.

PREPARATION OF THE SPECIMEN

This is similar to that followed in the preparation of museum specimens which are to be stored in kaiserling (K) 3, but it is necessary in the first place to cut a thick slice of the fresh specimen, avoiding distortion of the organ, at the site which is to be mounted. This should be laid on a piece of lint or thickish cloth on the bottom of the fixing tray, with another cloth and a sheet of glass laid over it in the fixative to avoid warping; the absolute minimum of pressure, however, must be used. Such a slice in solid tissue should be at least 10 mm. thicker than it is intended to mount, to allow for the final trimming down; in soft permeable tissue like lung 20 mm. is better.

The thickness of the mounted slice is a matter of choice, and very thin sections can be mounted effectively, as in the beautiful preparations of Gough.[1] We have found that, to give an appearance of solidity and verisimilitude, both as regards the capsule or periphery of the specimen and where hollow spaces or tubular structures figure in it, a final thickness of 6–8 mm. appears to be the most suitable. Slices showing much engorgement with blood must be washed before fixation, and this is perhaps best done in saline solution, to prevent lysis and staining of tissues.

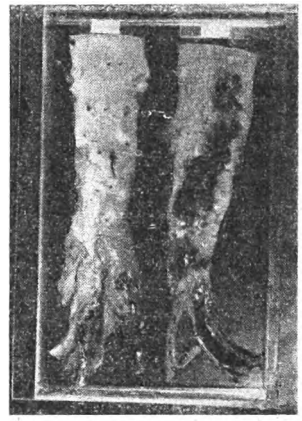

Fig. 3—Atheroma with ulceration and adherent clot.

Fixation and Shaping

This process has far too many problems to be discussed at length here. The object of the original slice is to enable the fixative to enter rapidly from both sides and to permeate the tissues throughout before they are altered by autolysis or decomposition. The pieces of cloth lying in contact with the tissue should be renewed after the first 24 hours; otherwise the coagulated exudate on them may form an impermeable layer. A parallel slice undergoing fixation at the same time can be cross cut every day or so to find out when fixation is complete and the slice is ready for paring down. Incomplete fixation is likely to be followed by oozing and discoloration of the mounting medium.

An alternative to the original slice, where large solid organs such as the liver are concerned, is to wash out the contained blood through the hepatic veins and then to inject K1 under slight pressure, tie off, and immerse the organ in K1. The tissue will then become fixed throughout in a few days. The difference between such treatment and the mere putting of the organ into K1 needs to be seen to be appreciated. In the latter case a thin fixed crust of about 5 or 6 mm. is formed

1. Gough, J. *Occup. Med.* 1947, 4, 86.

overlying a central dark soft mass, and further penetration is both difficult and unlikely to produce a picture comparable to that on the surface.

The slice when fully fixed is now cut to the proper size. This is done on a board having adjustable rails of perspex or glass rod on it to hold the specimen and guide the knife, as figured by Anderson.[2] It is convenient to have two boards, one with the rails giving the correct thickness for mounting, and one with rails slightly thicker. A flat surface is cut on the fixed slice using the higher rails, and then by reversing the slice onto the other board and cutting away the other rough surface, the final thickness is obtained. A long, very sharp and rigid knife (a "ham knife") is suitable for this purpose, and the specimen should be cut as far as possible in one sweep from heel to tip of the knife. It is necessary to set the front guide rail close to the front edge of the board to give freedom to the hand and knife handle, the second rail being brought forward until it touches the back of the specimen. The shaped slice is now washed, recoloured in alcohol, washed again, and put into arsenious glycerin or K3 ready for mounting.

MOUNTING THE SPECIMEN

Preparation of the Frame.—We have simplified this by standardisation, and the required elements—two sheets of perspex 30 × 20 cm., and strips 1 cm. square—are purchased in bulk already cut to measure. The parts are stuck together with a fairly liberal streak of 'Diakon,' the four rails being first attached to one sheet, forming a shallow tray, which should be left to dry for an hour or so. After the specimen has been arranged and fixed to the tray, the other sheet of perspex is applied and attached in the same way. We arrange for a $^3/_4$-in. margin of each plate to be left free, one on either side, to permit handling and for binding into the portfolio. The top rail of the case has had already a narrow drill-hole bored at one end, and through this a large needle is inserted, and the cell, now stood up vertically, is filled by gravity from a suspended transfusion bottle containing melted Delepine's jelly.

Setting Up the Specimen.—The specimen requires support by one or two small studs or spikes of perspex which are stuck down on to the back sheet in such positions that they will support the specimen at the sides, or they can be actually pushed into or through it. This is necessary because the cell has to be filled in a vertical position so that all bubbles may be collected at the top and removed through the drill-hole. The hole is finally plugged with a small rod of perspex dipped in diakon.

In working out this method we have been greatly helped by our assistants Mr. H. Butcher and Mr. L. Pettit.

APPENDIX

Delepine's Glycerin Jelly Method.—Fix the specimen by any one of the dependable methods. Restore the colour in spirit. Place the specimen in arsenious glycerin until ready for mounting. Mount it in Delepine's jelly.

Delepine's Jelly.—Soak Coignet's gelatin 42·5 g. in water until soft. Squeeze out surplus water, and dissolve gelatin with 150 ml. of saturated solution of arsenious acid in a steamer for 20 min. When the gelatin has been dissolved, cool it and then add the whites of two eggs well whisked. Return the solution to the steamer until it becomes clear (30–45 min.). Filter, add the filtered gelatin to 443 ml. of hot glycerin. The careful addition of dilute gentian, or methyl violet reduces the yellow colour of the gelatin. This is best done with a drop-bottle against a background of artificial light to make the end-point more readily seen.

Arsenious Glycerin

Saturated arsenious acid	400 ml.
Glycerin	600 ml.

The solution of arsenious acid should be made in a fume chamber. Saturation point is about 1%.

2. Anderson, J. How to Stain the Nervous System. Edinburgh, 1929.

The Act in Action

4. THE DENTAL SERVICES

AT the beginning of this year the Dentists Register contained 15,160 names. Some of those registered are, however, not in general practice, and Mr. S. D. Cox, assistant secretary of the British Dental Association, puts their number at about 2500. By this reckoning England, Wales, and Scotland between them have some 12,500 dentists practising on their own; and of these just over 9800 have so far entered the new service.

The number of dentists, never too great, is now much too small. The total has fallen steadily during the last four years; and while the post-war intake to the dental schools will soon raise the rate of additions to the Register, this gain is likely still to be offset by deaths and retirals. Over 4500 are registered under the Acts of 1878 and 1921. Many of these are due to retire soon; and since they are outside the normal flow of gain and loss of those with registrable qualifications, their withdrawal will tend further to deplete the Register. In 1946 the Teviot Committee [1] reckoned that with an intake into the profession of just over 800 a year—which would mean an intake into the dental schools of nearly 900—it would take 20 years to achieve a total of 20,000 dentists. The dental schools, confined in much the same way as are the medical schools, are at the moment powerless to arrange for the training of such numbers.

PUBLIC DENTAL SERVICE

It was against this dark background that the new dental service started on July 5. Plainly some plan had to be followed to ensure that treatment was given to the most needy; and the profession agrees that special consideration should be granted to the expectant mother, the child, and the adolescent. Mr. A. H. Condry, secretary of the Incorporated Dental Society, put it this way: "Dental treatment is, in general, not curative: it is preventive and restorative. Thus it follows that treatment should be applied at the earliest possible age." This principle has been conceded; and yet ironically the public dental service, which exists to serve the priority groups of children and expectant mothers, is the branch which has come nearest to breaking.

In one area at least 30% of the dentists in the public service have resigned in order to enter private practice. Moreover, a further number have handed in resignations which are pending, and others have changed from whole-time to part-time employment; there are virtually no new entrants. The immediate reason for the threatened collapse of this service is the neglect to equate the salaries of the dentists employed to the terms of the Spens report; but the roots of the trouble go deeper. Twenty years ago a dentist starting in the public service was offered £450 a year. (Even now he sometimes receives only £650 a year, with the chance of increase up to £900, plus cost-of-living allowance.) The reward has never been sufficient to attract enough men and women to enter the service as their life's work; and authorities have had to rely largely on the assistance of those who spent a short time in it for the sake of experience. Thus even at July 5 there was insufficient staff.

The dangerous drift since then has been allowed to continue unchecked for two main reasons. First, not only the local authorities but two Ministries—Health and Education—contribute to the salaries, and none of these three parties seems eager to seize the initiative. Secondly, the local authorities are unwilling to promise an increase which can be honoured only by requiring

1. Final Report of the Inter-Departmental Committee on Dentistry. Cmd. 6727. H.M. Stationery Office. 1946.

rate-payers to dig deeper into their pockets; and they fear that any such increase would cause "imbalance" with the remuneration of other professional and technical personnel, who might then claim for themselves a similar increment.

An emergency group of dental officers in the public service has lately been set up to get the position righted; and their demand for a Whitley council is likely soon to be met. The tardiness in establishing such a council is largely attributable to the conditions laid down by the other professional bodies, which insist that the council should be one of dentists only, and that the matters on which it cannot reach a final conclusion should be defined and limited, so that matters concerning dentists are not referred to a general council.

THE GENERAL PRACTITIONER

The cost of the dental services in the first nine months was originally estimated at just over £7 million. Now, it seems, the cost is running at the rate of about £28 million per annum.[2] Possibly with this in mind the Minister of Health has made it known that the dentist in private practice earning under the Act at a rate above £4800 gross will have the excess reduced by half in the new year.[3] The resulting protest from the professional associations derives less from disinclination to accept the cut than from indignation that they were not first consulted. Moreover, officials of the Public Dental Service Association point out that so far they have no evidence that more than two or three dozen dentists are earning amounts beyond those recommended in the Spens report. The proposed reduction does not, however, run counter to the Spens recommendations, which suggested a net income of £1600 for dentists working a 33-hour week at the chairside for 46 weeks in the year (with 6 weeks for holidays and illness); with the 20% betterment which has been conceded the net income is £1920. The justice of the report, whose terms have been accepted by the Minister, is acknowledged on every hand. Most dentists agree that 33 hours a week at the chairside (to which must be added some hours at other work) are enough. Here much depends on physique; and it has to be remembered that on average members of the profession are fairly old. Four years ago Mr. Cox established that the mean age of civilian practitioners was 52, and officers of the Public Dental Service Association set the present average at something over 45.

Hitherto, in an attempt to meet the demand, dentists have sometimes worked considerably more than 33 hours at the chairside—in some instances up to 75% more—and earnings have been correspondingly increased, a few gaining gross incomes at the rate of £12,000 or more a year. It has been agreed that expenses shall be reckoned at a general rate of 52% of gross income; but individual dentists point out that the percentage varies with the locality and the service provided, and with the size of the practice. In future there will be less attraction in these long hours; and there will also be less inducement to persuade people to receive free treatment. It is still too early to judge the proportion of patients benefiting by the service; but the experience of one man with a mixed practice may perhaps indicate the general trend. He says that whereas formerly he treated 10% of his patients under the National Insurance scheme, he now treats 10% as private patients. Nearly all patients in the professional classes have eagerly seized the chance to use the service; the 10% of private patients consists mostly of tradespeople, who prefer to pay rather than accept what they fear may be "utility" service.

The fees payable to the dentist under the Act range from £1 for a simple filling up to 30s. for a compound filling. If more than one filling is done at a single sitting the dentists may earn at almost—so to speak—double rate; but against this gain has to be set the difficult filling taking more than one consultation. Before the start of the scheme one of the greatest sources of income was the supply of dentures. Now a fee of 10 guineas is payable for supplying and fitting a complete set. In the hospital service the cost of a set is fixed at £4 10s.; and if this is taken as the average, the dentist's fee is £6. Normally four consultations precede the fitting; these take some dentists only about 1¼ hours, but most are occupied in this way for 3 hours, and to this must be added the time taken by subsequent adjustments. In complicated cases, or where the dentist aims at an exact reproduction of the previous dentition the profit is much less.

The determination of income by items of service has, perhaps above all else, accounted for the decision of some to remain outside the service. Many of these achieve an unusually high standard; and yet in the service they would gain no more than their less able colleagues. Their refusal also springs often from pride and a sturdy individualism, which prompts them to plan and carry out the treatment they think necessary without reference to an estimates board. They cast a thoughtful eye back on their Service days when they were esteemed officially not by the quality of their work or the severity of the conditions they chose to treat, but by the number of fillings they made per month (which had to reach a certain minimum). They reason that what holds for one public service must sooner or later apply to another, and they are persuaded that circumstances will not compel them to join the service, at least for many years to come.

Many who joined did so with grave misgivings; yet their way has been made unexpectedly easy. The Dental Estimates Board has proved so far very tolerant, allowing a degree of clinical freedom which dentists never expected. Authority has shown itself sympathetic in other directions. For example, dentists may now save time by using a facsimile stamp in place of a signature, provided that this is supported by initials; and arrangements are being made for limited emergency treatment to be carried out without the full charting of the dental state which is at present a first requirement.

The dental practitioner has his difficulties however; and foremost among these is that of supplies. X-ray films have become very scarce, and other materials and apparatus are almost equally hard to obtain. Suppliers complain bitterly of repeated refusals to permit importation of equipment. Before the war this was imported principally from the U.S.A. and Germany. Germany is again prepared to meet some of our needs; but licences are refused on the score that the granting of them might disturb the dollar balance. A similar ban is exercised on imports from France, which can offer a certain amount of equipment.

SPECIALISTS

The dentist has long been concerned that he is allotted less than his due status. This is largely rectified by the conditions under which he is now engaged in the Health Service; and the report on the specialist services, to be published shortly, is likely to augment this favourable trend by sustaining the parallelism with the medical profession first observed in the E.M.S. On the other hand, it is feared that the report may encourage part-time specialist work at the cost of whole-time work and to the detriment of the "temper" of hospital routine. The other outstanding difficulty in the specialist services is that of filling academic posts; this difficulty is, of course, shared by the medical schools.

DENTAL ASSISTANTS

Figures quoted by Mr. Condry show that some time ago at least 90% of the community were in need of dental treatment at any given moment, while only 10%

2. Leading article, *Brit. dent. J.* Nov. 19, p. 236.
3. *Lancet*, Dec. 11, p. 938.

were receiving it; the remaining 80% went untreated. The full extent of the need indicated by these figures has not been disclosed by attendances on dentists in the first months of the service. Many dentists, booked up for three months or more ahead, already make special provision for seeing emergency cases at once, and expectant mothers and children with the least possible delay. More time might be found for these and for others by the further employment of chairside assistants. Such assistants, if competent, can often save 5–10 minutes in a half-hour consultation. In the public service almost every dentist has an assistant; but this does not yet apply to private practitioners.[4] Another possible method is dilution of the work through assistance from hygienists. The encouraging experience of the R.A.F. with hygienists has prompted some to hope that these may be employed in civilian work on such duties as scaling (though amendment of the Dentists Acts would first be necessary). The dental associations are opposed to such a course; and they oppose even more firmly the suggestion, from a few dentists, that technicians should be employed on the mechanical and technical aspects of clinical dentistry. A still smaller group of dentists favour this plan accompanied by revision and enlargement of the dentist's training with greater orientation towards medicine, so that each dentist would be an expert consultant. Either plan would call for the transfer of practice to clinics, to which the majority of the profession objects. The fear in many minds is that with clinics would come a whole-time salaried service. Nevertheless, clinics would bring to an end payment by items of service, which many find degrading; and they would also end the possibility of abuse. Two main abuses are now possible: one is to charge for a filling completed at a previous consultation, and the other is to charge for an X-ray picture that has not been taken.

The importance of the technician has been underlined by the great demand for dentures since July. The technician's position has been much improved of recent years through the efforts of the National Joint Council, set up with the coöperation of the dental profession, which now ensures that only indentured apprentices enter the craft. Whereas before the war technicians earned a precarious £3 or £3 10*s*. a week, they are now certain of a £6 10*s*. minimum, and with the ability supplement most get £10–15. This has had the important effect of attracting a better type of recruit. Mr. W. A. Warrington, representing the associated dental technicians section of the Union of Goldsmiths, Jewellers, and Kindred Trades, reports that of 10 apprentices lately placed by him 8 had matriculated.

Great Britain has some 7000 technicians, of whom about a third are self-employed; and the joint council has lately formed a "fair list" of accredited technicians in this field. Technicians wish to establish themselves as dental auxiliaries; and in fact the joint council has received a draft Bill calling for their registration. At the present time the supplementary training of apprentices is carried out by polytechnic schools; but arrangements for the further training of adult technicians are scanty, and there is now a strong moment towards setting up an Institute of Dental Technology for this purpose.

Technicians are too few for the new need; and their number will not increase rapidly because the joint council meanwhile restricts the intake of apprentices to the rate of 1 to every 3 qualified men. The Denture Service Association claims that it could help to fill the gap. This association speaks for the owners of about half of the 500 premises occupied with the repair of dentures by private contract with the public. These businesses employ, it is stated, a large number of technicians formerly apprenticed to dentists. The association says that, given participation in the service, its members are willing to have their employees submitted to a test of technical proficiency; they are also willing to stop advertising and to guarantee that, where need exists, people will be referred to dentists; but they are not prepared otherwise to abandon their independence. Like the three dental associations, the dental-technicians' unions are opposed to the inclusion of these premises in the scheme.

4. *Lancet*, Nov. 27, p. 875.

CONCLUSION

The general dental practitioner is free to accept or refuse patients as he wishes; and once a particular contract is completed he can treat as a private patient one who formerly attended under the Health Service. In general he is pleased with the operation of the Act in its first months; but he remembers that the British Dental Association has persistently advised its members not to enter the service. The three main objections of this and the other associations are: (1) that the profession should have a greater measure of clinical freedom; (2) that a system of grants-in-aid should be followed; and (3) that no full-time salaried service should be possible without an amending Act. The impairment of clinical freedom has hitherto been less than was forecast, largely owing to the leniency of the Dental Estimates Boards. The principle of the grant-in-aid, though still cherished by many, particularly as it could check abuse on either side, is unlikely to be conceded. There remains the doubt about a full-time salaried service. The selling value of practices has already fallen by 20% or more; and the question of compensation, should a full-time service be started, is unanswered.

Disabilities

19. ULCERATIVE COLITIS: COLOSTOMY

WHEN the question of my having a colostomy was raised years ago I used to say—and I nearly meant it—that I would rather be dead. In the five years since mine was done, as an urgent necessity, I have occasionally doubted whether life is worth living, but never because of the colostomy: financial difficulties, or the illnesses of my family, have weighed far heavier on my mind.

I fancy it comes to this. How much trouble a colostomy will give can be gauged from the state of your bowel beforehand. If you are normally of a constipated or regular-after-breakfast habit there is a good chance that your colostomy will be well-behaved and easily managed. If, on the other hand, you have been having 10 loose motions daily for years you must expect a stormier voyage; though, judging from my experience, anything will settle down in time.

* * *

I started ulcerative colitis suddenly in 1933, when I was 30 and had been 3 years in general practice. Those who look for an emotional background to these cases would, I think, have searched vainly in mine. True, I was not long married, with our first son on the way, and the junior "dogsbody" of a busy country practice. But I was happy, secure, conscious of moderate success in my work, well off (i.e., not losing more than my capital could correct), comfortable in a way that now seems fantastically opulent, and not grossly overworked—that came later. No; the cause was undoubtedly a mild dysentery which I shared with half the village; but, while the village cleared up in a day or two, I became chronic. There were two red-letter days after the acute attack when I was *constipated* (think of it): then I took a dose of salts, and judging by appearances it might well have been acting for the next ten years.

At first my loose inside was no great inconvenience. I tried the various astringents of the pharmacopœia,

chalk (which worked a bit), and even iron. But I soon found that only opium could be relied on, and that in an amazingly small dose. For a year or two 5 minims of chlorodyne (tint. chlor. et morph. *B.P.* 1885) thrice daily was my maximum dosage (about gr. $^1/_{20}$ of morphine). Without it I could not leave home in safety; with it I could live normally with only a tiny anxiety. So I took it and went on with my work, with golf, tennis, dances—all the round which was middle-class country life before the war.

The trick, I found (and I commend it to others), was only to take the chlorodyne after my bowels had acted. You see the point? This is an insurance against overdosage and also against very embarrassing "accidents," because these super-disasters happened only when one's colon had become overdistended and a meal or a hot drink made it suddenly contract. Hence the waits, which drove my wife wild, for my bowels to act before I could take my medicine and join her at the pictures. Now and then, when only time was passing, I would risk it, with results which need not be described but (largely because my wife made fun of them) were more farcical than tragic. There was that time, for instance, when I left my pants and braces in a Hastings lavatory. . . .

This phase lasted three years, during which my "trouble" hardly varied: there were no exacerbations, remissions, or complications, until one day "the spots" started. These were petechiæ round my ankles, which in 24 hours developed into half-crown-size ecchymoses, accompanied by exquisitely tender swellings in one or more muscles (usually in a calf but sometimes in an arm), and in another 24 hours had faded. These "spots" recurred punctually every 16 days for about five months, each time rendering me hors-de-combat for one day. Scurvy? Yes, I think so, because in the end a bottle of ascorbic acid tablets finished them. But by then they had finished me, at any rate as a G.P.; because they forced me to "take proper advice," and that was to retire for a time.

For five months I lay in bed, charting my motions—only 10 today, 25 today, not so good—without any opium. Then I got out the chlorodyne again and retired to a Devon beach for a year.

* * *

The scene changes to 1942, with me doing an "evacuated" journalistic job, little inconvenienced by the looseness. Then gradually I began to develop an obstruction. That is, I no longer needed the opium, and in a month or two had to strain increasingly hard to get anything through. With this I had such bellyaches as I hope never to feel again. When even enemas failed I knew it was the surgeon's turn. He agreed—there was a rectosigmoid stricture—so I started 1943 with a colostomy on Jan. 1.

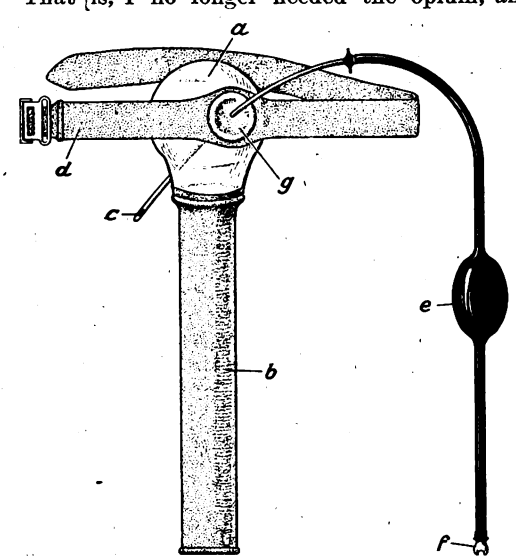

Fig. 1—Colostomy washout apparatus, consisting of plastic dome with two openings, a small one for inserting a catheter and a larger for the exit pipe. The whole is held on by a webbing belt. The maker is Donald Rose, of 36, George Street, Portman Square, W.1.

That was the worst year, because until near its end I could not control the colostomy. I tried washouts with a catheter and kidney-dish—twice; and each time spent an hour afterwards mopping the walls and ceiling. One might as well have held a bucket below a fire-hose nozzle to catch the jet. I tried increasing the opium; but it no longer took effect. So I wore a belt with a bag during the day and slept wrapped in cellulose wadding and rubber sheets. I still worked, in a secluded corner near the window.

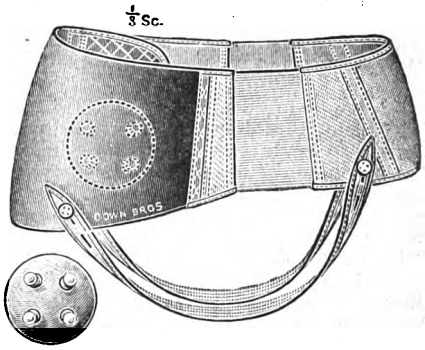

Fig. 2—Simple calico colostomy belt with rubber or plastic insertion and St. Mark's shield. I now prefer an even simpler, narrower all-rubber belt which is free of clothing coupons. The belts are made by Messrs. Down Bros.

In those bleak months my wife and I loathed Charles, as we called the colostomy; but we loathed it impersonally, not as part of me. The illusion of an isolated existence is easily maintained, because the extruded bowel besides having, it seemed, no decent feelings also has no feeling, except for its own contractions. Then, miraculously, almost in the twinkling of an eye, all was well. In October, 1943, I was operated on for pyloric stenosis (that is another story). After this a friend told me of the washout cup (fig. 1) which I have used ever since, and in a week I could exchange my bag for the simple belt and St. Mark's shield illustrated in fig. 2, and "accidents" became a rarity. Now my day is as follows:

> Get up at 6.30, change into a sweater and stockings, put on my washout cup, and retire to the lavatory with a $1^1/_2$-gallon can of warm water, a chair, a quart jug, some cellulose wadding, and a *book*. (That is the great joy: it isn't even a wasted half hour, for one can read.) With the jug on the chair, and the book propped behind it, I slowly pump in the water, 1–2 pints at a time, letting and if need be encouraging it to squirt out again between injections. One soon learns to know when no more need be done, and at that stage I pummel and prod myself to ensure that all the water is out. This is an important step for the rest of the day's comfort. Then I clip the end of the exit pipe with a large paper-clip, and come out to shave. If any water is left in it usually appears during this process. If one is doubtful, a few toe-touching exercises will help. It only remains to remove and wash up the cup, have a bath, cover the colostomy with a good pad of wool, and apply the belt. One should be ready for breakfast at 8 and have no further trouble all day. At night I renew the dressing and wear a linen binder instead of the belt.

What can I do with a well-controlled colostomy? Anything I could do without it. Even staying at a hotel, provided it has a bathroom and w.c. combined, presents no difficulties. Through one's clothes the belt is quite unnoticeable, and there is no smell whatever. Before July 5 dressings were expensive, for I use about $1^1/_2$ lb. of cotton-wool and $^1/_2$ lb. of cellulose wadding weekly; but now even that little burden has been lifted.

In England Now

A Running Commentary by Peripatetic Correspondents

THE problem of presents is here again in an acute form. For the very young and very old it is fairly easy; they are pleased with most gifts. What matters is the receiving of a present: what happens to it afterwards is often unimportant. An old gentleman I knew had all the ties and socks and handkerchiefs he wanted and he re-read his old books. So his wife just bought a box of linen handkerchiefs for his Chistmas present and then stored them away for presentation again next year. He was always delighted at being remembered and never suspected the wiles of his wife. It used to be, and perhaps still is, the custom to take a present when visiting a newborn baby. I know of one pair of knitted bootees which went from family to family on a new housing estate and were eventually presented to the original donor when her second child was born.

* * *

To me, as a doctor's wife, the greatest disaster of the new service is the unfortunate instruction to patients on the new cards: go to the surgery whenever you can and ring early if you cannot. They do indeed try to ring early; they queue for the line, and they tend to avoid having to do this by ringing earlier and earlier. The result is that I am usually not dressed by nine o'clock, let alone having time to wash or have breakfast; even when the "staff" are not down with chickenpox, the early morning is the time when I am single-handed and least able to run a telephone exchange. The instructions imply that someone will be available to deal with calls, and the patients, oddly enough, take it for granted that this is so since July 5.

More crippling still is the notion that surgeries are now chronically overcrowded and that all minor troubles had therefore best be handled by telephone. All these people demand to speak to the doctor personally, and many of them feel that they are doing him a kindness by ringing up and so saving him a proper consultation (and themselves a long wait). The really considerate want to save him visits too by trying to explain their troubles at length and getting advice by telephone, and I am quite helpless against them. I have not the time to explain (nor have they the inclination to hear) that they would in fact force him to spend half an hour doing a five-minute job badly if I did fetch him to the telephone; and that surgery would be a farce if the telephone were allowed to interrupt every consultation. Nor, though qualified, can I pass myself off as the doctor and advise on the spot, since my domestic emergency surpasses anything these people have any experience of. The best I can do is to bully them into parting with their name and address, put the receiver down before they can say any more, hope they will think we have been cut off, and have them visited that day. It's a horrible job and puts me in the wrong all round. Only the fact that there are no more bills to send makes life bearable; but the patients naturally think that I have become abrupt and unfriendly because I am now "part of the service!"

I have seen it mentioned that doctors' households enjoy a measure of priority in the matter of domestic staffing; and this is just sufficiently true to give one a nice, though false, feeling of security; it breaks down when it comes to securing the actual domestic. The way it works is that the local labour exchange, having satisfied themselves of one's need and genuine claim to priority, undertake to send along for interview any domestic who happens to come into the open market, and to "direct" her to work there in any domestic capacity required (regardless of the fact that none of them can cook and hardly any are safe with children). If domestics ever got into the open market for good reasons, the arrangement would no doubt work admirably; in my experience the reasons, though highly varied, are never good. I have interviewed tuberculous girls, pregnant girls, dwarfs, and epileptics; and I finally engaged an Irish girl whose real desire was to serve behind a bar, but who could be directed into domesticity. A bull in a china shop is the first analogy that comes to my mind, the only "china" to survive at all being the children. The same sort of thing, with variations, happened with her successor of the uncontrollable temper, and since then I have merely longed for the bliss of peace and no more interviews. I should be interested to know how many doctors' wives have benefited from their claim to domestic priority.

* * *

The hospital was large, modern, and well-appointed, but the lift had stuck midway between the sixth and seventh floors. The five men had pressed the buttons and rattled the gates for some time in vain.

"Where did you want to go, Sir Charles?" asked the tall one who looked like a matinée idol. The famous cardiologist shrugged wearily. "Some case Pulse-Palpable asked me to see for him in Fourteen; sounds like a heart-block after a coronary thrombosis, but he can't make out the E.C.G. And you?" he concluded politely. "Oh, I'm going the same way, sir, to see a query aphasia or dementia. May have to call you in, Alec." He glanced indolently at a bespectacled man with a dome-shaped forehead. "Well, if you want me," said the psychiatrist, "I've got a chap to see that sounds like an Alzheimer in Fourteen, so I can kill two birds." The fourth man had been pacing from side to side and peering into the lift-shaft. "What a confounded waste of time this is!" he burst out. "Got to be at Moorfields by four. I only came up to look at some fellow's discs too."

The ruddy-faced elderly man in the raglan murmured sympathetically, "I'm rather busy myself—I'm a G.P." The others smiled politely, and he went on, twisting an old felt hat in his big hands, "One of my patients is in here, pretty ill, poor chap, and I promised his missus I'd look in and see him. Used to be a hefty fellow, too; played for years in our local soccer team. He was a jolly good goalkeeper, old Jack. Robinson his other name is; perhaps some of you gentlemen know him?" They shook their heads. The lift gave a jerk. As it started slowly to ascend, the four consultants glanced hastily at the "Request for Opinion" cards in their hands. All four cards read: *Robinson, J. Male. C. of E.* 25,392. *Wd.* 14.

* * *

The district officer rang up to say that a Dyak had just dropped dead in the bazaar, a few yards from his office window. He added that the victim had terrible convulsions before dying and was clutching a bottle of our hospital medicine in either hand. Thinking to myself that the usual heavy outpatient attendances would probably be lessened for the next few weeks, for news travels fast here, I agreed to perform the suggested necropsy on the following day.

When I was doing a ward round next morning, proceedings were interrupted by the entrance of the Chinese chief clerk, looking extremely perturbed. He announced that about twenty Dyaks, each with his parang,* were picketing the mortuary, did not intend to allow a post-mortem, and would like blood money into the bargain as the hospital had supplied poison in place of medicine. The district officer was summoned, and after a parley with the Dyaks we went to inspect the exhibits. The bottle of cough medicine was untouched, but two ounces of lin. methyl salicyl. was missing from the other bottle. The superficial appearance of the corpse suggested asphyxia. Both the dispenser and the dresser concerned had taken pains to ensure that the deceased knew which bottle was which, and he had himself requested a supply of liniment as an afterthought to receiving the other medicine for his sore throat. Honour was satisfied by the issue of a certificate saying "Cause of death unknown. Foul play not suspected." We felt that the loss to forensic science of the necropsy was offset by the fact that, locally, one head is better than none.

* * *

"You know, dear," said one of the patients in the doctor's waiting-room to her friend, "the X rays you get on this new service are no good. They don't use the same voltage or something as they do for private X rays."

* Midway between a billhook and a meat chopper.

Letters to the Editor

PENICILLIN THERAPY OF MIXED SKIN INFECTIONS

SIR,—Although the application of penicillin cream to surface lesions infected with streptococci (Lancefield's group A, C, or G) usually eliminates this organism rapidly, occasional failures occur. For example, Colebrook [1] has noted failure in the penicillin treatment of burns infected with streptococci and *Staphylococcus aureus*. It has been suggested that a possible cause of such failures may be an associated infection with penicillinase-producing organisms.[2] We wish to present direct evidence that in a mixed infection with penicillinase-producing *Staph. aureus* and streptococci, the latter organisms, although sensitive, are rarely eliminated by local penicillin therapy. Emphasis is laid on *Staph. aureus* because it is so very commonly present in large numbers in streptococcal lesions.

The evidence is derived from the bacteriological sampling of skin lesions infected with both streptococci and *Staph. aureus*. The lesions were: (1) chronic vesicular eczema (10 cases); (2) skin-sensitivity reaction (7 cases); (3) leg ulceration, varicose or traumatic (6 cases); and (4) miscellaneous—infective dermatitis, seborrhœa, &c. (10 cases). Although streptococci were not primarily responsible for the condition their presence was usually manifested by undesirable clinical effects—exudation, crusting, or œdema. The lesions were treated by the daily application of penicillin cream or jelly (400 units per c.cm.), and swabs were taken at various intervals during therapy. Cultures were made aerobically on penicillinase-blood-agar plates, anaerobically in penicillinase-nutrient broth, and also in most instances, on gentian-violet media. The criterion of penicillinase production was the ability of a 24-hour broth-culture to inactivate 30 units per ml. of penicillin during 3 hours' incubation at 37°C.

The bacteriological results are shown below, the data being based on all swabs taken between the 8th and 21st day of penicillin therapy.

	Penicillinase-producing Staph. aureus	
	Absent	*Present*
Elimination of streptococci—		
"Successes"	8	1
"Partial successes" ..	7	4
"Failures"	3	10
Total patients	18	15

The patients have been divided into two groups according to whether or not penicillinase-producing *Staph. aureus* was isolated from the skin lesion at any time during treatment. Each of these groups has been subdivided into three categories. The "successes" are those patients whose lesions never yielded streptococci after one week's treatment; the "failures" are those whose lesions yielded, on at least one occasion, more than 20 colonies of streptococci; and the "partial successes" are an intermediate group in which, after treatment, streptococci were isolated in very small numbers, often being detected only by the broth-subculture technique. Inspection of these results shows that much greater bacteriological success was obtained in the absence of penicillinase-producing *Staph. aureus* than when this organism was present. Statistical analysis shows a significant association between the isolation of penicillinase-producing *Staph. aureus* and the persistence of streptococci in the lesions. This association is highly significant both when the results in the intermediate groups are regarded as "failures" (by factorials $P = 0{\cdot}018$) and when they are regarded as "successes" ($X^2 = 6{\cdot}6$; $P<0{\cdot}02$).

Although the figures quoted prove merely an association, the simplest explanation of the finding is that penicillinase from the staphylococci is destroying the locally applied penicillin.

The failure to eliminate streptococci was generally associated with clinical failure of penicillin therapy. The correlation between the presence of penicillinase-producing *Staph. aureus* and clinical failure was, however, less striking. This is only to be expected, as the streptococci were usually secondary invaders and variations in the underlying condition might well obscure the picture. There is sufficient clinical evidence, however, to support an opinion that local penicillin therapy of skin lesions with a mixed infection of streptococci and penicillinase-producing *Staph. aureus* is likely to fail in about two-thirds of the cases. Although the application of more concentrated penicillin preparations might secure the removal of streptococci in a few cases, a satisfactory method of dealing with such a mixed infection is the local application of another chemotherapeutic agent such as dibromopropamidine.[3]

M.R.C. Industrial Medicine and Burns Research Units, Birmingham Accident Hospital.

C. N. D. CRUICKSHANK
J. R. SQUIRE
ELIZABETH TOPLEY.

1. Colebrook, L. (personal communication).
2. Fleming, A. Penicillin. London, 1946; p. 88.
3. Wien, R., Harrison, J., Freeman, W. A. *Brit. J. Pharmacol.* 1948, 3, 211. Bull, J. P., Ross, W. P. D., Topley, E., Squire, J. R. *Lancet*, Nov. 6, p. 747.

THE GENERAL PRACTITIONER

SIR,—I was interested to note the discrepancy between your finding that the public welcome the National Health Service, and Dr. Weston's impression that they do not. My own experience is that the discrepancy is apparent rather than real; patients will vote for or against the service according to their grasp of its true intentions. It has not been easy for them to get such a grasp, and now that most of them have their medical cards, and have assimilated the printed instructions, it has become impossible.

The idea of getting something for nothing is sufficiently startling for people to wonder what might be behind it. I spent most of June and July explaining that what is behind a free health service is the general recognition that health should be the birthright of everyone; that the nation no less than the individual would benefit if attention to health were made independent of finance and other irrelevancies.

The response to this gospel was an evident desire to take my word for it, tempered by the suspicion that there must be a snag somewhere, if only one knew where to look for it. I averred categorically that there was no snag, at least from the patients' point of view, and that any rumours to the contrary should be ignored. Then came the cards to give the lie to my preaching, to confirm the patients' worst suspicions, and to sow distrust where confidence had begun to grow. Back came the patients—some dismayed, some aggressive, all disappointed—to show me page 2: "There, doctor, what did I tell you? I would rather go on paying you, if you don't mind, than have the wife come to the surgery every time she gets one of her headaches. She has no-one to look after the children, and we should not like you to feel that you've been called out for nothing."

This covers Dr. Weston's experience, I think, but it does not show what the patients think of the new service; it shows what a fatal blunder it was ever to allow the service to become associated with restrictive rules which no-one could fail to dislike. In so far as these have come to be identified with the concept of caring for health on a national scale, the vitality of the service has been destroyed, and it is hard to imagine a counter-measure which might restore it.

However lenient a view one may take of the injunctions on the new medical cards, their effect has been wholly deplorable. The attempt at regimentation is a complete break with tradition in medical practice, and is as unpopular in theory as it is undesirable at the present stage of administrative imperfection; it is a denial of the confidence which now, more than ever, should have been the basis of the doctor-patient relationship, since the patients' loyalty and friendly coöperativeness was the only real insurance doctors had against abuses of the service. Where once a message to the doctor seemed all that was needful, the patient must now make it his first concern to cater for the supposed convenience of his doctor. To this end he has been constituted judge of fitness or otherwise for a journey to the surgery and any exposure it may entail, and he is asked to act on this judgment. Worse still, he is virtually directed to make use of facilities provided by health centres which have

yet to be built. It is hardly surprising that he feels he is paying pretty dearly for the freedom from financial obligation, and that he is ready to blame the scheme and all its works for his discomfiture.

No-one expected to escape difficulties and hardships while the new health service was being helped to its feet; it was generally recognised that so vast a piece of social legislation could never hope to find an administrative machine geared for the job in advance; but there were enough people who welcomed the scheme on any terms, and who were eager to make good the initial defects by exerting themselves in any way or degree that seemed to be called for. These willing horses included Dr. Weston's housekeeper and her opposite numbers in other medical households; they worked gamely enough in the past and they would be game still, had not the administration planted the proverbial cart so firmly before the horse by "affording" the facilities without the centres. It is not possible to will an adequate telephone service into being while one is obliged to do something else, nor is it possible to derive any satisfaction from the heroic failure to adapt a small and understaffed private house for the smooth running of large outpatient sessions —particularly when the "outpatients" attend under duress.

It seems that the authors of "General Information" succeeded in paralysing the good will of nearly everyone whose devoted services were essential to the success of the National Health Service. Everyone, that is, except the doctor who is sufficiently emancipated to dismiss a gathering of gloomy patients with the genial assurance that they will all be visited at leisure, if they will be good enough to leave their names and addresses with him. The sigh of mass relief with which tortured humanity greets this announcement more than repays his "unnecessary" trouble; it also suggests that the authors aforementioned might do well to consider what, by contrast, deserves to be called "necessary" trouble.

PRACTITIONER.

WELFARE OF THE HOUSEWIFE

SIR,—Dr. Instone in her article on the housewife (Dec. 4) has put on paper what has long been well known over the teacups by women of all income-groups. No doubt the subjective nature of some of the observations is open to criticism, but the general picture is unfortunately true. May I make a plea for a similar survey of a comparable sample of men? With so much talk of shorter working hours, improved industrial environments, and so on, it is often forgotten that men in all strata of society now do many hours of homework after (and before) their recognised day's work. Many household chores which used to be regarded as the perquisite of the gentler sex are now thrust upon broader shoulders, and bathing the baby is no longer a woman's privilege. I have an impression that the percentage of anxious strained faces among househusbands would be as high as Dr. Instone found among her housewives.

London, E.C.3. ALAN WATSON.

AGRANULOCYTOSIS

SIR,—Some time ago we published the case-records of two patients with agranulocytosis who had a return of granulocytes to the circulating blood within 48 hours of starting folic-acid therapy.[1] In your issue of Dec. 4 Dr. Waelsch described two similar cases together with three others in which spontaneous remission took place. Since the occurrence of such spontaneous remission in this disease is not in dispute, the value of Dr. Waelsch's paper would seem to us to lie mainly in the addition of two further examples of a happening which, as we said in our article, may be merely a coincidence. We do not follow the argument which leads him to conclude that "closer study suggested that this improvement was a spontaneous remission." There is no law of nature which requires that therapeutically induced remissions should be distinguishable from natural remissions by their characters.

Agranulocytosis is a symptom which may arise as the end-result of different pathological processes. If it be wrong to compare drug agranulocytosis with the agranulocytosis of nutritional deficiency, then surely it is equally naïve to draw conclusions on the therapy of drug agranulocytosis from what happened in a patient with pernicious anæmia. At present what we would claim for folic acid in agranulocytosis is that there is as much indication for giving it as for giving pyridoxine, and rather more than for giving the highly toxic pentose nucleotides.

Department of Medicine, University of Manchester. D. A. K. BLACK S. W. STANBURY.

1. *Lancet*, 1947, i, 827.

ILLUSIONS WHILE FALLING ASLEEP

SIR,—I wonder whether any reader has come across and successfully treated the following minor complaint.

Within the last few months a number of patients have mentioned a curious sensation in the head and limbs just before falling asleep at night. They feel as though they are swelling to twice their usual size, and only by touching the parts concerned can the unfortunate victims reassure themselves that these have not reached elephantine proportions. Though distinctly unpleasant and lasting up to about 15 minutes, these attacks do not seem to be of sufficient importance to warrant a visit to a doctor, for they have only been mentioned to me in casual conversation. In each case the patient has been above the average in intelligence. All emphasise the acute unpleasantness of the attacks.

Exmouth. ARMOREL NETTELL.

PENILE CARCINOMA AND CIRCUMCISION

SIR,—Sir Ernest Kennaway has called my attention to a mis-statement in my lecture given to the Eighth International French Biochemical Congress, and published in your issue of Nov. 27. I stated that "in Moslems, who are circumcised in early boyhood and never as babies, the incidence of carcinoma of the penis is the same as in the uncircumcised non-Jews." What Sir Ernest Kennaway said was: "Cancer of the penis does not occur after circumcision on the eighth day according to the Jewish practice, but occurs in later life in Moslem populations, where the operation is carried out between the 3rd and 14th years." As Sir Ernest points out, there are no statistics available on the frequency with which this occurs. This, however, does not affect the argument developed in my lecture.

E. C. DODDS.

SIR,—Professor Dodds, in his excellent critical survey of Nov. 27, discusses the common theory of long-term action of carcinogenic factors. Some of the evidence given by him appears, however, to be open to question. Referring to a study by Kennaway,[1] he says that Jews, who are circumcised soon after birth, never develop carcinoma of the penis, in striking contrast to Moslems, who are circumcised in early boyhood. He adds:

> "This suggests that the carcinogenic potentiality is conferred on the epithelium of the penis during the first few years, and that the carcinoma which develops forty or fifty years later had its foundation when the child was uncircumcised."

And Kennaway points out:

> "The failure of the operation deferred until the 14th year to give the protection given by it when carried out on the 8th day suggests that the trail of the cause does not then avert the development of cancer at a much later age."

I do not think the evidence for such an argument is conclusive. There seems to be no sure proof that in the uncircumcised adult with penile carcinoma malignant change really began in the first years of life.

Certain industrial forms of cancer seem to arise after long "incubation" periods; but it seems impossible that the surgical removal, in early infancy, of the prepuce —a protective structure—should prevent the later development of carcinoma on the glans, the retroglandar sulcus, or the skin of the shaft. On the contrary, I suggest that the removal of the prepuce may expose the penis to all manner of carcinogenic "irritation." It might be argued that the preputial mucus is carcinogenic; but then why is vaginal carcinoma so rare in women,

1. Kennaway, E. L. *Brit. J. Cancer*, 1947, 1, 335.

despite the vaginal mucus and the preputial mucus transferred during intercourse?

My main objection, however, is different. How does Kennaway explain the astonishing fact that Jewish women hardly ever develop carcinoma of the cervix—a form of cancer dreadfully prevalent in other peoples? (In negroes carcinoma of the cervix is more frequent even than carcinoma of the breast—at the Hospital for Negroes in St. Louis five times more frequent.) Only one explanation remains—racial differences in susceptibility to cancer of the various tissues. In animal experimentation such a difference is recognised as existing even between different strains of the same species; and in man this difference is particularly evident in respect of penile cancer. Ngai [2] has reported that in Mongols cancer of the penis accounts for 18¾% of all cases of carcinoma, whereas in Britain it accounts for only 1½%. Thus I conclude that the determining factor is not circumcision but specific racial susceptibility.

London, N.W.3. HANS BAB.

HUMAN TOXOPLASMOSIS

SIR,—Dr. Jacoby and Dr. Sagorin end their excellent report last week with the sentence: "Unfortunately there are in England at present no facilities for performing the antibody neutralising test, and in our opinion the provisions of such facilities is essential." This is perhaps putting it rather strongly. In this laboratory we have been working with the neutralisation test;. and other laboratories are probably doing likewise. This test is not simple to interpret. We should therefore like to increase our experience and would be grateful if physicians who suspect toxoplasmosis would get in touch with us.

Bacteriology Department, The University, Sheffield. C. P. BEATTIE.

HOSPITAL BIOCHEMISTS

SIR,—Your correspondent "PH.D." (Dec. 4) is labouring under a serious misapprehension. He can rest assured that at a salary of £1500 per annum a hospital biochemist with medical qualifications would be expected also to be chemically qualified.

A medical graduate with experience in biochemistry can act as a medical consultant in matters where biochemistry is concerned. The additional salary he commands is, therefore, recognition of his additional usefulness. A chemist with limited medical knowledge is in many ways worse than one with none at all. He cannot hope to be more than a high-grade technician as far as his medical colleagues are concerned. There is to my knowledge one notable exception to this rule, and his ability has been recognised by his appointment to one of our more important university chairs of chemical pathology. The remarkable rarity of such an exception can be appreciated only by those who are themselves medically qualified. I have yet to meet the university graduate in chemistry who is better technically than the fully trained laboratory technician holding the F.I.M.L.T. or A.I.M.L.T. in biochemistry. Nevertheless, a salary for a science graduate of £750–1000 per annum is far in excess of that paid to the senior technician.

I have no personal axe to grind. In addition to a chemical qualification I hold higher degrees in both biochemistry and medicine.

CLINICAL BIOCHEMIST.

ACUTE ATROPINE POISONING

SIR,—After my experiences with the cases of atropine poisoning reported by Dr. Buxton and myself in your columns on Aug. 7, I was very interested in the reactions of my own small daughter to the instillation of atropine eye-drops.

She is just 4 years old, and had to have her eyes atropinised recently before examination for a suspected error of refraction. She had two drops of 1% atropine sulphate instilled into each eye three times a day for 5 days. On the 1st day she had difficulty with near vision, but appeared to get over this. On the 3rd day she had bright red patches on her cheeks and her mouth became dry; she had difficulty in swallowing dry food. By the 4th night she was becoming very restless and easily tired, and called out once or twice in her sleep. On the 5th night she slept very little and talked almost continuously, occasionally crying out and shouting. Her speech was rational and, for the most part, calm, but she changed from one subject to another as though talking in a dream. She repeated nursery rhymes which she had not heard for a year or more. Whenever I went to her she was ready to jump out of bed and play, as if it were the middle of the day, and talked excitedly. She did not want comforting as she does when she calls out when she is poorly. As morning approached she fell asleep and did not awake until 11.30 A.M. She was puzzled at waking up so late and did not remember anything that had happened during the night. Apart from the dilatation of her pupils she appeared to be normal.

It would be interesting to know how common this type of reaction to atropine eye-drops is in children. Those of my colleagues with whom I have discussed the question are certainly unfamiliar with it, but perhaps the ophthalmologists see it more frequently.

Woolton, Liverpool. RICHARD B. WELBOURN.

2. Ngai, S. K. *Amer. J. Cancer*, 1933, **19**, 259.

Parliament

QUESTION TIME

Nutritional Standard

Sir WALDRON SMITHERS asked the Minister of Food why his department informed the United Emergency Fund for Britain that Britain was living on marginal constitutional standards and expressed anxiety for the physique and health of our people; and what steps he was taking to remedy the situation described.—Mr. JOHN STRACHEY replied: In August we were asked by the U.E.F.B. to give as accurate an account as we could of the state of the national nutrition. We replied, as we have repeatedly said before and since, that our present diet, though nutritionally adequate, left little margin and that we were making every effort to supplement it within the limits of our financial strength. This in part we have succeeded in doing as the recent increases in the distribution of sugar and fats bear witness.

Mr. SIDNEY SHEPHARD asked the Minister what was the calorific value of rationed and points foods at the most recent date; and what were the comparative figures for the years 1944, 1945, 1946 and 1947, respectively.—Dr. EDITH SUMMERSKILL replied: The calorific value of the foods at present on domestic rations plus the allowances of milk and eggs to a normal adult at the present time is approximately 740 calories a day. The figures for the same foods for December 1944, 1945, 1946, and 1947, are 730, 710, 720, 620, respectively. In December, 1946, bread was rationed and in December, 1947, both bread and potatoes were rationed. Both these and also preserves have now been taken off the ration. The average quantity of points foods available has provided 150 and 200 calories daily during these years.

National Health Service in Scotland

Mr. JAMES CARMICHAEL asked the Secretary of State for Scotland if he would submit a report on the work of the National Health Service in Scotland, including some detailed evidence of the earnings of doctors, dentists, and opticians; and the difference in the cost of denture treatment and of artificial dentures and glasses compared with costs for similar services prior to the commencement of the National Health Service.—Mr. ARTHUR WOODBURN replied: A report on the health service will be included in the next annual report of the Department of Health for Scotland. Mr. CARMICHAEL: Is not the Minister aware of the serious increase in charges to the State and the necessity for an immediate examination? A medical officer in Scotland has already indicated that in his area dentists are now earning on an average £15,000 per annum. Glasgow corporation received a report to the effect that while formerly they paid 8*s.* 4*d.* for schoolchildren's glasses they are now paying £2 10*s.* Surely, that calls for immediate action. Mr. WOODBURN: A great many stories go about, and there are facts accumulating which perhaps are a little unsettling, but these matters are receiving the careful attention of the responsible committee. In due course they will be examined, and action taken, if necessary.

Mr. J. HENDERSON STEWART: As the report of the department is not likely to be presented to the House for many months, and as the matter is urgent—for example, some doctors in my district have suffered such serious cuts in their incomes that they cannot meet their responsibilities—is there not a case for a special interim report?—Mr. WOODBURN: I met the representatives of the doctors on Friday, and it is rather curious that they did not mention this matter. I should have thought that they would have been the first people to have brought it to our attention if it had been necessary to do so.

Mr. CARMICHAEL: If the Minister has evidence prior to the submission of this report, has he sufficient authority to alter the conditions regarding opticians and dentists?—Mr. WOODBURN: Action has already been taken with regard to one set of factors mentioned, and of course administrative action will be taken where necessary.

Discontent among Public Dental Officers

Mr. CARMICHAEL asked the Secretary of State for Scotland what reports he had received regarding the local authorities' clinical services with particular reference to the dental service and the discontentment at the staff remuneration in contrast to the incomes being earned by those engaged on similar work under the National Health Service and what action he intended to take to ensure that all local authorities' health services were maintained in the highest level with well qualified and contented staffs.—Mr. WOODBURN replied: I am aware that some authorities are having difficulty in maintaining their dental services at full strength because of a drift of public dental officers to general dental practice. I am encouraging the local authorities who are the employers of public dental officers and the dental associations to enter into negotiations about salaries. In the meantime I should like to pay tribute to those dentists who are continuing to carry on their important work in the public service.

Infant Mortality in Scotland

Replying to a question Mr. WOODBURN gave the following figures comparing infant mortality in Scotland and in England and Wales.

Infant-mortality rate (deaths of infants under 12 months per 1000 live births)

Year	*Scotland*	*England and Wales*
1947	56	41
1948—		
1st quarter	51	41
2nd quarter	43	31
3rd quarter	40*	28

*Provisional.

Exchequer Grants to Medical Schools

Mr. SOMERVILLE HASTINGS asked the Chancellor of the Exchequer what proportion of the cost of medical education in England and Wales was paid by taxation.—Sir STAFFORD CRIPPS replied: These figures are only available for London as in that case the medical schools receive separate allocations of grants. In 1946–47, the latest year for which figures are available, approximately 55% of their cost was met by Exchequer grants. This figure takes no account of financial assistance given from the Exchequer to individual medical students.

Artificial Insemination

Mr. T. E. N. DRIBERG asked the Prime Minister if he would consider the appointment of a Royal Commission to examine the social and legal implications of the practice of human artificial insemination, including A.I.D., with special reference to the problems of legitimacy and inheritance involved; or extend the terms of reference of the Royal Commission on Population to include this subject.—Mr. C. R. ATTLEE replied: I should prefer first to see the general report of the Royal Commission on Population which I understand is in the final stages of drafting.

Mr. SYDNEY SILVERMAN: Is the Prime Minister aware that in an answer given on behalf of the Attorney-General on these matters it was said that the question of an inquiry into the legal implications of this decision was being considered? Does the present answer mean that it is not being considered until after the Royal Commission on Population has reported?—Mr. ATTLEE: I said in regard to the setting up of any Royal Commission that I should prefer to see the general report of the Royal Commission on Population first.

Artificial Limbs

Lord WILLOUGHBY DE ERESBY asked the Minister of Pensions how many private firms were manufacturing artificial limbs in July last; how many had now entered into contract to supply artificial limbs under the National Insurance Act; and how many persons insured under the National Insurance scheme had chosen to be fitted with an artificial limb or limbs from any of these now contracting firms.—Mr. ARTHUR BLENKINSOP replied: In July last there were 19 private firms manufacturing artificial legs in addition to the main contractor to the Ministry. Of these 13 have now entered into contract with my department to supply patients under the National Health Service Act and negotiations are proceeding with 3 others. Up to Nov. 19, 597 National Health Service patients have chosen to be fitted with artificial limbs made by one or other of 11 of these firms. The contracts with the remaining 2 firms were only recently concluded.

Rheumatism Research

Replying to a question Mr. ANEURIN BEVAN stated that research in rheumatism was being carried out at the following centres:

Acute Rheumatism.—Canadian Red Cross Memorial Hospital, Taplow (clinical and laboratory investigation of rheumatic fever); Sheffield, Bristol, and parts of Lincolnshire (social investigation of notified cases of acute rheumatism in children); University College Hospital, London (experimental study of changes in the blood and tissues in rheumatic fever).

Chronic Rheumatism (Arthritis, &c.).—Manchester University (clinical and laboratory investigation of chronic arthritic disorders, and of rheumatic disease in miners); Leeds University (clinical and laboratory investigation of chronic rheumatic diseases); Royal Free Hospital, London (clinical and laboratory investigation of chronic rheumatic diseases); Hospitals in London, Bristol, Leeds, and elsewhere (special statistical inquiry into the clinical and social aspects of rheumatoid arthritis); Maclean Laboratory, Hospital of St. John and St. Elizabeth, London (investigation into immunology of patients with arthritis).

He added that investigation was also taking place at a number of hospitals where treatment is carried out, such as Liverpool Royal Infirmary; Bristol Royal Hospital and the Royal National Hospital for Rheumatic Diseases, Bath; St. Stephen's Hospital, London; and West London Hospital.

Mosquito Campaign in Cyprus

Replying to a question Mr. D. R. REES-WILLIAMS stated that recent reports show that the extermination of anopheline mosquitoes in Cyprus should be substantially complete by the end of this year.

Dentists' Remuneration

Mr. H. G. MCGHEE asked the Minister what alterations he proposed to make in the remuneration of dentists under the National Health Service.—Mr. BEVAN replied: With the dental associations I am undertaking a full review of our present translation of the Spens Committee into fees for services. Meanwhile, as it is obvious that some dentists are earning far more than that committee ever contemplated, I am adopting a temporary arrangement whereby fees are reduced by half after a dentist reaches an income of £4800 gross—or £1000 in excess of the point at which the Spens committee said the risk of bad dentistry began. Doctors already have a limit, in the number of patients allowed on their lists.

Alien Dentists

Dr. S. SEGAL asked the Minister of Health how many dentists with foreign qualifications had been refused registration in this country; and whether he would consider the possibility of their recruitment for the school dental service.—Mr. BEVAN replied: Approximately 1200 since 1935, when foreign dentists began to enter this country from the Continent in appreciable numbers. The Minister of Education has no objection to the employment in the school dental service of any foreign dentists provided that they are legally entitled to practise dentistry in this country.

Dr. SEGAL: Where any doubt may exist about the qualifications, could special facilities be granted for retraining, in order that they may equip themselves for entry into the school medical service?—Mr. BEVAN: Dental schools in this country are already fully occupied in training our own people.

Mr. VERNON BARTLETT asked the Minister why permission to practise in this country was still withheld from 33 dentists,

refugees from Nazi oppression, now naturalised and living in this country.—Mr. BEVAN replied: The conditions on which foreign trained dentists may practise in this country are prescribed by the Dentists' Acts, and the duty of ensuring that these conditions are fulfilled rests with the General Medical Council.

Parkinson's Disease

Dr. SEGAL asked the Minister how many British subjects had been enabled to travel to Kassel to undergo the Voeller treatment for Parkinson's disease; on what basis they were selected; and what the results of treatment are to date. —Mr. BEVAN replied: No British subjects have so far been permitted by the United States authorities to travel to Germany for treatment by Dr. Voeller. I am arranging a full investigation into Dr. Voeller's claims. If these are substantiated I will see what can be done to ensure that the treatment is available to all sufferers from the disease. Dr. SEGAL: Could the Minister give some indication of the time when the report may be made available so that some of these people may look forward with perhaps some degree of justified hope to some remedy for their position?—Mr. BEVAN: I obviously could not give any date, because the experts who are investigating these claims must not be unduly hurried by Parliamentary pressure. They must satisfy themselves that there is something in the claim before any further steps can be taken.

Amendment of the National Health Service Act

Colonel M. STODDART-SCOTT asked the Lord President of the Council if he would give some indication when the promised Amending Bill to the National Health Service Act was likely to be introduced, as it was promised last session and there was no mention of it in the King's Speech. —Mr. HERBERT MORRISON replied: That Bill is under consideration. I cannot say when it will be forthcoming, but it will not be this side of Christmas. The hon. member can be assured that it is not overlooked. I have every anticipation that it will be produced this session.

Health Centres

Dr. L. COMYNS asked the Minister of Health how many applications for permission to build health centres had been received from local authorities, how many such schemes in the London area had been approved as new structures and as adaptations of existing buildings, respectively; and whether he was satisfied that sufficient such centres were being constructed.—Mr. BEVAN replied: I have proposals for 2 new centres and have approved 1, in London. Discussions are going on in about 20 other cases. So far there have been no adaptations of old buildings approved. There are, however, a number of existing dental or medical clinics which have been maintained under the new Act. I am certainly not satisfied, but progress is governed by the building situation.

Specialists' Domiciliary Visits

Mr. L. W. JOYNSON-HICKS asked the Minister whether he was aware that medical specialists were, under the operation of the National Health scheme, limited to making a total of 25 visits per quarter in a given area upon patients; and what arrangements there were for the treatment of the patients in that area when the specialist had fulfilled his schedule.—Mr. BEVAN replied: There is no limit on visits. Remuneration has a provisional ceiling for each quarter while longer term arrangements—which will date back—are being worked out. The situation in the last part of the question can be considered if and when it arises.

Public Health

Diphtheria Immunisation

IN the first six months of this year more children were immunised against diphtheria by local authorities than in any half-year since the end of the war. They numbered 347,000, bringing the grand total for England and Wales to 7,567,574. The total for the important "under-five" age-group during the first half of the year was 288,000. The target for the year is the protection of 635,000 babies before their first birthday; because of the higher birth-rate, this is 45,000 more than that set in 1947.

Obituary

ARTHUR ROBINSON

M.D., LL.D. EDIN., F.R.C.S., F.R.C.S.E.

Professor Robinson, who had been living in the South of England since he retired from the Edinburgh chair of anatomy in 1931, died at Eastbourne on Dec. 3.

Born at Manchester in 1862, he was educated at Edinburgh University where he graduated M.B. with honours in 1883. He at once turned his attention to anatomy and in the same year he was appointed demonstrator to Sir William Turner. After two years he returned to Manchester as demonstrator in Owens College, and later he became lecturer in the Victoria University under Prof. A. H. Young.

In 1896 Robinson came to London on his appointment as the first whole-time lecturer in anatomy at the Middlesex Hospital. He quickly established his reputation as a rising young anatomist, and at short intervals he moved to the chairs of anatomy at King's College, London (1900), the University of Birmingham (1905), where he was also subdean of the faculty of medicine, and finally to Edinburgh (1909), where he succeeded D. J. Cunningham. In all these posts he displayed his talent for organisation and his powers as a teacher, while continuing to conduct important researches in his chosen field of comparative embryology. In 1920 he was Struthers lecturer of the Royal College of Surgeons of Edinburgh—he had received the fellowship in 1912—taking as his subject Prenatal Death; and the Royal Society of Edinburgh awarded him the Neill prize for 1925–27 for his contributions to comparative anatomy and embryology. From 1920 to 1922 he served as president of the Anatomical Society of Great Britain and Ireland. He was a fellow of King's College, London, and in 1924 he was elected to fellowship of the Royal College of Surgeons of England as a member of over 20 years' standing. He received the LL.D. from the University of Edinburgh on his retirement.

Of his work as an anatomist, J. C. B., to whom we are indebted for much of this memoir, writes: "Robinson's first paper on the position and peritoneal relations of the mammalian ovary appeared in the *Journal of Anatomy and Physiology* in 1887; others followed, and in 1890 he was awarded a gold medal for his M.D. thesis on development in two rodents. His work on the comparative anatomy of the placenta is embodied in three Hunterian lectures which he delivered to the Royal College of Surgeons in 1903. But as early as 1888 he was collaborating with A. H. Young in morphological studies including the development of the vascular system; and in 1902 they jointly contributed to the first edition of Cunningham's *Text Book of Anatomy*, being responsible for the sections on general embryology and the vascular system. Robinson himself succeeded Cunningham as editor of this work, and also of the *Manual of Practical Anatomy*, and he was responsible for the editions between 1910 and 1932. His editorial labours took up much of his time, but he continued to pursue the developmental problems that interested him, such as the formation of the ovarian follicle, the presence of lipoids in mammalian ova, and the development of veins, the last a subject on which he was a recognised authority.

Professor Robinson's preparations for retirement in 1931 were clouded by serious eye trouble which gave rise to much anxiety. But his friends were relieved to learn that a good measure of sight had been spared to him. His resilient spirit enabled him to overcome the disability that remained; and in these later years of his long life he quietly enjoyed the general reading for which during his active professional days he had had so little time."

E. B. J., a colleague who was long associated with him, adds: "Arthur Robinson was brisk and agile in all his movements—his students used to call him 'Dancing Arthur.' He was also alert and active in mind, and he displayed an immediate interest in any subject that was brought up. Ready and adroit in argument he was a competent advocate, and he held decided opinions —tersely expressed—especially on politics.

"Both staff and students found in him an understanding and helpful counsellor, and he was always

accessible. As a second-professional examination approached, the unofficial tutorials which he gave, himself, to small groups were greatly appreciated; and, at all times, there was admiration for the speed and deftness with which he illustrated his lectures on the blackboards.

"In the year before he retired he learned to drive a motor-car; for he intended to spend part of his leisure wandering round the country in his car with his wife. But in his last summer of service the retina of one eye became detached; a cataract in the other eye was not then ripe for removal; and the first year of his retirement was spent in darkness—but without a grumble. It is noteworthy that, after light came back to him, his handwriting was more legible than it had ever been. Up till that summer, he played golf with zeal and zest during the whole of his sojourn in Edinburgh, except that he refused to touch a club while the Kaiser-war lasted. In his holidays and in his retirement after sight was restored to one eye, he was fond of long walks and also of gardening—he would have liked to have been a farmer—and as the 'incurable malady,' old age, grew upon him, his chief regret was that he was forced to curtail these activities."

Professor Robinson married Emily, third daughter of John Baily, in 1888, and she survives him.

WILLIAM HENRY BROAD

M.D. LPOOL

Dr. W. H. Broad, whose death at the age of 73 is announced, was well known in Liverpool as an orthopædic surgeon and as an anthropologist.

He was born and educated in Liverpool at the Institute and the university. After graduating in 1900 he held house-appointments at the David Lewis Northern Hospital and at the Royal Infirmary till in 1901 he received a Robert Gee fellowship which he held while acting as junior demonstrator in anatomy at the university. In the following year he was awarded a Holt fellowship, in physiology. The next two years he spent on travel, visiting the United States, Canada, Australia, and the Cape. At Stockholm and Berlin he attended clinics in orthopædic surgery and he returned to Liverpool to settle in consultant practice. Soon he was attracted to the treatment of injuries, chiefly by physiotherapeutic measures, and his interest in this branch of medicine remained with him until his death.

For many years he was in charge of the physiotherapeutic department of the David Lewis Northern Hospital, and during the 1914–18 war, as a major in the R.A.M.C., he was responsible for the rehabilitation department of the orthopædic centre at Alder Hey. A recognised authority in this branch of medicine, he became in the late war a regional consultant adviser in physical medicine in the Emergency Medical Service, being chiefly concerned with the hospitals in the North-Western area. He was an associate member of the British Orthopædic Association, and also a member of the Massage Advisory Committee set up by the Ministry of Pensions, and he often examined for the then Chartered Society of Medical Massage and Gymnastics. His *Rules of Massage* appeared in 1918.

"But a bald list of his achievements," adds a colleague, "is no indication of the character of the man. He was always a good doctor, who worked unceasingly for his patients and his hospital, and many improvements in treatment can be traced directly to his thoughtful suggestions."

Outside his work Broad was keenly interested in anthropology, and he was a fellow of the Royal Anthropological Institute. For him anthropology was a second career rather than a hobby. As early as 1901 he had described aboriginal Australian skeletons, and his later writings included *Heredity and Skull Form* (1913) and *Prehistoric Man* (1914). For several years he was also lecturer in physical anthropology at the university. For a time he was a member of the Liverpool county council and he was also a former president of the Liverpool Literary and Philosophical Society. His wit as a raconteur was appreciated at any social function.

Dr. Broad married Miss C. M. Hawkes, of Adelaide. The loss of their only son during the late war was a blow from which he never fully recovered.

Notes and News

REPRESENTATION OF SPECIALISTS AND CONSULTANTS

THE exploratory committee set up last July at the conference of representatives of the Royal Colleges, the Royal Scottish Corporations, and the British Medical Association, met at the Royal College of Surgeons on Dec. 10 with Sir Lionel Whitby in the chair. It was agreed that:

(1) It is essential in the interests of the consultants that a joint committee of the bodies concerned should be established to speak for consultants with one voice.

(2) The terms of reference of the joint committee should be: (*a*) to represent consultants and specialists in the impending negotiations with the Government on matters arising out of the National Health Service Acts and the report of the Spens Committee on the Remuneration of Consultants and Specialists; (*b*) to prepare and to submit for the consideration of its constituent bodies a scheme, including terms and reference, for the future work of the committee.

(3) Where a constituent body disagrees with the view of the joint committee on a proposal put forward to the committee, the constituent body shall be entitled to have its view represented to the Government, provided that, before any such representation is made, a conference between representatives of the joint committee and the constituent body is held in an endeavour to reach agreement.

(4) The joint committee should appoint joint secretaries to the committee, one nominated by the colleges and corporations jointly, and one by the British Medical Association.

(5) On the question of the composition of the joint committee it is suggested that it is desirable that in the representation of constituent bodies on the joint committee there should be representatives of both teaching and non-teaching interests.

The following composition of the committee is agreed: Royal College of Physicians, 3; Royal College of Surgeons, 3; Royal College of Obstetricians and Gynæcologists, 2; Royal College of Physicians of Edinburgh, 1; Royal College of Surgeons of Edinburgh, 1; Royal Faculty of Physicians and Surgeons of Glasgow, 1; Consultants and Specialists Committee established by the British Medical Association, 6.

NATIONAL (WAR) FORMULARY

THE N.W.F. Committee has decided that the third edition of the formulary shall be amended as follows:

Emulsion of liquid paraffin *B.P.C.* shall be deleted and replaced by emulsion of liquid paraffin *B.P.*

The synonym for emulsion of liquid paraffin and magnesia shall be deleted.

The suffix to emulsion of liquid paraffin with phenolphthalein shall be deleted and replaced by *N.W.F.* In the latter two preparations the emulsion of liquid paraffin that will be used will now be the *B.P.* emulsion.

It has been agreed that Jan. 1, 1949, shall be the date on which this amendment will come into operation.

INTERNATIONAL BIOLOGICAL CONTROL

ENTOMOLOGISTS from 10 countries, who lately met in Stockholm under the auspices of the International Union of Biological Sciences, have sent a resolution[1] to UNESCO and F.A.O. urging the need to provide "facilities for the development of basic research on biological control which will lead to the greatly extended use of natural enemies to control insect pests and noxious weeds, so helping to conserve world food resources." In support of their resolution the members of the Stockholm symposium point out that though insecticides have proved a powerful means of reducing losses of food their use involves a continued expenditure of money and labour. They are also not without danger to man and the domestic animals and may damage the crops they protect. The use of natural enemies for the control of insect pests and weeds, on the other hand, is economical but entomologists are handicapped by their meagre knowledge of the important natural enemies that exist in different parts of the world. An international organisation is thus essential, for biological control can best be effected by introducing natural enemies from

1. *Science*, Nov. 5, p. 512.

one region to another. The Stockholm resolution suggests that the following services should be set up at once; a documentation service for the collection and dissemination of pertinent information; a taxonomic service to identify natural enemies; a survey service to study the natural enemies in major regions; and later an application service to collect, breed, transport, and acclimatise natural enemies in regions where the nations concerned are unable to carry out this task. The work of the international organisation, the resolution ends, would be an extension to other countries of what is already being done in Britain and in America, and it would coöperate with all existing institutes.

EXPERIMENTAL PANCREATICOGASTRECTOMY

ADDRESSING the Liverpool Medical Institution on Nov. 25 Mr. David Annis said that in pancreaticoduodenectomy for carcinoma of the head of the pancreas or of the common bile-duct, after excising the head of the pancreas, the terminal common bile-duct, and the duodenum it was necessary to re-establish the biliary, intestinal, and pancreatic flows. An experimental study had been made to find a better site for the reimplantation of the remaining pancreatic tail after excision of the head. The pyloric end of the stomach was selected because the reaction is acid and there is no enterokinase to promote the action of trypsin. In six dogs the pancreas was divided at the neck and the cut surface of the tail implanted through a hole in the anterior wall of the pyloric end of the stomach. All the dogs recovered from the operation. One dog died on the 51st day; five were well and well-nourished when killed on the 15th, 45th, 45th 49th, and 66th day. Pancreatic amylase was collected from the implanted pancreatic tail. Some atrophy of the implanted pancreas took place in three dogs. In the dog killed on the 66th day there was continuity of epithelium between the gastric and pancreatic-duct mucosa.

ASSISTANT NURSES

WOMEN with the appropriate nursing experience who failed to apply for admission to the roll of assistant nurses before the closing date (Feb. 3, 1946) now have another chance to do so under the waiver rule recently passed by the General Nursing Council. The new closing date is Dec. 31, 1948, but this concession applies only to women who are at present engaged in nursing duties. The closing date for applications from assistant nurses with "intermediate qualifications"—that is those who have obtained appropriate experience since March, 1943—is Jan. 1, 1949.

The Ministry of Health [R.H.B. (48) 91] appreciate that many hospitals are at present employing probationers and assistant nurses who will not have completed the prescribed period of experience in time to claim enrolment, but there will be no objection to regional hospital boards continuing to employ these women at their present rates of pay for the time being. The Ministry hope that revised arrangements for the training of assistant nurses, which are being considered by the General Nursing Council, will attract this staff and other nursing auxiliaries to take the training and gain admission to the roll. But if they fail to do so further consideration will have to be given later to regularising the position of these nursing auxiliaries.

OLD AND NEW

THE Hospitals Year-Book for 1948 [1] is a meeting-place of the past and the future, and it will be of special value as a reference work this year while the new groupings and provisions of our hospital services are still unfamiliar. The directory section has been doubled in size, and the hospitals are shown, not only under their old headings of voluntary and municipal, but also in their new array under regional hospital boards and boards of governors. The two directories have cross-references, and any hospital may quickly be found under either system. This section also includes lists of the regional areas, the disclaimed hospitals, and the members of the three health service councils. Short surveys of the Health Acts for England and Wales, for Scotland, and for Northern Ireland are included.

Besides these records of fact the yearbook contains a series of special articles on aspects of the new service from different viewpoints, including one by Sir Allen Daley on the work of local health authorities. In another section are reproduced memoranda, from the British Hospitals Association with other bodies, on such subjects as the recruitment and training of nurses, and appointments for outpatients.

1. Edited by J. P. Wetenhall, B.A. From the British Hospitals Association, 52, Green Street, London, W.1. 1948. Pp. 319. 21s.

MEDICAL WAR RELIEF FUND

DURING the year 1947–48 this fund has distributed £6663 among 42 applicants, 20 of whom had previously received help. As in earlier years, most of the grants were made to help doctors to re-establish themselves in civil practice (18 applicants) and widows with the education of children (15 applicants). A grant which is to be paid over a period of time or is for school fees, is administered through the Royal Medical Benevolent Fund, and 12 grants amounting to £1696 were made in this manner. From time to time the distribution subcommittee reviews the progress of cases helped and every effort has been made to keep in touch with all the cases where children are concerned and to ensure that their education is progressing. The statement of accounts in the annual report shows that the fund still has a substantial unspent balance and, as has already been announced, the committee thinks it unnecessary to seek further contributions at present.

ON ARRANGING FILM SHOWS

Two new leaflets give practical help to those responsible for arranging film shows. *Notes on How to Borrow Films* gives detailed instructions on how to set about borrowing and returning films listed in catalogues. *Notes for the Secretaries of Medical Societies on Organising Medical Film Programmes*, to which we referred on Aug. 28, is even more detailed: armed with this pamphlet secretaries can confidently set about arranging their first film show, for guidance is given on programme planning, organisation of hall and projector, entertainment tax, and other problems, and six specimen programmes are included. Both pamphlets are published by the Scientific Film Association, 34, Soho Square, London, W.1; the first is free, the second costs 1s.

University of London

The governing body of the British Postgraduate Medical Federation have appointed Mr. L. E. C. Norbury, consulting surgeon to the Royal Free Hospital, to be regional adviser in postgraduate medical education for the North-West Metropolitan hospital region.

University of Dublin

On Dec. 9 at the school of physic, Trinity College, the following medical degrees were conferred:

M.D.—Emanuel Howitt, Sheila Sheehan.
M.A.O.—J. D. Llewellyn-Jones.
M.B., B.Ch., B.A.O.—M. D. Bamber, S. D. Boland, E. M. Clein, G. N. Constable, John Diamond, Winifred D. Eadie, P. F. Eustace, M. H. Fruithof, E. A. Jackson, J. S. P. Lane, W. H. Leon, J. K. McCall, Peggy Moore, K. C. Mullen, Dorothy I. Ogden, T. M. W. Redman, Ivy P. Robinson, S. F. Shilliday, Olivia M. Welsh.

Royal College of Physicians

Dr. C. J. Gavey, will deliver the Goulstonian lectures at the college, Pall Mall East, S.W.1, on Tuesday and Thursday, Jan. 11 and 13, at 5 P.M. He is to speak on the Cardiology of Old Age.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Dec. 6, with Dr. W. R. Snodgrass, the president, in the chair, the following were admitted to the fellowship:

John Douglas Aitchison, Robert David Campbell Brackenridge, James Howie Haldane, George Johnston, Walter Phillips Kennedy, Hector Robert Ferguson Macdonald, John Rankin, qua physicians; Hugh Alec Benjamin, Jacob Cohen, William Young Cornock, John Malcolm McBride, James Dunlop McCardel, David Moffat Macdonald, William Macintyre, Neil McLean, Roderick George MacLeod, Robert George Main, Alister John Miller Mathieson, Abraham Bernard May, Kenneth Miles Mayall, Ian Pinkerton Munro, Thomas Anderson Ramsay, Robert Paul Schach, James Moffat Scott, Donald Malcolm Sinclair, Robert Baury Watson, Thomas Murray Welsh, William Frame White, qua surgeons.

Commissioned Rank for Australian Pharmacists

The *Pharmaceutical Journal* (Dec. 4) reports that the Australian army has accepted the principle that every pharmaceutical chemist serving in a professional capacity in the Australian Army Medical Corps shall hold a commission. The supervision of the storage of drugs and medicines, as well as their dispensing and distribution, are to be undertaken only by registered pharmaceutical chemists.

Royal College of Surgeons of England

At a meeting of the council held on Dec. 9 with Lord Webb-Johnson, the president, in the chair, the honorary fellowship was conferred on Viscount Nuffield, honorary medallist of the college, and on Prof. J. R. Learmonth, surgeon to H.M. Household in Scotland and regius professor of clinical surgery and professor of surgery in the University of Edinbugh.

Sir Reginald Watson-Jones was appointed Arthur Sims Commonwealth travelling professor for 1950. Mackenzie Mackinnon fellowships were awarded to Mr. W. J. Atkinson and Dr. C. F. Hawkins. Dr. Horace Evans was elected a Hunterian professor.

Diplomas of fellowship were granted to the following:

K. M. MacLeod, Maurice Ellis, Erling Troensegaard-Hansen, A. B. Dempsey, E. P. Clarke, C. L. Clinton-Thomas, Myer Glick, C. T. A. Burgess, L. F. W. Salmon, C. R. Savage, Thomas Fenwick, D. H. Campbell, P. W. Hunt, K. P. S. Caldwell, J. L. Temple, R. N. Grant, J. S. A. Linton, M. F. Pilcher, D. P. B. Turner, D. A. Barley, B. L. N. Morgan, L. B. Cohen, A. C. Higgitt, J. V. Morris, J. H. E. Verdon, G. B. R. Walkey, R. D. Wilkins, H. M. Jones, E. H. M. Foxen, Edwin Haigh, J. G. Brockis, J. A. L. Davies, J. C. Fulford, Owen Daniel, R. N. Ticehurst, J. F. R. Withycombe, G. W. Taylor, D. H. Randall, P. H. Huggill, P. F. Jones, P. G. Large, B. W. T. Pender, J. M. Davis, John Andrew, K. E. D. Shuttleworth, R. J. Williams, R. L. B. Roberts, E. J. M. Weaver, D. L. B. Farley, M. J. Roper-Hall, G. J. Hadfield, J. A. MacDougall, Appacutty Sinnatamby, I. W. Ball, F. J. Damato, S. J. H. Miller, J. M. G. Nixon, J. L. Wright, Austen Young, P. F. Howden, G. C. Jennings, T. H. Wilson, P. L. Brunnen, E. M. Cortis, Walter Gordon, G. H. Levien, C. W. D. Lewis, Amulya Kumar Saha, Jean R. C. Burton-Brown, C. T. Collins, J. G. Gow, T. S. S. Gregory, J. D. Morgan, Christopher Parish, D. L. Shaw, T. H. Tweedy, C. B. R. Mann, H. G. Smith, Masood Ahmad, H. M. Bradmore, J. W. E. Raine, Sangarapillai Rajanayagam, J. B. Blacklay, B. H. Courtice, J. R. Kirker, K. R. Lothian, Ian Monk, E. H. Paterson, D. A. Sarsfield, R. E. Shaw, Pritamsingh Ahluwalia, Russi Dhunjishaw Anklesaria, Krishan Dev Koshal, W. A. McAlpine, Marion J. Phillips, J. V. Ellis, P. G. Laing, Douglas Tooms.

A diploma of membership was granted to T. McKendrick and D. A. G. Williams, and the following diplomas were granted jointly with the Royal College of Physicians:

D.T.M. & H.—B. N. A. Beetles, Manzoor Ahmad Chowdhry, Joan E. Jermyn.

D.M.R.-D.—J. W. Pierce.

D.A.—O. H. E. Bayles, Om Dutta Bhati, John Bullough, Louis Clement, Patricia F. de C. Coles, Elsa R. Cooper, J. A. L. Cooper, D. H. Couch, Jacob Davidson, Eleanor Davies-Jones, Eric Fowler, Ilse R. Hadelmayr-Kuhn, W. K. Jones, E. J. Leighton, Bertha A. McDougall, Thomas Magner, J. M. Marchant, A. J. Merry, A. A. McC. Miller, L. E. Mosscrop, G. P. Murtagh, D. K. W. Picken, W. L. Price, Silvia W. Pyddoke, L. W. Ritchie, F. L. Robertshaw, J. G. Robson, J. E. Schofield, W. R. Scott, Doris N. A. Smith, J. K. Sugden, J. H. Wakely, Pamela Westhead, David Zuck.

D.I.H.—J. W. Webb.

American Medical Association's Fighting Fund

The American Medical Association is to raise a fighting fund of $3\frac{1}{2}$ million to finance health-education programmes and to oppose "socialised medicine." According to a B.U.P. report, the association's board of trustees, meeting in St. Louis, decided to ask each of the 140,000 members to contribute $25. The association has pledged itself to oppose "any form of compulsory sickness insurance." Its educational programme, the board said, would stress "the advantages of the American system in securing a wide distribution of a high quality of medical care." Criticising the proposals of Mr. Oscar Ewing, the Federal Security Administrator, in favour of socialised medicine (see *Lancet*, Oct. 9, p. 574), the board stated: "It has been demonstrated that the voluntary method provides a better and less costly service and avoids the imposition of enormous taxation."

Proposed Rheumatism Centre at Harrogate

A scheme to establish a rheumatic treatment and research centre at Harrogate has been submitted to the Minister of Health by the Leeds regional hospital board. The *Manchester Guardian* (Dec. 9) says that the scheme would take five years to complete, cost £500,000, treat 8000 patients a year, and provide 900 free beds. The proposals are designed to meet, in the first place, the needs of the immediate area; but the board is reported to have said that "if the project is fully developed the facilities for diagnosis, treatment, and research provided may well prove to be of national if not international importance." The first stage will be to recondition the Royal Bath Hospital to accommodate 150 bed cases; then it is intended to take over three hotels to house ambulant patients; and finally the Royal Bath Hospital is to be extended to provide beds for a further 250 patients. The Royal Baths would remain the property of the corporation; and private patients could still be treated there. The plan calls for a school of physiotherapy at Harrogate.

Legg Lecture

The first of these lectures, founded in memory of Thomas Percy Legg, surgeon to King's College Hospital from 1910 to 1930, was given on Dec. 3 by Mr. Denis Browne, who spoke on Principles of Surgery Exemplified in the Story of Hare-lip and Cleft Palate.

British Association of Physical Medicine

A course of lectures for candidates preparing for part II of the diploma in physical medicine is to be given at 5 P.M. on Tuesdays and Thursdays from Jan. 4 to Feb. 10. Further details can be had from the hon. secretary of the association, 45, Lincoln's Inn Fields, London, W.C.2.

Veterinary Congress

The 14th international veterinary congress will be held at the Central Hall and at Church House, Westminster, from Aug. 8 to 13 under the presidency of Sir Daniel Cabot. The main theme of the congress is to be the present world food situation. Further particulars may be had from the organising secretary, Lieut.-Colonel J. A. Gordon Roberts, 10, Red Lion Square, London, W.C.1.

Information Services Committee

Arising out of the Scientific Information Conference held last June, the council of the Royal Society has set up a standing committee on information services "to advise on means of improving existing methods of publishing, abstracting, indexing, and distributing scientific information" and on how the recommendations of the conference should be fulfilled. Sir Alfred Egerton, F.R.S., is to be chairman of the committee, and the members will include Dr. G. L. Brown, F.R.S., and Dr. G. M. Findlay.

International Neurological Congress

The 4th International Neurological Congress will be held in Paris from Sept. 5 to 10, 1949. The main topics of discussion are to be the thalamus and its pathology; electroencephalography and electromyography; virus diseases of the nervous system; and surgery of pain. The British national committee, which has been constituted by the section of neurology of the Royal Society of Medicine, is as follows: president, Dr. Anthony Feiling; secretary, Dr. Macdonald Critchley; treasurer, Dr. M. J. McArdle; other members, Dr. Douglas McAlpine, Dr. W. Ritchie Russell, Dr. G. Smythe, and Sir Charles Symonds. Further information may be had from Dr. Critchley, National Hospital, Queen Square, London, W.C.1.

Diary of the Week

DEC. 19 TO 25

Monday, 20th

HUNTERIAN SOCIETY
7.30 P.M. (Talbot Restaurant, 64, London Wall, E.C.2.) Prof. John McMichael, Dr. Alice Stewart: Toxic Jaundice.

Tuesday, 21st

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. F. Ray Bettley: Cutaneous Reticulo-endotheliosis.

EDINBURGH POST-GRADUATE BOARD FOR MEDICINE
5 P.M. (Royal Infirmary.) Dr. A. P. Meiklejohn: Nutrition in Europe during the War and After.

Births, Marriages, and Deaths

BIRTHS

ASHER.—On Dec. 3, the wife of Dr. R. A. J. Asher—a daughter.

ATTENBOROUGH.—On Dec. 6, at Farnborough, Hants, the wife of Dr. John Attenborough—a daughter.

BURBIDGE.—On Dec. 1, at Stamford, to Dr. Elizabeth Burbidge (née Newton-Clare), wife of Mr. J. L. Burbidge—a son.

CRANLEY.—On Nov. 24, in Malta, the wife of Surgeon Lieut.-Commander W. J. Cranley, R.N.—a daughter.

FRANKLIN.—On Dec. 8, at Edgware, the wife of Dr. C. B. Franklin—a son.

SLOMINSKI.—On Dec. 7, in Grenada, B.W. Indies, the wife of Dr. John Slominski—a daughter.

TULK-HARN.—On Dec. 6, in London, the wife of Dr. Richard Tulk-Hart—a daughter.

MARRIAGES

COLES—MACBEAN.—On Nov. 12, at Accra, Gold Coast, John Frederick George Coles to Dorothea Fraser MacBean, M.B.

GREENFIELD—BECK.—On Dec. 4, at Rushden, Northants, Dudley Greenfield, M.D., to Isabel Agnes Beck.

DEATHS

BLAYNEY.—On Dec. 4, at Watford, William Blayney, M.R.C.S.

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THE AIMS OF MEDICINE*

E. D. ADRIAN
O.M., M.A., M.D. Camb., F.R.C.P., F.R.S.
PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF CAMBRIDGE

IN Marlowe's play *The Tragical History of Dr. Faustus* the first scene opens with Faustus alone in his study at the University of Wittenberg. He is already famous for his learning, but the time has come to decide whether he should settle down as a philosopher, a doctor, a lawyer, or a theologian. He dismisses philosophy as empty disputation. Medicine seems attractive at first for reasons which even now have not lost all appeal, though we might be loth to state them quite so openly:

> "Be a physician Faustus, heap up gold
> And be eternised for some wondrous cure."

But then he reflects that "The end of physic is our bodies' health," and that does not satisfy him. He has already discovered remedies

> "Whereby whole cities have escaped the plague
> And thousand desperate maladies been eased,
> Yet art thou still but Faustus and a man.
> Could'st thou make men to live eternally
> Or, being dead, raise them to life again,
> Then this profession were to be esteemed.
> Physic farewell."

After this it is not surprising that he finds theology and the law equally futile, and so he turns to the black arts and sells his soul to the Devil. Faustus was hard to please and suffered for it. We have chosen a less exciting career, and though we cannot make men immortal there are few of us who come to regret our choice. But in these days Faustus might think differently. The rewards of necromancy would not seem so attractive, for natural science has deprived the Devil of that particular bait. On the other hand, social science would have hard things to say about the elixir of life—its economic and political consequences might be worse than those of the atomic bomb.

The fact is that with advancing knowledge the prospect in every direction has become less rosy and less extensive. What are the prospects for medicine? We need have no doubt that its practice now is a worthy and satisfying occupation; but it is worth looking ahead and considering what it is likely to become.

Our task at present is to keep men healthy and free from pain and to give them a reasonable span of active life. It keeps us fully occupied, and on the whole we are reasonably successful. There is a great deal more to be found out before we shall be able to guarantee most people a healthy life and a painless death, barring accidents; yet medical science has progressed so rapidly in the past hundred years that in another hundred there should be very little bodily disease that we cannot prevent. That side of the picture is bright enough; but there is the other, that of the diseases of the mind—not so much the gross disorders of thought but the conflicts which all of us suffer to some extent. We ought to aim at making men not only free from bodily pain but also as contented as the circumstances will allow them to be. In this field the advance is likely to be slower and the prospects are less certain. Disorders of the spirit seem to involve theories and ways of prevention and treatment which must take us into quite new fields, away from the laboratory and the hospital ward and into the psycho-analyst's parlour or even into the psychosurgeon's operating-theatre.

Before we venture so far, however, I must try to justify so much optimism about diseases of the body. It may seem far too rash to suggest that in a hundred years or so the progress of medical science will have emptied the hospitals of all the ailments which we have to treat now, with the result that nothing but traffic accidents and psychoneuroses will be left. The layman who has a cold in his head or pains in his joints may say that medical science has not progressed at all, so far as he is concerned. But the fact is that in these last hundred years medicine has advanced quite as rapidly as all the other branches of natural science, and that is saying a great deal.

PROGRESS OF MEDICINE

A hundred years ago electricity was just beginning to be used outside the laboratory and chemists were still not agreed whether they should write the formula of water as HO or H_2O. There was very little basic science on which to build physiology or pathology. The doctors of that time, like the chemists, were just as good, probably better, observers than we are now, and just as sharp-witted; but they had a far smaller range of significant knowledge to which their observations could be related. So medicine was largely skilled prognosis based on history and clinical signs rather than on laboratory findings. Micro-organisms were unknown, and young men and women died of consumption in the natural course of things. But the change had already begun, in medicine as in physics and chemistry. Cholera was spreading in Europe, but a recent epidemic in London had been traced to sewage-contaminated water, and Chadwick was trying to force public-health measures on an apprehensive but indignant public. Anæsthetics had just begun to make new possibilities for surgery, though Lister did not introduce antiseptics until 1865. Physiology was still mainly the anatomy of the circulation and the study of frog's muscle; but it was beginning to move, for the effect of the vagus on the heart was discovered in 1845.

Contrast that picture not with what we know nowadays about disease but with what we can actually do to prevent and treat it, and I do not think anyone can be dissatisfied at the progress of medicine, or anything but optimistic about its future. It is not merely that most of you can confidently expect not to die young—it would have been a different story in 1848—but the important thing is that the advance goes on and is now going faster than ever it did before. In the last ten years, for instance, the sulpha drugs and the antibiotics have come into use, with the result that pneumonia and cerebrospinal meningitis and septicæmia have lost most of their terrors. Operations on the most vital organs—the heart and lungs and brain—have passed the experimental stage. Anæsthetics have become almost a pleasure instead of an ordeal, and morbidity from severe injuries was far less in the second world war than in the first. These are some of the advances which are most dramatic because they help to cure the sick man, but the advances in prevention have been no less remarkable. Large areas of the world are becoming safe and comfortable to live in because the insect carriers have been marked down and destroyed or antidotes found for the diseases they bring. The cure of scrub-typhus by the antibiotic chloromycetin is the latest example. If all goes well—and wars which stop short of destroying civilisation altogether seem if anything to accelerate the advance—the medical student of the year 2050 will have very few of the existing bacterial and protozoal diseases to study. They will be curiosities, as gout, smallpox, and tertiary syphilis are to most of the present generation.

No doubt the doctors of the next hundred years will have other cares. We cannot be sure that they will know how to stop the virus diseases. New plagues may arise, as epidemic encephalitis arose in 1918. The disorders of the elderly body—cancer, paralysis agitans, heart disease, and the failure of sight and hearing—

* Opening address of the session at the Welsh National School of Medicine on Oct. 5.

may still menace our retirement. A pessimist might list a great many chronic ailments which we have not yet begun to understand because it is so much harder to trace the causes of slow changes than of rapid. He could also point out that we have always been too optimistic, and that very few of the advances made have fulfilled all expectations. The discovery of antitoxins seemed at first to hold the key to the treatment of bacterial disease, but there are only two diseases—tetanus and diphtheria—where they can be used. The vaccines raised the same hopes and have had only a limited success. The hormones and vitamins can be used with great effect but they cannot be used for everything. Even penicillin and the sulpha drugs are not cure-alls.

UNIVERSAL REMEDIES

The argument would be good if all our hopes had to be centred on one particular line of advance. It is true, and a pity, that many such hopes have been dashed, but the really encouraging thing is that nowadays the failures scarcely matter because the advance is on such a wide front. Medicine is already so much of a science that we have almost ceased to think of it as magic. But it was magic to begin with, and the idea is so deep-rooted that it is difficult to give up the hope of finding the elixir of life or—what comes very close to it—a universal remedy and a universal cause for disease. We have, even now, to be very careful to get it out of our heads that each new method of treatment will cure everything. In the nineteenth century the tendency was far greater. Almost universal claims were made for Hahnemann's homœopathic system of treatment—*Similia similibus curantur* (like cures like)—for water cures and nature cures, and for the treatment of the spinal lesion of the osteopaths. And more orthodox medicine was little better. All harmful agents were to be extracted from the body by bleeding and purgatives in the age of Broussais, and not so long ago toxæmia was the root of all evil and the surgeons dealt with it by removing everything they could get at, including the large intestine.

Naturally the public has always taken to the idea of universal remedies. Many of us can recall our reverence for the family physician of our childhood bringing the magical stethoscope out of the top hat and prescribing the tonic which would make us well again; and the chemists' shops with the mysterious bottles of coloured fluid in the windows, and the astrologers' signs, where you could buy the rings which would charm away the rheumatism, and where you might expect that they would have some of the elixir of life under the counter. With so much magic in the air it was not surprising that some of the claims made for new treatments reflected the same kind of day-dreaming; but the glamour has worn thin in a scientific age, and the great thing to be thankful for is that we can afford to do without it. We can be sceptical about universal remedies without losing our belief that almost all bodily disease will find some remedy, or, better still, that we shall find some way of preventing it.

MENTAL DISEASES

No doubt some mental diseases will disappear in the same way. General paralysis of the insane is already a rarity because it has been traced to an infection which can be prevented or cured. There are others depending on chronic poisoning or on vitamin deficiency which should be equally amenable, and others where the symptoms run a definite course suggesting some bodily disorder as their cause. The deterioration of the schizophrenic and the cycle of manic-depressive psychosis have not yet been related to any organic change, but there is nothing about them to make us stop looking for some physical cause. What we have to fear is not that we shall be unable to deal with such definite disorders, but that, in spite of all we can do, many sane people will still be tormented by their hopes and fears. This is where the prospect is still rather uncertain. Have we really advanced very much in the treatment and prevention of neurosis in the past hundred years, and are we advancing now? A great deal has been said and written recently about the men and women of the Victorian age. Many of the great ones of that time have been displayed with human failings and misfortunes. They did not get on with their children, they had grievances, or they drank too much. But on the whole they and our own grandparents do not seem to have had worse difficulties, to have been less well balanced and less contented than we are now. In spite of modern nurseries some children still fear the dark, and stammer, and bite their nails, and some grown-ups sleep badly and commit suicide.

It is difficult to compare then and now, and statistics do not help. If there were any they would almost certainly show a great increase in neurotic illness during the present century, but that would be mainly a matter of more confident diagnosis. We believe now that a great deal of indigestion, headache, lassitude, all the symptoms in the patent-medicine advertisements, may be due to mental rather than physical causes, and many of the unexplained illness of the Victorians would now be classed as functional. To have recognised this is certainly an advance. I remember Dr. James Taylor, the friend of Hughlings Jackson, telling me of the introduction of Babinski's sign into clinical neurology in 1898. Before that there was no simple test to distinguish a functional paralysis of the legs from an organic paralysis due to a lesion of the pyramidal tract. Babinski showed that after a pyramidal lesion the great toe moved up instead of down when the sole of the foot was scratched. His sign was a godsend to the neurologist; it must have kept many patients from a lifetime in bed and spared their relations the trouble of nursing them. Nowadays most doctors can be trusted to recognise the commoner manifestations of neurosis, and hysterical paralysis is so easily recognised that it is rarely attempted. But, when hysterical paralysis was more common than it is now, there was nothing so flattering to the young neurologist as the almost miraculous recovery he could produce in a patient who seemed hopelessly bedridden, and nothing so deflating as the realisation that the patient was not much the better for having the use of his limbs again, that he was in fact a good deal more unhappy than before, when he had some obvious claim to sympathy. Here, for example, is an extract from a recent paper on spasmodic torticollis, a curious complaint which seems to have a psychopathic origin:

> A patient had been treated by a partial analysis and had lost all his spasms. He wrote later: "In the last few weeks I have had no movement in my neck, but I would much rather have it because I now have terrific anxiety. I can't sleep, and when I sleep I have nightmares. I would much rather have my torticollis and have the movements of my neck."

These functional symptoms, most of which can be dispelled in one way or another, are certainly less common than they were thirty years ago, but I am not sure that the less striking disorders, such as headache and nervous dyspepsia, are treated more successfully because we know that they are neuroses. The statistics are certainly rather alarming. It has been stated, and not contradicted, that from a third to a half of all medical invalids discharged during the war were discharged on psychiatric grounds, and that in conflict the figure might rise to three-quarters of the casualties. In industry a survey of 3000 workers showed 10% had had definite disabling

neurosis and a further 20% minor neurosis causing absenteeism during the six months before the investigation; 30% of the patients attending medical outpatient clinics are said to be really cases of psychiatric disorder; 1 child in 30 is likely to spend some time in a mental hospital, and 1 in 10–15 will have a nervous breakdown.

There is nothing here to encourage the belief that we are treating these disorders much better now than they were treated fifty or a hundred years ago. It looks as though recognition of their cause has not done much to remove it, and we should certainly find it hard to produce convincing evidence of a real improvement in the way neurosis is dealt with. But, in spite of that, I think everyone who has had much experience in these cases would agree that there has been a real improvement. There are certainly encouraging signs.

There was the much smaller incidence of gross hysterical symptoms and of persistent severe neurosis in the recent war compared with that in the 1914–18 war, and there is the much greater appreciation by everyone—public as well as doctors—of what neurosis can do. After all, it is only within the last fifty years that psychological medicine has had an adequate theory to build on. Before Freud there were descriptions like Weir Mitchell's "neurasthenia" and Janet's "retraction of the personality," but nothing that held out much prospect of explaining the particular symptoms which the neurotic patient happened to develop. Today every film-goer knows about the unconscious—at least about its more respectable manifestations—and another sign of more widespread knowledge was told me by a magistrate who said that nowadays it is almost the rule for a convicted prisoner to ask for more favourable consideration because of the psychological mismanagement of his early childhood.

The small incidence of neurosis in the war was due largely to the more effective weeding-out of the men who would not have been able to stand the strain. In peace-time the strains are less intense, but we are not braced to meet them as we are in war. The same kind of vocational selection will certainly help in peace, but no-one supposes it will banish neurosis entirely; and for the treatment of severe illness the methods which psychological medicine has evolved are either very elaborate, like psycho-analysis, or else dependent on the personality and enthusiasm of the doctor. There will always be successful psychotherapists whose effectiveness depends not on the particular theories they hold but on their general relation to their patients, much as there will always be mothers and nurses who will bring up their children well without considering how they are doing it. What we still lack in psychotherapy, as in infant training, are the definite rules which can be learnt and applied by all of us, the formula which will make it possible to treat the patient on the intellectual level without any emotional exchanges. Greater understanding of psychological processes will make that easier, but there is not much indication that the methods required for dealing with an obsession will ever be as straightforward, as reducible to a formula, as the methods needed for a streptococcal infection.

OLD AGE

There is one class of mental trouble which is in a special category and where the prospects are on the whole much better. In the near future we shall have to think not only of the people who go through life with what is called the psychopathetic temperament but also of the large number of normal but elderly people whose lives we have prolonged. There is one of Swift's satires in which Gulliver on his travels comes across the miserable people known as the Struldbrugs, who were born with the mark of immortality on their foreheads and were immune from death but not from old age and all its consequences. It is not a picture we can afford to neglect when we congratulate ourselves on having extended the range of life. All of us, whatever our temperament, may have good cause to be unhappy, when we are old, because we have lost our friends and are not wanted, or because we are losing our hearing, our memory, or our self-control. Let us therefore hope that we shall soon have learnt how to look after the ageing body so that nothing much goes wrong with it until the final complete break up. We must learn to emulate the car manufacturers whose products were constructed to give good service for three years and then to break down so comprehensively that the owners were spared all the anxiety of repairs and had no other course but to order the new model. It is not too much to expect that we shall soon know enough to avoid the particular habits which make us live too long for comfort, which keep our hearts going after our mind has failed. At all events the problems of old age are primarily physical, a matter of arteries and cell degenerations rather than of repressed hopes and fears.

PREFRONTAL LEUCOTOMY

In the present state of our knowledge the former sort of disorder seems more likely to be preventable and curable than the latter; but one can make too much of the distinction between mind and body, and the recent trend in psychiatry has been towards the physical treatment of mental trouble. In fact one recent development aims at the mind by deliberate interference with the structure of the brain. This is a branch of neurosurgery which is still in its infancy, and no-one would be rash enough to guess how it will grow. But already it raises important issues with which the medicine of the future will be more and more concerned.

In a sense the issues are not so new. Medicine has always claimed the right to treat disorders of the spirit. When the temperament and emotional state were related to the colour of the bile, they bled and purged the sanguine and choleric, and tried to lighten the dark humours of the melancholic. So now, when we carry out a prefrontal leucotomy in a patient whose anxieties are too much for him, we are not trying to alter his character any more than the medieval physicians did in their day. However, the fact remains that we can do it more effectively and more permanently. By destroying the nerve-fibres in the frontal lobe of the brain we can make people less anxious, less preoccupied with the unfortunate state of the world, less worried by their doubts and failures. They become care-free, self-satisfied, less sensitive, less of a burden on themselves and other people. Sometimes the results are far less satisfactory, but Moniz's operation has had spectacular successes which cannot be overlooked. It has been used for other things besides the obsessions of the psychasthenic. Prefrontal leucotomy can be done, for instance, to make the pain of inoperable cancer more bearable; for, though the pain is still felt, the effect of the leucotomy, when it succeeds, is to make it no longer so distressing. No-one would grudge that sort of relief; but in the relief of anxiety we shall have to go rather carefully. The problem is to decide where to stop—how much responsibility to leave. Rylander has cited some interesting cases to show what may happen. The nurse who worried herself into a breakdown about the treatment of her patients became after a leucotomy a happier but a less careful nurse, better fitted probably to look after a convalescence than a serious illness. The mechanic whose spare time is spent in sociology and economics settles down to football pools and family life. No doubt we shall learn in time to remove just the right amount of morbid anxiety so that the patient becomes reasonably care-free and also reasonably careful. After

all, they had the same sort of doubt when anæsthetics were first introduced, arguing that pain in childbirth was good for the character. We seem to have decided now that all bodily pain is evil and should be suppressed, and perhaps we ought to feel the same about mental pain. Hamlet would no doubt have led a happier life after a leucotomy, and the state of Denmark might have been little the worse.

REGIMENTATION

This problem of mental health and responsibility is not bound up with any particular method of treatment. It is well illustrated by what happens after a leucotomy, but any method of influencing the mind must involve some idea of the sort of mind to aim at. We have fairly clear ideas of bodily health, we can decide when medical aid is worth while to bring the bodily efficiency back within the accepted range. And we are not likely to make too standardised a product. So far as the body is concerned, the extreme variations which are likely to go are all things which will not be missed, like the adenoid face, the bandy legs of rickets, and the signs of congenital syphilis, that have now almost disappeared. But mental health is a much more difficult matter. If it can only be achieved by a comfortable uniformity, by ironing out all the rough experiences of our mental development, by making us unambitious and contented with our lot, we might very well hesitate to try to impose it. How much unhappiness and discontent should be regarded as within the acceptable range for a particular person? When does eccentricity and antisocial conduct become a matter for medical care? To what lengths should we go in bringing up our children so as to prevent their becoming saints or rebels, to ensure their settling down comfortably as respectable citizens? If medical psychology advances with the rest of medical science it may well give us the power of influencing these things to a far greater degree than has ever been possible before. Even now, for instance, UNESCO has teams of psychologists engaged in research on the tensions which lead to war. If the spirit of aggression could be prevented by adding some pacifying vitamin to everybody's diet, should we take this step to prevent it? I suppose we should if it were quite certain that some countries would not veto the proposal for their own citizens.

Clearly this kind of decision, which involves altering the character of mankind, will involve medicine in heavy responsibilities. But the prevention of serious mental disturbance, like that of bodily disease, is bound to involve more and more interference by the medical profession in the lives of people who do not regard themselves as ill, and in the upbringing of their children. The Ministry of Health may be called on to ensure healthy food for the mind as well as for the body. Not too much news about murders and suicides, as well as enough vitamin D in the margarine. There may have to be more and more regulation of our mental activity, the hours we keep, the colour of our rooms, and the music we should listen to. There would be nothing very new in such proposals except their aims. After all, in Plato's republic the only kind of music that was to be permitted was martial music to encourage the aggressive spirit of the citizens. It is at least a sign of grace that we are now led to think of a world where the aggressive spirit will not be so essential to survival.

Would this sort of interference with the mind be too great a price to pay for increased mental stability? Few of us would want to be the priests of a new religion which will dictate how men ought to use their minds, even though we believe that they might use them better than they do now. But, whether we like it or not, we have to face the prospect that the control of individual liberties by experts must become more and more an accepted part of civilised existence—and the experts will be the doctors and psychologists as well as the economists and politicians and lawyers.

After all, prevention—and that is what the medicine of the future must aim at—cannot but involve a great deal of control of what people may do. Even now we impose countless regulations on the public: they may not spit in railway carriages, they may not enter certain countries without inoculation and vaccination, and the quality of their food and their houses and sanitation is decided for them. How long shall we allow them to sneeze in public or to drive a car when they are angry or sleepy? As we come to know more and more about prevention of disease and accident we shall have to make more and more regulations to see that they are prevented.

And our functions must extend to more than the prevention of disease. If infant mortality is greatly reduced in countries where the birth-rate is high and the standard of life low, there will soon be too many people to feed. Already the control of malaria is beginning to increase the population to an alarming extent in certain areas. We can scarcely rely on the famines and wars of the next hundred years to keep the population of the world within limits. It must be controlled somehow by propaganda, by economic pressure, even by penalties or drugs. However it is done, birth control will be a medical concern, though the problem of adjusting the population to the resources of the country will call for all kinds of expert knowledge and for decisions at the highest levels of government.

It is easy to paint a horrible picture of the cold-blooded doctor and scientist of the future prescribing every detail of the lives of a population which has been made docile and uniform by correct dieting and upbringing (if not by operations on the brain), and has been adjusted as regards numbers so that there is a place for everyone, and everyone in his place: there have been many utopias which seem to have been devised to produce just that kind of society, and very few people can have wanted to live in them. But the prospect is really not so bad. The human brain confers on us not only an amazing power of controlling our circumstances but also an amazing power of becoming adapted to them. Our activities nowadays are already regulated to make us fit into an extremely complex framework. There are all sorts of things we must and must not do, but we have learnt to accept most of them without really giving up any of the freedom and variety of our lives. Most of the new controls which have been imposed by the State have seemed at first to be an unwarrantable intrusion on the private lives of the citizens; but after a time, if the control has turned out to be reasonable and necessary, it has become part of the normal framework, and people have ceased to resent it. You have only to read the outcries which greeted the early attempts to impose education and sanitary legislation on this country to realise that our standards of what constitutes liberty can change fairly rapidly, and that no-one is much the worse when they do. We are just as resentful over new controls which seem to deprive people of their personal freedom, but we do not give much thought to the old ones. Though we may have more forms to fill in and more cards to carry about, I think most of us feel, and are, as free as our grandfathers, as angry at everything which seems an encroachment on our liberty, and as superior to the inhabitants of other countries where they have a different list of restrictions, or where they are not encouraged to grumble so much.

THE FUTURE

The doctors of the future will be in authority over mankind and cannot expect to be popular. Since there will be little serious illness, they will miss the gratitude which comes their way when they happen to have done their job without bungling. They will be accused of

interfering in matters which are outside their special province and blamed when anything goes wrong because they have not interfered. And, although we can confidently expect that they will make mankind much healthier, it will need constant vigilance to keep it so—perhaps a constant struggle to prevent new diseases or variations of old ones, at any rate constant research and a good deal of disappointment.

We can confidently expect that mankind will be kept much healthier in body and, in spite of the doubts I have expressed, we can look for a great improvement in mental health as well. I should like to think that mankind will be the happier for this, yet as a biologist I am not so sure. Mankind will be more active no doubt and longer-lived; there will be less absenteeism in industry and fewer patients in mental hospitals—they will be better specimens of the genus *Homo sapiens* in fact. But happiness or even contentment is another matter. The adaptability of the living organism has been mentioned already to explain why we are not constantly discouraged at some of the inconveniences of life nowadays; it explains also why we are not constantly happy at the thought of the diseases we are escaping. In man adaptation is largely the affair of the brain. Living cells in general show remarkable powers of adapting themselves to their environment so that they can continue with their normal cycle of activities in all sorts of circumstances; but in the complex organisms, and in man in particular, the individual cells do not need a wide range of adaptation, for the organism can keep the immediate environment relatively constant. With man the immediate environment of the cells is perhaps the most narrowly adjusted of any mammal, but our brains have made it possible for us to live in an immense variety of conditions. Owing to the contrivances we make we can live in places where it is very hot or very cold (outside the immediate surroundings of our bodies), where there is no daylight, no food, and no oxygen. In the last hundred years we have constantly extended the range of our environment. For a cat it is a house, some roof-tops, and a garden; but for a man it is no longer a village or even a country. We can travel as fast as sound, we can hear what is said 1000 miles away, and we shall soon be able to see what is happening there as well. Yet these changes in the scale of our activities are at once assimilated by the brain and are accepted as the natural way of life. They cause no permanent change of mood, and we have no reason to suppose that we are happier than our grandfathers because we can do so many things that they could not. So with increased health: we suit ourselves to the world we are in and to the experiences it gives us; we have less disease and live longer now than they did a hundred years ago; there is much less chance that our children will die young, or that we shall have to face a great deal of pain; and we have all sorts of facilities for living comfortably—better food, fewer unpleasant smells, and so on. But I do not think anyone would be bold enough to say that the world is a happier place for us now than it was then—apart altogether from the particular circumstances of these last few years. Undoubtedly the many people who lived in such miserable conditions in the industrial districts a hundred years ago, and the many who were dying of famine in Ireland in 1846, must have suffered conditions too extreme for adaptation; but an improvement in health will not prevent overcrowding and famines, and did not prevent the widespread unhappiness of the workless twenty years ago.

For this reason I think we shall be deluding ourselves if we suppose that what we are going to do in the next hundred years will lead to a permanent increase in the happiness of the human race. I fancy that life will be much the same mixture of happiness and unhappiness that it is now—that our moods must always tend to oscillate about a position of equilibrium which does not greatly depend on external circumstances. And our brains will always tend to drive some of us to act up to the limit of what is possible. Medical science may give us more control over the mind as well as over the body, but it will not be able to change the general principles which govern its working. For the present I think we had better leave happiness out of it, though our contributions to that will not be worth nothing at all. What we can be sure of giving is a more vigorous life for mankind and a greater freedom from physical pain; and if we can give more than this, so much the better for everyone.

ENVOI

If Dr. Faustus had to make his choice now, would he find medicine any more to his taste? He might still heap up a certain amount of gold as a specialist, but he would still have no hope of making men immortal or raising them to life again. On the other hand, he was ambitious and eager for new experience and for power over his fellows; and the medicine of the future would give him opportunities for influencing mankind in new and unexpected ways, of controlling their general character and the kind of lives they would lead. He might find himself charged with the task of regulating the increase of population and of trying to control heredity and environment in such a way that there would be just the right proportion of rebels and eccentrics to keep the human race from stagnating. He might become a psychiatrist, for he would find that the study of the human mind raises problems worthy of even his ability. And of course if he turned to the laboratory there would be the immense field of research into all the processes of life, with all the new methods of investigating them.

For us ordinary people that I am sure will be more than enough. For Dr. Faustus I am not so sure. His subsequent career in Marlowe's play suggests that, if he chose a scientific career, it would be in physics with its cosmic problems rather than in physic with its human ones. Mephistopheles might then tempt him with all the possibilities of atomic disintegration, and the play might have an even more spectacular end. Mephistopheles will no doubt supply the appropriate temptations for those of us who have chosen medicine, but he will not be able to persuade us that its future practice will become less interesting, and that its future aims will not be worth pursuing with all the energy we can give.

A DRUG SENSITISING THE ORGANISM TO ETHYL ALCOHOL

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EXPERIMENTS in these laboratories with diethylthiuramdisulphide [bis (diethylthiocarbanyldisulphide)]—formula $(C_2H_5)_2$ N C (S).S.S.C (S) N $(C_2H_5)_2$—showed that people who had ingested 0·5–1·5 g. of this substance (an otherwise inert dose) developed characteristic symptoms when they subsequently drank even small amounts of alcohol. These symptoms include a feeling of heat in the face, followed by an intense flushing, located principally in the face but spreading in some cases to the neck and upper part of the chest and arms or even to the abdomen. A constant effect is dilatation of the scleral vessels, making the person look "bull-eyed." These are followed a little later by palpitations, and sometimes slight dyspnœa. After larger doses of alcohol nausea and vomiting often develop. If nausea is intense, blushing gives way to pallor. These symptoms, which are usually accompanied by headache, are very unpleasant. They disappear, however, within a few

hours, generally leaving the person rather sleepy. After the alcohol has been oxidised, the person feels completely well again, and all complaints are usually relieved by a short nap.

Similar symptoms follow the intake of alcohol combined with some other drugs, the best known of which is cyanamide (Koelsch 1914, Mellinghoff and Thomas 1939, Gärtner 1939, 1944, Thiery 1942). Ingestion of the fungus *Coprinus atramentarius* in combination with alcohol gives rise to similar symptoms (Fischer 1945). In rare cases of idiosyncrasy to alcohol similar symptoms appear without any other drug being taken.

In collaboration with Dr. Valdemar Larsen of these laboratories, and with Dr. Erling Asmussen and Dr. Gunnar Jørgensen of the Laboratory for the Theory of Gymnastics, University of Copenhagen, we have further examined this peculiar effect of diethylthiuram-disulphide (trade name 'Antabuse').

TOXICITY

Tetraethylthiuramdisulphide is relatively non-toxic. The lethal dose in animals is reported to be 3 g. per kg. of body-weight (Henzlet and Irvine 1921). In experiments in our laboratory daily doses of 10 mg. were given to rats, and 60 mg. to rabbits, for more than three months without any notable effect on the blood picture or otherwise. In clinical trials single doses of up to 6 g. and daily doses of 0·25–0·60 g. for several months were given without producing any subjective or objective symptoms apart from those following the ingestion of alcohol.

RESPONSE TO ALCOHOL

Normal people usually show no effect or only slight symptoms after taking 10–20 g. of alcohol—e.g., 30–60 ml. of gin—but, if a person has taken 1·0–1·5 g. of antabuse

EFFECT OF ALCOHOL IN NORMAL PEOPLE WITH AND WITHOUT PREVIOUS TREATMENT WITH ANTABUSE 1·5 g.

—	Before intake of alcohol	½ hr. after intake of 60 ml. of gin (43 % by vol.)	
		Not treated with antabuse	Treated with antabuse
Respiratory dead space (ml.)	121 [1]	138 [3]	154 [3]
Ventilation in litres per litre of oxygen consumption	19·1 [4]	19·1 [3]	23·1 [3]
Alveolar CO_2 (%)	5·35 [1]	5·40 [3]	4·42 [3]
Oxygen consumption (ml. per min.)	264 [4]	270 [3]	324 [3]
Cardiac output (litres per min.)	6·02 [4]	5·76 [3]	8·64 [3]
Pulse-rate (per min.)	65 [4]	64 [3]	90 [3]

1. 13 experiments in 4 persons. 2. 4 experiments in 2 persons.
3. 6 „ „ 4 „ 4. 14 „ „ 4 „

the previous day, symptoms develop mainly involving the circulatory and respiratory systems. Circulatory effects are the facial vasodilatation already described, pulse-rate raised to 120–140 per min., and a slightly increased cardiac output (figs. 1 and 2). No significant change in blood-pressure has been observed, except for a slight fall in a few instances. Respiratory effects include an increase in the dead space, increased pulmonary ventilation, and a corresponding reduction in alveolar carbon dioxide. The main results are given in the accompanying table (after Asmussen et al. 1948a).

The extent of the vasodilatation can easily be registered objectively by measuring the skin temperature of the face. Within less than 30 min. of taking alcohol this rises to 1°C or less below the body temperature. The

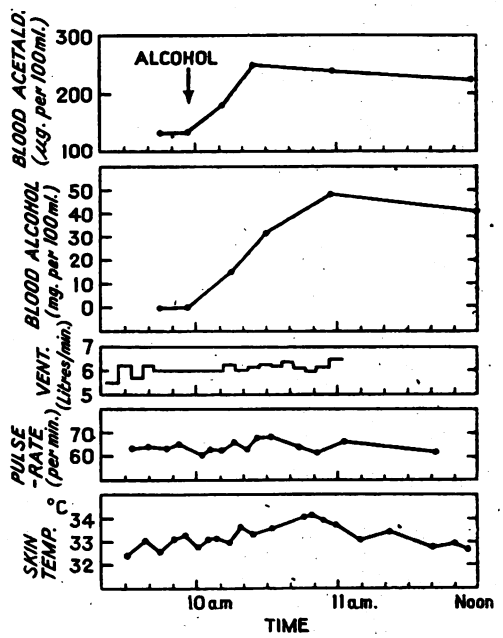

Fig. 1—Effect of 40 ml. of gin on ventilation, pulse-rate, skin temperature of face, blood alcohol and blood acetaldehyde in a normal person.

magnitude of the increase naturally depends on the skin temperature before the intake of alcohol.

The effects start 7–12 min. after the ingestion of alcohol and are maximal after about 30 min. (fig. 2). Flushing is the most sensitive symptom and is generally seen with a blood-alcohol level of about 15–20 mg. per 100 ml. The increase in ventilation and pulse-rate is first noted when the blood-alcohol level reaches at least 25–40 mg. per 100 ml. The effects are independent of the route by which the alcohol is given (Hald et al. 1948).

In experiments on animals Larsen (1948) noted no definite effect on blood-pressure, but pulmonary ventilation increased 20–35% after the administration of alcohol to animals previously treated with antabuse, whereas no change was seen in untreated animals given the same dose of alcohol.

The lethal dose of alcohol was determined in mice or rats, and only a slight reduction was seen in groups previously treated with antabuse compared with non-treated animals.

The characteristic effect of alcohol does not appear unless the antabuse is taken at least three hours earlier; in some clinical trials this latent period was as long as forty-eight hours.

ABSORPTION AND EXCRETION

The absorption of antabuse from the gastric intestinal tract is not complete. In man about 20% of a given dose is excreted in the fæces during the following two or three days, and the same tendency is seen in rabbits and dogs. The elimination of antabuse is very slow in man. No antabuse is excreted unaltered in the urine, and after the intake of 1·5–2·0 g. by mouth no increase in the S/N ratio was detected in the urine during the next eight days.

Owing to the slow elimination the effect of a single dose lasts rather a long time. If the increase in skin temperature after the intake of 40 ml. of gin is taken as an indicator, the action of antabuse 0·5 g. lasts three or four days, 1·0 g. five or six days, and 1·5 g. seven or eight days.

No experiments have yet been done to find out if the protracted action is due to slow absorption from the

intestinal tract or to fixation in the tissues after absorption. The latter alternative is the more probable.

MODE OF ACTION

Several hypotheses to explain the similar effects of cyanamide have been suggested (Le Monaco 1918, Hesse 1921, Dittrich 1924, Glaubach 1926, Thiery 1942). All of them, however, seem poorly founded, and we have been unable to reproduce the observations on which these hypotheses were based when antabuse was given to animals.

Some of the effects observed are very similar to those of histamine, but no rise in blood-histamine level was found after the administration of antabuse and alcohol. Moreover, bronchodilatation was observed, whereas histamine produces bronchoconstriction (Asmussen et al. 1948a).

The symptoms can, however, be fully explained by an increased formation of acetaldehyde after the taking of alcohol by people previously treated with antabuse. Small amounts of acetaldehyde are found in the blood even in normal people after taking alcohol (Stotz 1943). In people who have taken antabuse the blood-acetaldehyde level rises to about two to five times that in normal people who have taken the same dose of alcohol (figs. 1 and 2). Further, up to nine times as much acetaldehyde can be isolated and identified as 2, 4-dinitrophenylhydrazone from the expired air of antabuse-treated people as in normal people given the same amount of alcohol under the same conditions (Hald and Jacobsen 1948).

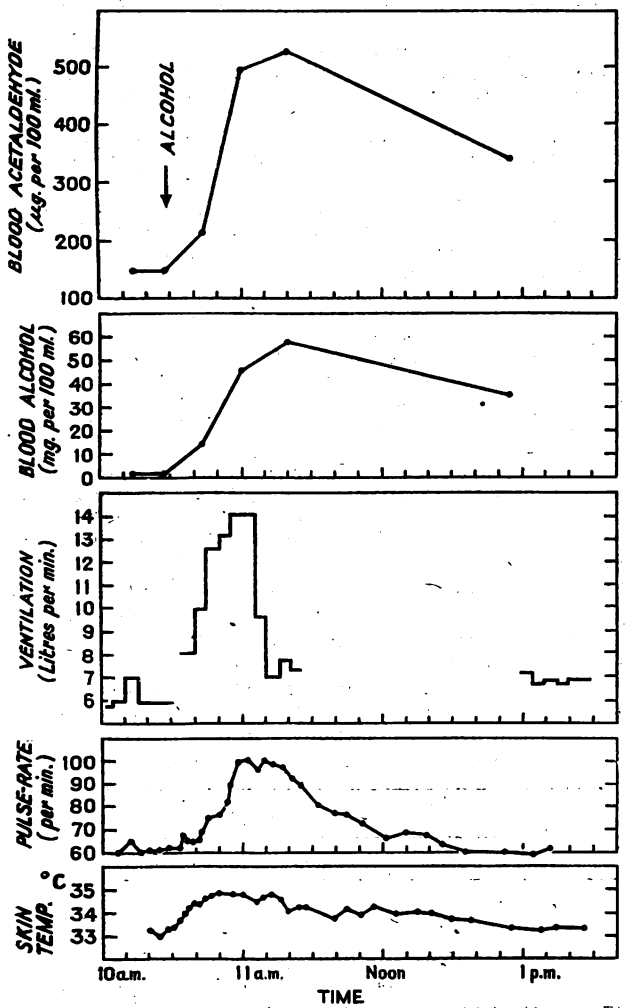

Fig. 2—Effect of 40 ml. of gin on ventilation, pulse-rate, skin temperature of face, blood alcohol, and blood acetaldehyde in a person who had taken tetraethylthiuramdisulphide 1·5 g. the previous day.

Handovsky (1934) has shown that acetaldehyde increases the ventilation and heart-rate, but it is not known at what blood-acetaldehyde levels these effects appear; nor do the few published reports on the pharmacology of acetaldehyde describe its effect on the peripheral vessels in man. By means of continued intravenous infusion of acetaldehyde Asmussen et al. (1948b) have shown that at blood-acetaldehyde levels corresponding to those found in antabuse-treated people after taking alcohol the same qualitative and quantitative effects are elicited: flushing of the face and upper part of the chest, increased ventilation, reduced alveolar carbon dioxide, raised pulse-rate, and an increased dead space (fig. 3). Even in rabbits Larsen (1948) observed increased ventilation at blood-acetaldehyde levels corresponding to those found in antabuse-treated animals given alcohol. Acetaldehyde accumulates very rapidly after the intake of alcohol in antabuse-prepared animals; within 3 min. after the intravenous administration of alcohol to antabuse-treated rabbits a considerable increase in blood-acetaldehyde was noted.

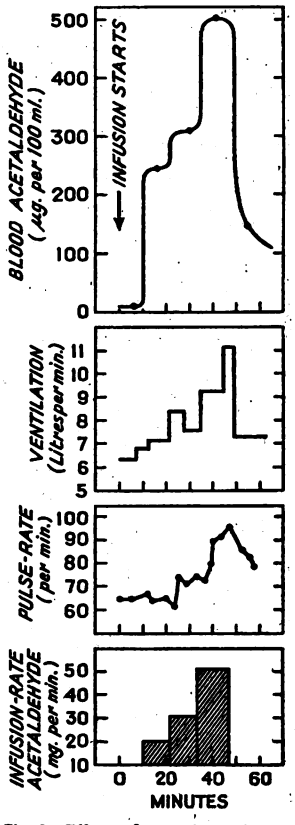

Fig. 3—Effect of acetaldehyde on ventilation and pulse-rate in a normal person.

It is difficult to explain why antabuse causes acetaldehyde to be formed in higher concentrations than normal after the ingestion of alcohol. The elimination-rate of alcohol as measured by blood-alcohol levels was the same in normal people and in people treated with antabuse. In rabbits also no difference between the two groups was observed. Our experiments show that acetaldehyde is eliminated at the same very rapid rate regardless of whether the animals have been treated with antabuse or not. This observation accords well with the fact that the blood-acetaldehyde level is not raised in antabuse-treated animals before the administration of alcohol.

It must then be supposed that only part of the alcohol consumed passes, during oxidation, through the intermediate stage of acetaldehyde. In-vitro experiments made by Lutwak-Mann (1938) support this suggestion. Perhaps after treatment with antabuse, the normal elimination of alcohol is partly or completely blocked, and under the influence of the alcohol dehydrogenase a higher proportion of alcohol than normal is oxidised to acetaldehyde. Another possible explanation is that the alcohol hydrogenase is highly activated by antabuse, but further experiments are needed to solve this problem.

SUMMARY

The organism is sensitised to alcohol after intake of tetraethylthiuramdisulphide (antabuse).

Alcohol given to persons previously treated with this otherwise innocuous substance produces dilatation of

the facial vessels, increased pulmonary ventilation, raised pulse-rate, and general uneasiness. The symptoms appear to be the result of an increased formation of acetaldehyde from alcohol.

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TREATMENT OF ALCOHOLISM WITH A SENSITISING DRUG

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HITHERTO treatments for chronic alcoholism have given poor or transient results. The most successful has been psychological treatment, and except for the use of apomorphine in the aversion treatment, no drug has proved at all effective. However, the discovery by Hald and Jacobsen [1] that the intake of tetraethylthiuramdisulphide ('Antabuse') sensitises the organism to even moderate doses of alcohol makes it possible to develop a medical treatment for alcoholism. Concurrently with the examination of the pharmacological effects of this substance I have studied the clinical effects of antabuse on alcoholics. My experiments have now run for about six months and, though this is far too short a time for a full assessment, the results seem promising enough to be worth publishing.

From December, 1947, to May, 1948, 83 patients have been treated with antabuse. So far no harmful systemic effects on liver, heart, kidney, or blood-forming organs have been observed; nor have any untoward side-effects been noted which could be attributed to antabuse.

The general scheme of treatment has been mainly as indicated in the 3 illustrative case-records given below.

After careful physical examination and study of the medical, psychiatric, and social background, the patient is given 1·0–1·5 g. of antabuse and is told to continue with 0·5 g. daily. He is told that he will become ill if he drinks alcohol, and is asked to return for a second interview two or three days later. The patient takes two or three drinks either the night before or immediately before the second interview to show the effect of the treatment. Sometimes the patient will already have taken the alcohol before this time, often in larger amounts than recommended and with a violent reaction, which is beneficial from a therapeutic point of view. A few patients, mostly heavy drinkers, can take considerable amounts of alcohol before the effect appears. In such cases the medication is continued and the patient is tested in the same way at intervals of four to six days. The tolerance for alcohol is, however, gradually reduced.

Thus, for example, after taking antabuse 1·5 g. the previous day and 0·5 g. the same morning, a heavy drinker took nine drinks (under control) during an hour. He blushed and had a raised pulse-rate but nevertheless wanted to continue drinking. Five days later he was tested again and took twenty-six drinks before he had an explosive and copious vomiting. Like all serious cases he was admitted to hospital during the beginning of the treatment. After the second test he was discharged from hospital but continued the treatment. A few days later, after only two drinks, he had to break away from a lunch with his fiancée in a restaurant and take a taxi home. A few days later he became ill even after a single drink.

Such patients are exceptions; most feel so uneasy after four or five drinks taken in one or two hours that they never want to repeat the experience.

When the characteristic effect is observed, the patient is told to continue the treatment and is seen at least once a week at first and at longer intervals later on. It is very important for the patients to keep in contact with the doctor, or for their relations to report to him, so that the effect of treatment can be controlled. In milder cases the patient sees the doctor in his consulting-room, but sometimes it is necessary for the doctor to visit the patient's home.

RESULTS

The patients studied here had sought treatment for alcoholism more or less voluntarily, either at a psychiatric department or as private psychiatric patients. All alcoholics seen since December, 1947, have been given the treatment and are included in this report. They are divided into four groups:

Group A: the 32 patients in this group benefited sufficiently from the treatment to continue on a token dose (often only 0·0625 g. a day) after a few weeks' observation period. Later their treatment was controlled by telephone. These patients can increase their dose when they know they will be tempted to drink.

Group B: the 29 patients in this group see the doctor in his consulting-room at regular intervals and are encouraged to continue the treatment. Their blood and urine are examined, and further dosage is fixed to meet each patient's requirements. The dosage in this group must be sufficient to prevent the patient from taking more than one or two drinks at a time.

Group C: the 13 patients in this group are more psychoneurotic than those in groups A and B and are therefore more difficult to follow. Their desire to be treated is not always genuine, and it often requires an effort on the part of the doctor and the patient's relations to make them continue the treatment. The general impression is that even these difficult subjects have been helped to some degree, but a very long observation time is necessary before definite conclusions can be drawn. No doubt the treatment would be still more effective if legal measures could be taken, but for the present this is impossible in Denmark, in contrast to Sweden and Norway.

Group D: in 9 cases the treatment has failed. Most of these patients have serious psychic defects. All of them have shown the characteristic symptoms after intake of antabuse and alcohol, but they have lacked interest in the treatment and have refused to continue it.

The results are given in the accompanying table. The rather high figure in group C in the first column is due to the fact that the treatment was first tried on a group of psychoneurotic heavy drinkers on whom a series of other treatments had failed. Subsequently a larger less homogeneous group was also treated. It is possible that some of the patients treated for only a short time may be transferred to another group after a longer observation

Group	Duration of treatment			Total
	4–7 months	2–4 months	1–2 months	
A	8	11	13	32
B	6	10	13	29
C	8	1	4	13
D	3	5	1	9
Total	25	27	31	83

For the meaning of the groups see text.

1. Hald, J., Jacobsen, E. *Lancet*, Dec. 25, p. 1001.

period: but experience has shown that it is fairly easy to judge to which group a given patient belongs, from his psychological history and a comparatively brief observation.

ILLUSTRATIVE CASE-RECORDS

Case 1 (group A).—A woman, aged 43, was an only child of upper middle-class parents; she had been brought up mainly by her mother, who had rather spoilt her. In her youth she showed good faculties but was shallow and lazy. She was always good-natured. After being employed in several different jobs from the age of 19 she married at 25 and had one child. At the age of 13 she underwent an operation for Graves's disease, of which she retained no symptoms.

Her good economic position enabled her to enjoy society life and parties. Her addiction to alcohol developed since 1939 but increased considerably since 1946. At first she took only wine at parties, but later she also drank beer and brandy and continued drinking on returning home. When treatment began she was taking an average of ten drinks a day. In January, 1948, a psychiatrist advised treatment in a clinic for a year, but she refused. Her first interview with me was on Jan. 24, 1948.

On examination nothing remarkable was found. At first the patient refused treatment, saying she did not want to be abstinent for the rest of her life, but finally she was persuaded to try it. She was given antabuse 1 g. and told to drink alcohol the same night. Six hours after taking the antabuse she drank a pint of beer and a glass of rum. She blushed but showed no further symptoms. Two hours later she drank about 2 pints of beer. Shortly afterwards she noted severe blushing of the face and the upper part of the chest, palpitation, and an unpleasant feeling of dyspnœa. A little later, feeling sleepy she went to bed and slept soundly the whole night. She felt perfectly well next morning and continued to take antabuse 0·25 g. daily.

At various parties in the next few days she sipped wine but discovered that she had no desire to drink. She blushed after a single mouthful of claret. Her abstinence might be explained by her desire to avoid the humiliation associated with the blushing, but she insists that this is not the deciding factor, and that she has lost the taste for wine and spirits.

In the following month a daily dose of antabuse 0·125 g. was sufficient to make the patient blush after a single glass of wine. She refused a second glass, to avoid the uneasiness she felt the first evening.

On March 1 she attended a dinner party at which several doctors were present. Because she was too shy to reveal her abstinence and wanted to take a couple of drinks without blushing, she was allowed to omit the antabuse for four days before the party. After a single glass of light wine, however, she blushed so much that one of the doctors jokingly asked if she was going to have german measles. The effect faded in half an hour, but she did not take any more drinks that evening.

She now continues to take antabuse 0·0625 g. daily. Occasionally she has two or three drinks at parties with a faint blushing effect, but generally she does not want to drink. On April 8 she and her husband affirmed that she had regained her psychological stability. She has once more become interested in her home and has no inclination to spend too much time at parties. She is in excellent humour, sleeps better than she has for many years, and is willing to continue treatment, though she now finds it unnecessary.

Case 2 (group B).—A man, aged 39, had been a master baker since he was 23. From the age of 25 he began to take alcohol to increase his self-confidence, courage, and energy. He took various types of spirits, even denatured industrial spirit. In 1940 and 1944 he was admitted to an asylum for alcoholics, but for only a few months each time. In 1944 he was treated unsuccessfully with apomorphine. In 1947 a professional hypnotist treated him by suggestion. After this the patient abstained from alcohol for a few months, but later he began drinking as before. In January, 1948, he took about a dozen drinks a day, often starting early in the morning, with the result that his wife had to look after the bakery. His first interview with me was on Jan. 9, 1948.

On examination he was a pale fat pyknic man with characteristic tremor of the hands and he smelt of alcohol. Psychologically he was submissive and aware of his disability. He seemed miserable, tired, depressed, and unreliable, and subconsciously minimised the extent of his alcoholism.

Treatment and Progress.—Treatment was started with antabuse 1 g. followed by 0·5 g. daily. In the ensuing month the patient's reports did not agree with those of his wife, but apparently he still drank though not so much as before, and he developed blushing, dyspnœa, palpitation, &c., after alcohol. He became uneasy and had to rest often, partly because of the alcohol intake, but mainly because of the added effect of antabuse. He also regained sobriety more readily.

After six weeks of this treatment the patient and his wife agreed that his desire for alcohol had disappeared. He became more cheerful, felt well and could do his work again. Taking alcohol, he said, produced colicky pains in his epigastrium, throbbing in his head, and a "hangover" but only for a few hours.

He now takes antabuse 0·125 g. daily. He drinks no alcohol but takes a little more coffee and smokes somewhat more. Emotionally he seems better balanced. He is content with the result of his treatment, and he looks better and shows no tremor of the hands.

Case 3 (group B).—A man, aged 41, whose father, paternal uncle, and paternal grandfather had probably all been alcoholics, had had an unhappy childhood. His mother died when he was 8 years old, and his father remarried. Relations with his stepmother were not cordial. He was backward at school. He entered his father's house-painting firm and had no other special interests. After his father's retirement he found it difficult to keep the firm on the same level as before. He felt inadequate, and from the age of 28 began to drink increasing quantities of alcohol, until 10–20 drinks a day became normal to him. In 1947 he was sentenced to fourteen days' imprisonment for driving a car while intoxicated. This was probably why he came for medical treatment on Jan. 26, 1948.

Treatment and Progress.—Antabuse was given in the same doses as in case 2. Here also there were discrepancies between the statements of the patient and of his wife during the first weeks of treatment, but since March 1 he has been completely abstinent (with the exception noted below) and continues with 0·125 g. of antabuse a day. He readily takes his medicine and is satisfied with the result.

On April 15 he went to see his dentist and took no tablets that day. Next day he had lunch with a man he had met in jail when they were undergoing sentence for the same offence. The patient thought he ought to take a couple of drinks; and, since he was eager to avoid blushing, he took no tablet that day either. The result was that he suffered only a transient indisposition and continued to drink all day.

Next morning the patient was inclined to continue drinking, as he would have done before treatment, but instead he took 0·5 g. of antabuse and telephoned the doctor. When seen at 2 P.M. he showed the combined effects of alcohol and antabuse: intense blushing, pulse-rate 120 per min., and a feeling of dyspnœa. He was very nervous and eager that the symptoms should develop no further. He said he had taken only one drink on the way to the doctor, and he refused to take another though it was offered by the doctor.

A week later the patient's condition had so improved that he could continue on 0·25 g. of antabuse a day. He has taken no alcohol since. His incipient relapse was thus completely stopped.

COMMENTS

The follow-up is still too short to ascertain how long the results will last, or if any undesirable side-effects will follow the protracted use of antabuse. For this reason caution is advised in treating patients with organic diseases. So far, however, the treatment is promising, especially for the habitual drinker.

Naturally the treatment with antabuse must often be only part of a general treatment. In severe cases psychological analysis and psychotherapy are important, as always in the treatment of alcoholism.

SUMMARY

A treatment for alcoholism is described, based on the sensitisation to alcohol produced by tetraethylthiuram-disulphide (antabuse).

Since December, 1947, 83 patients have been treated, with promising results in 74 cases.

Further observation is required for complete assessment of the results.

PERITONEAL EFFUSION AS A COMPLICATION OF ARTIFICIAL PNEUMOPERITONEUM

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ARTIFICIAL pneumoperitoneum (P.P.) now holds an established place in the treatment of pulmonary tuberculosis. One of its important features is its relative freedom from complications: it may suffer from being, as it were, an indirect means of attack, but it carries less risk than more radical forms of treatment. Of the recorded complications, peritoneal effusion seems to be one of the commonest, and most writers refer to it though few give details or make special comment. In my experience it has occurred in 8 (3·58%) of 223 P.P. cases involving some 5800 refills. This represents only those cases in which fluid was detected, and no doubt the actual incidence is higher, since small quantities of free fluid in the peritoneal cavity are difficult or impossible to recognise. The incidence of detected effusions is low compared, for example, to that of pleural effusions in artificial pneumothorax (A.P.), and is not enough to contra-indicate the use of P.P. in suitable cases.

Clifford-Jones and Macdonald (1943) reported 1 case of peritoneal effusion in more than 60 cases of P.P., but Fowler (1941) had an incidence of 3·8% (56 cases).

Reporting 176 cases of P.P., Mallick et al. (1943) mentioned subcutaneous emphysema and shoulder pain as the only complications in their series. They had no cases of peritonitis, which they say is due to incomplete asepsis. They do not refer to peritoneal effusion at all.

Edwards and Logan (1945) described peritoneal effusions in 4 out of 50 cases treated by P.P. One of these had a febrile reaction to each refill, which led to abandonment of the treatment.

A large series of cases (710) was reported by Mitchell et al. (1947), who found peritoneal effusions in 52 patients (7·3%); 24 of these effusions were tuberculous. They pointed out that Ophuls (1926) found that 12% of patients dying of tuberculosis showed at necropsy peritoneal fluid without pneumoperitoneum. This is an interesting observation but does not necessarily bear on cases under treatment with P.P. Advanced cases of pulmonary tuberculosis are commonly complicated by abdominal tuberculosis, and it is probable that peritoneal effusions might also develop in such cases as part of a general anasarca associated with terminal cardiac failure. Mitchell et al. described also 1 case of fatal air-embolism (following a refill into the liver), and 2 cases of peritonitis of mixed infection (1 due to perforated tuberculous ulcer of the ileum).

Calix and Jacobs (1948) refer to the possible and well-recognised complications, and state that a peritoneal effusion develops in about 1% of cases, "occasionally leading to adhesive peritonitis and abandonment of this form of therapy."

I wish here to call attention to the importance of ascites in cases under treatment by P.P., and to a form of ascitic tuberculous peritonitis which differs from the classical tuberculous ascites and is more serious.

ILLUSTRATIVE CASES

Case 1.—A girl, aged 17, was admitted to Black Notley on Aug. 13, 1945, with exudative tuberculosis of both apices and left subapical region. An attempt to induce a left A.P. failed. In October, 1945, the patient developed an acute spread of exudative tuberculosis throughout the left lung, with rapid cavity formation in the mid-zone. The left phrenic nerve was crushed on Nov. 2, 1945, and P.P. was induced on Nov. 12, 1945. There was slow improvement until by August, 1946, the disease appeared to be quiescent. The phrenic nerve was crushed again on Jan. 3, 1946, and the patient was discharged on March 9, 1947, with her pulmonary tuberculosis fully quiescent. Refills were given at a London hospital until the end of April, 1947, when, on returning home after a refill, the patient felt ill and hot, and next day had rigors.

She was readmitted on May 2, 1947, very ill, flushed, toxic, and with a furred tongue and signs of peritoneal effusion: temperature 103°F, pulse-rate 120–140. 2½ pints of green slightly turbid fluid were aspirated. This fluid contained 55% lymphocytes, and gave a profuse growth of *Micrococcus tetragenus*, but no tubercle bacilli were seen on direct examination or culture. Radiography of the chest showed small areas of linear scarring in the left lung but no evidence of reactivation. The patient remained very ill, with persistent vomiting, and a further 1½ pints of (clear) fluid were aspirated from the abdomen on May 5, 1947. This fluid was sterile on ordinary media but contained 80% lymphocytes and showed tubercle bacilli both on direct examination and culture.

The patient appeared to have an ascitic type of tuberculous peritonitis, and laparotomy (Mr. K. Jacobi) on May 14, 1947, revealed adherent loops of small intestine, with free fluid and fibrinous strands. The peritoneum was œdematous, friable, and hæmorrhagic. No tubercles were seen, and the uterus and appendages felt normal. Hectic fever to 102°F continued, uninfluenced by laparotomy, and after a transient improvement in the general condition, the wound broke down, a fæcal fistula developed, and the patient rapidly went downhill and died on July 2, 1947. No evidence of reactivation of the pulmonary disease was found at any time.

Case 2.—A married woman, aged 33, underwent, at Black Notley, P.P. on July 24, 1946, and left phrenic crush on Sept. 2, 1946, for fibrocaseous tuberculosis. She discharged herself on Sept. 28, 1946, improved and symptomless, but with her pulmonary disease not fully quiescent. She attended a London chest hospital as an outpatient for refills and kept well until May, 1947, when she noticed swelling of her abdomen after larger P.P. refills (1500–1600 ml.).

Outpatient refills were continued until July, 1947, when she was readmitted to Black Notley. She was then afebrile but looked thin and ill and had a large peritoneal effusion. 6 pints of clear yellow fluid were aspirated on July 18, 1947, and 1¾ pints on July 22, 1947. The patient had no chest symptoms, and radiography showed tuberculous scarring in both lungs but no evidence of activity. No further refills were given, but 8 pints of fluid were aspirated on Sept. 11, 1947, and 3½ pints on Oct. 4, 1947. All these fluids showed a few lymphocytes only, and that aspirated on Sept. 11 gave a growth of *Mycobacterium tuberculosis* on culture and was positive on guineapig inoculation. No mass could be felt in the abdomen, and the patient was regarded as a case of tuberculous peritonitis of the classical ascitic type.

Laparotomy (Mr. R. Reid) on Oct. 24, 1947, showed the great omentum and intestines matted together with clotted lymph, and about a further pint of greenish opalescent fluid. No definite tubercles were seen, and the adhesions were not disturbed. No tubo-ovarian masses were felt. Convalescence was uneventful except for occasional brief attacks of vomiting and mild generalised abdominal pain. 3½ pints of fluid were aspirated on Dec. 6, 1947, and grew tubercle bacilli on culture. No further aspirations were required, and the patient was discharged symptomless on April 16, 1948. The chest condition remained quiescent throughout.

Case 3.—A girl, aged 18, was admitted to Black Notley on Nov. 4, 1947, with exudative tuberculosis of the left upper lobe. An attempt to induce a left A.P. failed. In February, 1948, she became sputum-positive for the first time, and a small cavity appeared in the left subapical region. Pneumoperitoneum was induced on Feb. 24, 1948, and the left phrenic nerve was crushed on March 15, 1948. Moderate elevation (2½ in.) of the diaphragm was secured, the patient became sputum-negative, and the cavity closed, but subdiaphragmatic peritoneal adhesions were noted on the left side.

On April 20, 1948, the patient complained of a bruised feeling in the abdomen and of transient diarrhœa, and shifting dullness was found in the flanks. Refills were suspended, and two days later an irregular fever, up to 102°F, began. An abdominal radiogram taken in the lateral position showed a fluid level about half-way up the abdomen, and a small quantity of clear green fluid was aspirated on April 26, 1948. Further aspiration on May 6, 1948, yielded 10 oz. only of clear green fluid with some difficulty, and there was thought to be pocketing of the fluid with matting of the intestines. The cells in the first fluid were about 50% lymphocytes, but no tubercle bacilli were found on direct examination or culture.

The second aspiration, however, yielded fluid which, though negative on culture, was positive on guineapig inoculation. The temperature subsided completely in twenty days, P.P. was abandoned, progress was uneventful, and the patient was discharged with her tuberculosis quiescent on Aug. 7, 1948.

Case 4.—A girl, aged 17, with moderately severe diabetes, had a left A.P. and adhesion section done at the London Hospital in August and September, 1947, followed by a left spontaneous pneumothorax in October, 1947, and a pleural effusion which contained tubercle bacilli. She was transferred to Black Notley on Feb. 6, 1948, the left A.P. maintained, and with a small tuberculous cavity in her right upper lobe. Pneumoperitoneum was induced on March 15, 1948, with a view to subsequent right phrenic crush (this was not done because of later developments). On April 14, 1948, the patient had a second spontaneous pneumothorax on the left side, followed by the rapid development of a tuberculous empyema, containing tubercle bacilli but not secondarily infected. This was treated by bi-weekly aspirations and washouts with 'Azochloramid-T' solution, and almost complete re-expansion was secured.

On May 25, 1948, the patient became febrile (100–101°F), but no cause could be found for this until June 1, when slight shifting dullness in the flanks was detected. A lateral radiogram of the abdomen revealed fluid, but paracentesis abdominis was unsuccessful. Aspiration of the chest yielded a small quantity of clear fluid, which was sterile. The fever mounted to 102°F, and two further attempts at abdominal aspiration were made. The second of these, on June 9, yielded 60 ml. only of fluid which contained tubercle bacilli on direct examination, culture, and guineapig inoculation. High fever continued, reaching 104°F, and great difficulty was experienced with the diabetes, the patient being unable to take diet owing to severe nausea and occasional vomiting. By June 30 her general condition was very grave, with toxic myocarditis (confirmed by electrocardiogram), and a course of streptomycin 0·5 g. twice daily was begun.

At laparotomy on July 2 (Mr. R. Reid) 24 oz. of turbid fluid was removed, the peritoneum being bright red and œdematous, with much matting, but no tubercles seen. A fragment of peritoneum revealed miliary tubercles, however, on section. After the operation the patient's condition slowly improved, but up to mid-August she remained seriously ill. The temperature fell to normal for 48 hours, two days after operation, but till mid-October continued as irregular remittent fever between 99° and 101°F. Since then there has been progressive improvement in the patient's general condition, and she is now afebrile and symptomless, though failing to gain weight in spite of adequate calorific intake and control of the diabetes. Streptomycin therapy was discontinued after twenty days, since no benefit was observed, and there has been no regression since its withdrawal. Serial radiography of the lungs has shown no substantial change since May, 1948, and no evidence of miliary tuberculosis.

DISCUSSION

These cases will suffice to show that the development of ascites in the course of artificial pneumoperitoneum may be a grave complication, which should be watched for. I feel that the recognition of a peritoneal effusion should in most cases decide termination of the P.P. The present cases bring out several other points of importance:

(1) A tuberculous ascites may occur in cases in which no evidence of activity of the pulmonary lesion can be found (cases 1, 2, and possibly 3). Two of the worst cases occurred in patients after discharge. This complication differs from the classical form of tuberculous ascites in that adhesive peritonitis develops early, with much matting of intestines and pocketing of fluid. Response to laparotomy is not as favourable as in the classical cases, but the operation may be indicated to remove quantities of fluid and reduce toxæmia. In my limited experience patients stand the operation well. If the process is well developed and associated with continued high fever, the prognosis is poor.

(2) Such a complication has so far not been observed to affect the pulmonary lesion.

(3) Refills should never be given in the presence of an effusion (case 2), and it is very doubtful whether any advantage is gained by giving very large refills (over 800 ml.).

(4) Probably the spontaneous obliteration of a P.P. which is occasionally seen is due to an adhesive peritonitis, associated with a small effusion which may not have been recognised clinically.

(5) A high proportion of these effusions contain tubercle bacilli. They were identified in all my cases in which fluid was removed from the abdomen—i.e., in 6 of the 8. The development of tuberculous peritonitis in pulmonary patients with no previous abdominal history, and in whom the pulmonary tuberculosis appeared to be arrested, may be difficult to explain. Peritoneal lesions may be blood-borne from a "quiescent" focus in the lung or elsewhere. The association of these cases with P.P. refills, however, makes it more probable that trauma is a real factor. Whether the refill needle ruptures a tubercle on the parietal peritoneum or the gut, or whether a more generalised trauma is produced which stirs into activity a latent tuberculous lesion somewhere in the abdominal cavity, it is not possible to determine.

However an effusion may be caused, there is no doubt that familiarity must not be allowed to breed contempt, and, though P.P. is relatively benign and harmless, it should be watched and handled with the care that any form of active treatment requires.

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HYPERTROPHY OF THE PYLORUS IN AN ADULT

WITH MASSIVE EOSINOPHIL INFILTRATION AND GIANT-CELL REACTION

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THE possibility that organic changes in the gastro-intestinal tract may be caused by allergic reactions is of great practical importance. The following case is reported because of its rarity and intrinsic interest. We have not been able to discover any published report of a similar case.

CASE-REPORT

A married woman, aged 27, a clerk, was admitted to hospital in February, 1946, with two weeks' history of constant circumumbilical pain intense enough to keep her awake at night, and of pain and a feeling of distension between the breasts immediately after taking food. She had vomited after every meal, and this had relieved the pain between the breasts. She had lost 2 st. in weight. Four years previously she had had a similar but less severe attack associated with melæna, but the symptoms had lasted a fortnight. Her appetite had been good between these two attacks, but eggs, pastry, and bacon caused indigestion. She had never had asthma or urticaria, nor had her father, mother, or two sisters. She denied ever having had syphilis, and the Wassermann reaction was negative.

She had a furred moist tongue and a pulse-rate of 130. There was slight tenderness to palpation in the epigastrium and the right iliac fossa.

Investigations.—With a provisional diagnosis of regional ileitis she was sent for radiography after a barium meal.

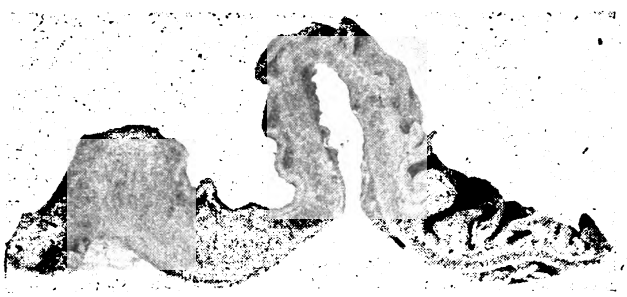

Fig. 1—Macroscopical section of resected part of stomach, showing great muscular hypertrophy.

Dr. J. L. Grout reported that the œsophagus was normal; there was a smooth filling defect involving the greater curvature of the prepylorus; the mucosal pattern was well formed in this narrowed portion of the stomach. Examination in the supine position showed that the filling defect was well defined, with a smooth convex outline. Six hours after the meal there was a small residue in the stomach, but the cæcum and ascending colon had filled. These appearances suggested that there was probably a hypertrophy of the prepylorus, but no malignant growth.

A blood-count showed Hb 120%, red cells 6,300,000 per c.mm., colour-index 1, white cells 17,000 per c.mm. (polymorphs 55%, lymphocytes 25%, monocytes 2%, eosinophils 18%). The only abnormality of the urine was a very faint cloud of albumin. The test for occult blood in the fæces was negative, and repeated microscopy of the fæces did not show any ova.

Course.—The patient remained afebrile but very ill and could not retain her food. Three weeks after admission the white-cell count was 11,800 per c.mm. (polymorphs 16%, lymphocytes 52%, monocytes 1%, eosinophils 31%).

Operation.—Laparotomy showed the pylorus to be greatly thickened. The serosa was reddened, and the whole wall of the duodenum and first 2 ft. of the jejunum were thickened, indurated, and friable. The spleen felt normal. Partial gastrectomy was performed, followed by anterior gastrojejunostomy and enteral anastomosis. Difficulty was experienced in invaginating the duodenal stump, owing to its friability.

Progress.—The patient progressed well and was discharged after a month. The leucocytosis and blood eosinophilia persisted. In November, 1946, she reported that she was two months pregnant. At that time a sternal puncture was normal, apart from a relative increase in neutrophils and eosinophils, and Casoni's skin test for hydatid disease was negative. Radiography of the chest showed no disease. The patient had a normal delivery in May, 1947, and has been well since.

SPECIMEN REMOVED AT OPERATION

Naked-eye.—The specimen is a portion of stomach, lesser curve 6 cm. long, greater curve 13 cm. long, with pyloric canal and an incomplete cuff of duodenum up to 2 cm. long. There is no visible abnormality of the mucosa, but there is translucent grey very wet thickening of the antral submucosa. The stomach wall is very rigid owing to great thickening of the muscular coat, which is 0·2 cm. thick at the proximal line of section, 0·8 cm. thick at a point midway along the lesser curve, 1·2 cm. thick in the antrum, and 1·8 cm. thick at the pyloric sphincter (fig. 1). At the pyloroduodenal junction the thickening rapidly diminishes, but there is some hypertrophy of the duodenal muscular coat which is 0·3 cm. thick at the most distal line of section.

The serosa is smooth but appears thickened over the antrum and pylorus, where it is firmly anchored to the muscle coat by pale striæ traversing the muscle-fibres. These striæ are most obvious on the cut surface of the pylorus, where they form laminæ enclosing big bundles of muscle-fibres.

There are a few pinkish nodes up to 1 cm. diameter near the pylorus, and a few small dark-red nodes along the lesser curve.

Microscopical.—Sections confirm that the thickening of the gut wall is largely due to hypertrophy of the muscle. Even the pale striæ, which give a pattern to the pylorus, are composed of muscle-fibres extending in unusual fashion to the serosa. There is a little increase of fibrous tissue round the blood-vessels and in the duodenal submucosa. The periarterial connective tissue of the muscle coat is infiltrated by broad bands of eosinophils, and there are scattered eosinophils between the muscle-fibres. The thickest band of eosinophils lies deep in the submucosa of the pyloric canal. Eosinophils are rare in the mucosa of the duodenum and pyloric canal and absent from the gastric mucosa and submucosa.

The submucosa of the prepylorus is greatly widened by a lake of lightly eosinophilic material apparently precipitated from a fluid exudate.

The intestinal mucosa is intact except in the pyloric canal, where there is surface erosion, and under the high power the remaining glands show the pleomorphism, distortion, hyperchromatism, and abundant mitoses common to regenerating epithelium. Deep in the bulk of the hypertrophied muscle of the pylorus are three follicles lying in a row in the connective tissue beside an artery (figs. 2 and 3). The follicles are graded in size but of uniform construction and consist of three zones. The central zone is composed of strongly eosinophilic necrotic material of uneven composition showing partly fragmented basophilic remnants of cell nuclei. The intermediate zone is composed of radially arranged giant-cells, partially separated from each other by big vacuoles spanned by interconnecting bridges of cytoplasm. The outer zone is narrow and composed of circumferentially arranged epithelioid cells.

Sections stained by Foot's modification of Perdrau's reticulin stain show that the centre of the follicle is strongly argyrophilic. There are no argyrophilic foci in any of the bands of connective tissue throughout the section to suggest early fibrinoid degeneration.

Many of the arteries running through the mass of hypertrophied muscle are hypertrophied, the muscle cells being swollen, vesiculated, and arranged in columns at right angles to the lumen. The nuclei of the endothelium are swollen, and the lumen contains plasma only. The nerve-fibres and ganglion cells appear normal.

DISCUSSION

Three findings in this case merit discussion: the massive eosinophil infiltration of the pylorus, the parterial giant-cell follicles, and the hypertrophy of the muscle coat of stomach, pylorus, and duodenum.

Massive Eosinophil Infiltration

Eosinophils are commonly found in the intestinal tract in chronic inflammations and are then most numerous in the mucosa. In our case the eosinophil infiltration was very different. The cells were rare in the mucosa but lay in broad bands between the muscle-fibres. Plasma-cell infiltration and fibrosis, the usual concomitants of inflammation, were almost absent, and

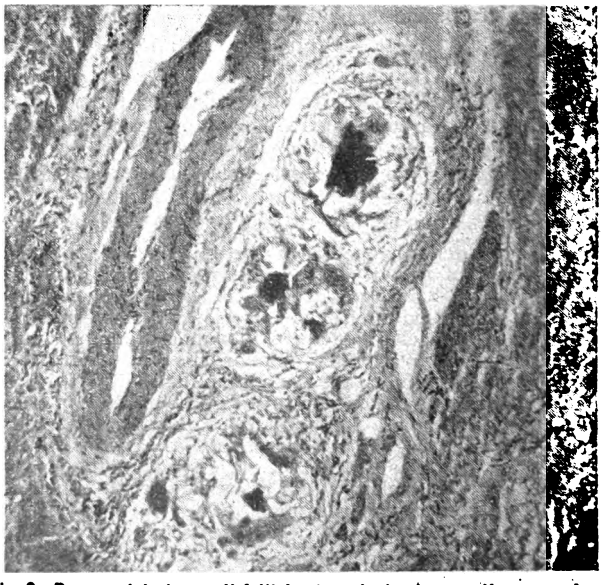

Fig. 2—Pararterial giant-cell follicles in pyloric ring: cells separating surrounding muscle-fibres are eosinophils. (× 70.)

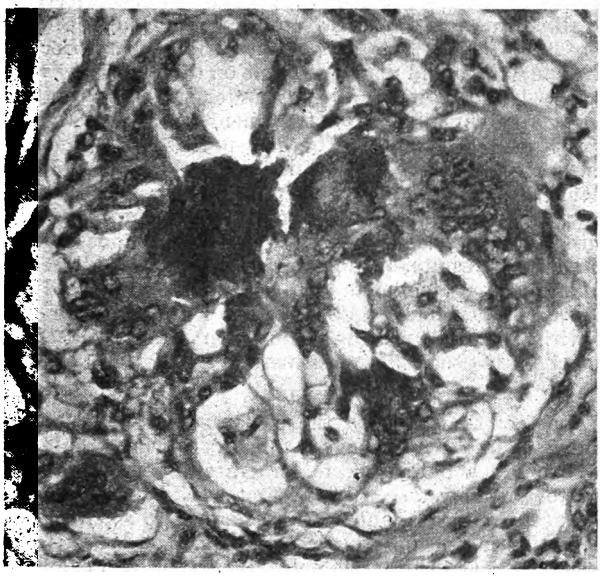

Fig. 3—Central follicle of those shown in fig. 2. (× 325.)

an unusual lesion was the lake of fluid in the prepyloric submucosa.

It is commonly accepted that localised eosinophilia is a relatively sure sign of an allergic reaction (Berger and Lang 1931, Knott and Bruce Pearson 1934), and that the eosinophils come from the blood and are not produced locally (Biggart 1932).

Pararterial Giant-cell Follicles

We have not met with follicles quite like this before. They were quite unlike tubercles, sarcoid, or the follicles of regional ileitis. They might possibly have been a reaction to a foreign body, and it was difficult to assess this possibility, for in repeated blocks no further follicles were discovered, and few sections were available from the original block in which they were found. One of these was stained with Weigert's elastin stain, but no elastic fibres were seen in the giant-cells. Frozen sections were not available. We considered the possibility that the follicles might represent a focus of early fibrinoid degeneration of allergic type, such as those described by Bergstrand (1946), with superadded peripheral giant-cell reaction, but in our experience of these focal degenerative lesions the argyrophilia of the collagen fibres is quickly lost as degeneration proceeds, and only exists as a marginal zone between the central area of necrosis and the surrounding collagen. In the follicles of this case the central zone was strongly argyrophilic and, moreover, was not fibrillar.

An interesting clue was discovered in a description by Šikl (1936) of four cases of eosinophil myocarditis developing after neoarsphenamine treatment of syphilis. The lesions, as described and illustrated, closely resemble those found in the pylorus of our case, but focal necroses were also present resembling those found in rheumatic fever. Šikl accepted the explanation of an allergic inflammation for his cases.

Kaijser (1937) described three cases to illustrate the importance to the surgeon of allergic affections of the alimentary tract.

The first was in a woman, aged 38, who had shown signs of skin sensitivity to arsphenamine when being treated for syphilis. A later course of neoarsphenamine was followed in ten days by severe colic, vomiting, and meteorism. At laparotomy a clear peritoneal effusion was found, and a segment of small gut 0·5 m. long was red, swollen, and œdematous.

The second case was in a man, aged 58, treated with neoarsphenamine for dementia paralytica. Nineteen days after beginning treatment he had severe nausea, pain, and vomiting. At laparotomy there was a peritoneal effusion and 190 cm. of the small gut was friable and swollen and was resected. Microscopy of the intestine showed numerous inflammatory cells, including eosinophils, throughout all coats.

The third case was in a man, aged 53, whose family had allergic manifestations, and who had pain and vomiting after eating onions. Nine days after gastrectomy for an ulcer 26% of his white cells were eosinophils. The stomach showed severe distal œdema with great swelling of the submucosa and widespread infiltration of plasma cells and eosinophils in the mucosa and submucosa.

These cases have been cited in some detail because we believe that they, together with Šikl's cases, are of importance in assessing the significance of ours. Kaijser pointed out that in his case 2, where eosinophil infiltration was mainly in the muscle, the "antigen" was parenteral whereas in his case 3, where the infiltration was mainly mucosal and submucosal, the "antigen" was presumably peroral.

Hypertrophy of the Pylorus

The commonest type of hypertrophy of the pylorus in adults affects the ring unevenly and is secondary to ulceration of the canal or the duodenum. The antrum may be hypertrophied owing to pyloric stenosis, but the duodenum is rarely affected. The even concentric hypertrophy found in our case was an instance of the "idiopathic" hypertrophy of the pylorus found in adults. This condition has been discussed fully by Klose and Bernstein (1932), who claim that the age-incidence (40–50) and the freedom of the subjects from symptoms in earlier years make it likely that it is not a missed congenital pyloric hypertrophy but a new development. Little is known about the causes of either the infantile or the adult form of this disorder; and, as might be expected, it has been suggested that they might be allergic responses. Pylorospasm due to food allergy in infants, simulating pyloric stenosis, has been described by Cohen and Breitbart (1929) and Balyeat and Pounders (1933).

SUMMARY AND CONCLUSION

The case is reported of a woman, aged 27, who developed pyloric obstruction, for which partial gastrectomy was performed.

The surgical specimen showed concentric hypertrophy of the muscular coat of the stomach, pylorus, and duodenum, with massive eosinophil infiltration of the pylorus and peculiar pararterial giant-cell follicles.

The evidence suggests that this is an example of a true organic intestinal allergic reaction. The woman did not tolerate certain foods well; she had constant blood eosinophilia and a localised tissue eosinophilia of the pylorus; and there were giant-cell follicles in the pylorus which closely resembled follicles found in the heart muscle of patients who have become sensitive to neoarsphenamine.

The microscopic sections were prepared by Mr. D. Bradey, and the photographs taken by Miss J. G. Brown.

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CALCIFEROL BY INTRAMUSCULAR INJECTION

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ONE of the greatest advances in dermatology in recent years has been the cure of lupus vulgaris with massive doses of calciferol (vitamin D_2). With this drug alone, without any local treatment, patients can be cured in a comparatively short time. It has, however, two serious disadvantages: it is badly tolerated by many patients; and it is dangerous because it can damage both blood-vessels and kidneys. For this reason all patients treated with calciferol should have serum-calcium estimations and kidney-function tests at regular intervals.

Since April, 1946, all tuberculous skin patients attending the lupus clinic at Belmont Road Hospital, Liverpool, have been treated with calciferol. For a proportion of these cases regular investigations were done, as follows:

(1) At the beginning of treatment, every fourth week during treatment, and the fourth week after all treatment had ceased, estimations were made of the erythrocyte-sedimentation rate (E.S.R.), by Wintrobe's method, the volume of packed red cells, the serum-calcium, the serum-inorganic phosphates, and the total and differential white-cell counts. The white-cell counts were discontinued after November, 1946.

(2) Weekly examination of the urine for calcium with Sulkowitch's reagent and occasionally a routine examination of the urine.

(3) Weekly record of weight.

(4) Weekly record of clinical progress and of toxic symptoms, if any.

(5) Record of blood-pressure at intervals.

(6) Urea-clearance test at the end of each course of treatment and four weeks after all treatment had ceased. In the case of patients on injections this was also done before treatment began.

(7) Lateral and anteroposterior radiograms of abdomen and lateral radiogram of one leg, at the end of treatment, to detect abnormal calcification, if any, in kidneys and arteries.

(8) The serum-alkaline phosphatase was estimated at intervals for patients on injections only.

The patients were photographed before and after treatment.

The patients investigated included 39 cases of lupus vulgaris (4 of which were later treated by injections because of toxic symptoms), 2 of lupus verrucosus, 2 of erythema induratum, and 1 of erythema induratum (a tuberculide) with generalised tuberculides. As controls were included 1 normal person, 3 with psoriasis, and 1 with tinea infection of the nails. Of the 39 patients with lupus 3 did not complete the course, 1 having developed kidney disease, 1 having had an amputation of the leg because a large tuberculous ulcer on her foot had undergone a malignant change, and 1 ceasing to attend as soon as he was cured. These 3 are not taken into account in the summary except in the percentage of cures.

TREATMENT

All cases were started on a daily dose of 150,000 I.U. of calciferol in the form of high-potency 'Ostelin' tablets (Glaxo) and were treated for six months. After an interval of twelve weeks a second course of treatment was given lasting five months.

Some patients could not take 150,000 I.U. daily owing to intolerance. For them at first the dose was reduced to 100,000 or 50,000 I.U. daily according to their tolerance, but later it was found more satisfactory to stop the treatment entirely for four weeks and then to resume the full dose of 150,000 I.U. daily.

After calciferol had been given by mouth for a few months, it was thought possible that the nausea and vomiting which seriously interfered with the continuity of treatment might be due to the action of the tablets on the gastric mucosa. To ascertain if this were so, it was decided to begin treatment with intramuscular injections for all new patients after November, 1946. The injections were first tried on 2 of the patients who had experienced extreme nausea and vomiting while on tablets. They were admitted to hospital and kept under strict observation during their first month of treatment. They were given injections of 600,000 I.U. of high-potency ostelin three times a week for the first three weeks, and their blood chemistry was checked weekly. After the first three weeks they were given one injection of 600,000 I.U. weekly, but later this was increased to two injections weekly with better results. The series of patients on intramuscular injections included 4 lupus patients who could not tolerate the tablets, together with 6 new lupus patients, 1 with severe erythema induratum (Bazin's disease), and 1 with psoriasis as a control.

RESULTS

The fact that none of the patients missed his or her tablets or injections speaks for itself. Nowhere could one have found a more cheerful or grateful set of patients. Improvement was seen in the first week of treatment in all except one case, and within a month to six weeks all ulceration had usually healed.

Of the 35 cases of lupus vulgaris treated with calciferol tablets, 22 (63%) were clinically cured, and the average time taken to affect the cures was eleven months. Of the remainder, 1 was 90% healed, 3 were 75% healed, 6 were 50% healed, 2 were 40% healed, and 1 was practically stationary. Of the 2 cases of lupus verrucosus 1 was cured in eleven months; of the 2 cases of erythema induratum 1 was cured in three months and 1 in six months. The case of erythema induratum with tuberculides was unsatisfactory.

Of the 6 cases of lupus treated with injections alone 3 (50%) were clinically cured in an average of four and a half months: 1 in three months, 1 in four months, and 1 in six and a half months. Another was almost cured in seven and a half months. Of the 4 patients who could not tolerate the tablets 2 were cured—1 in four months, and 1 in five months, after the injections were begun.

Pigmentation.—Temporary brownish pigmentation, which was often very unsightly, developed in the lupus areas of almost half the patients on tablets but not in any of the patients on injections.

Blood-pressure did not vary appreciably in any of the patients except in one woman who developed kidney disease, in whom the systolic pressure rose from 140 to 166 mm. Hg.

Weight.—The weight of the patients on tablets, apart from those who had symptoms of intolerance, was slightly increased. Of those on injections half lost and half gained weight.

White-cell Counts.—The differential white-cell counts were so variable that it was obvious after a few months that no useful information could be obtained from them.

Erythrocyte-sedimentation Rate.—At the start of treatment on tablets the E.S.R. was normal in 15 of the 32 lupus cases investigated. Calciferol appeared to have a distinct tendency to raise the E.S.R., for in many cases it rose with treatment and fell during the rest period. There was no correlation between the E.S.R. and clinical cure. For example, of the 17 cases with an abnormal E.S.R. in the beginning, 15 still had a raised E.S.R. at the end of treatment. Of these, 7 were cured clinically, 4 much improved, and 1 stationary. Intolerance to calciferol did not raise the E.S.R. Only 1 of the patients on injections had a normal E.S.R. before treatment started. With injections there was on the whole a tendency for the E.S.R. to rise at first and then to fall gradually, but in some cases the course was erratic. Patients were cured clinically whether the E.S.R. remained high or low or fell.

Volume of Packed Red Cells.—A slight decrease in the red-cell volume was a constant finding in every case of

the series on tablets, whether there was toxæmia or not. After cessation of treatment the volume of the packed red cells tended to increase. There was an increase in the volume in 5 of the 10 lupus cases treated by injections.

Serum-calcium.—The normal level varies from 9 to 11·5 mg. per 100 ml.) There was a remarkable difference between the amount of serum-calcium in the two sets of patients. The level rose in every patient on calciferol tablets in each course of treatment. There can be no doubt that the rise was due to the tablets, since the serum-calcium level invariably fell rapidly on cessation or reduction in the number of the tablets. It is essential that the serum-calcium level of all patients receiving massive doses of calciferol in tablet form for any length of time should be estimated at least every four weeks, because, though toxic symptoms coincide in every case with a raised serum-calcium level (over 11·5 mg. per 100 ml.), there are cases in which a raised serum-calcium level is not associated with toxic symptoms. The highest serum-calcium levels reached in the 10 lupus patients who were never toxic on tablets were as follows: 11·6, 11·9, 12·2, 12·3, 12·5, 12·6 (2 cases), 12·7, 12·9, and 14·4 mg. per 100 ml. Many patients are slow to recognise symptoms: thus a patient with a serum-calcium level of 15 mg. per 100 ml. had excessive thirst and polyuria which she entirely omitted to mention.

The essential feature of injection therapy is that there is little or no hypercalcæmia. The highest level reached was 12·2 mg. per 100 ml. by 2 patients on two occasions. This feature is emphasised by the fact that 1 patient, whose serum-calcium level repeatedly rose to 14 mg. per 100 ml. after four weeks on tablets, had a normal serum-calcium level while on injections, and 2 others, whose serum-calcium levels were 14·2 and 13·8 mg. per 100 ml. while on tablets, were normal throughout while on injections.

Toxicity.—Here again there was a remarkable difference between the two sets of patients. Of the 32 patients treated with calciferol tablets 22 had symptoms of intolerance. These varied from patient to patient. The commonest were loss of appetite, gastric discomfort, a feeling of weight or tightness over the abdomen and chest, headaches, dizziness, depression, extreme lassitude, nausea, vomiting, frequency of micturition, polyuria, excessive thirst, neuritis, palpitation, rheumatic pains, and breathlessness. In all cases the toxic symptoms coincided with a rise in the serum-calcium level, each patient having a certain level above which he or she exhibited symptoms of intolerance. These levels were as follows: 11·6, 12 (4 cases), 12·2, 12·3 (2 cases), 12·6 (3 cases), 12·7, 12·8, 12·9, 13 (2 cases), 13·1, 13·2, 13·7 (2 cases), 13·9, and 14·6 mg. per 100 ml. of serum.

Toxicity did not hinder cure, for 17 of the 22 patients who were toxic on tablets were cured clinically, and 4 of the 10 cases who were never toxic were cured.

None of the 10 lupus patients treated by intramuscular injections developed toxic symptoms. This was most remarkable in the 4 patients who had previously been treated with tablets. One of these had vomited so much during his first week of treatment with 3 tablets (150,000 I.U.) daily that he could never take more than 2 tablets daily—i.e., 700,000 I.U. weekly—yet on injections he had no symptoms of intolerance though he had three injections of 600,000 I.U.—i.e., 1,800,000 I.U. weekly—for the first three weeks and two injections of 600,000 I.U.—1,200,000 I.U. weekly—for the remainder of his course. Two of the other patients vomited so much on tablets that it had to be left to their own discretion to take what they could. However, on injections with a larger dose than they had ever attempted to take in tablet form they felt quite well.

Only twice during treatment by injection was there any semblance of toxic symptoms.

One patient after having injections for four months complained of headaches on returning home after her injections. Injections were stopped for a week, and the headaches ceased. She had no return of the headaches until two months later, when she complained of aching pain over the occipital region and at the nape of the neck. Treatment was discontinued for three months.

Another patient after having injections for seven months reported that on one occasion only she had the same feeling of nausea as when she was beginning to be toxic on tablets. Injections were stopped for a week, and she had no return of the nausea.

Serum-inorganic Phosphates.—(The normal level is 2–4 mg. per 100 ml. of serum.) There was no apparent relation between the amount of calcium and the amount of inorganic phosphates in the serum. The inorganic phosphates rose above the original level at some time during each course of treatment on tablets for every patient. Unlike the serum-calcium level, which fell in every case when calciferol was stopped or reduced in amount, the level of inorganic phosphates rose in some cases and fell in others after cessation of treatment.

The toxic symptoms do not appear to depend on the amount of inorganic phosphates in the serum. Some patients were toxic when this was as low as 2·4 mg. per 100 ml. (the serum-calcium level being raised); others were toxic when it was as high as 6·2 mg. per 100 ml. (the serum-calcium level being high); and others were not toxic when it was either 2·4 or 6 mg. and 2·8 or 5·6 mg. per 100 ml. of serum (the serum-calcium level being normal).

With injections also the inorganic phosphates rose above the original level for every patient some time during treatment.

These remarks also apply to the controls.

Blood-urea.—(The normal level is 20–40 mg. per 100 ml.). The blood-urea was raised by treatment in 12 of the 32 lupus patients who completed the whole course of treatment on tablets. It rose in 1 case to 56, in 1 to 51, in 1 to 47, in 3 to 45, in 3 to 44, in 2 to 43, and in 1 to 42 mg. per 100 ml. Of these 12 patients, 7 had toxic symptoms either at the time or just previously, and those 7 all had hypercalcæmia; 5 only showed hyperphosphatæmia (3 of these were included in the 7 with hypercalcæmia and toxæmia). The blood-urea level of 1 of the psoriasis patients rose to 45 mg. per 100 ml. and that of the normal control to 41 mg. per 100 ml. without hyperphosphatæmia, hypercalcæmia, or toxic symptoms.

The blood-urea level was raised in 2 of the 10 lupus patients receiving calciferol by injection; neither of these patients had toxic symptoms or hypercalcæmia, but both had a raised serum-inorganic phosphate level. The blood-urea was raised in these 2 cases to 47 and 69 mg. per 100 ml.

Urea Clearance.—This was not estimated for the patients on tablets at the start of treatment, so their normal kidney function was not known. It was first estimated before starting the second course of treatment. Comparison of the figures then obtained with those at the end of treatment showed that after treatment the kidney function was greatly diminished for all cases except 1 case of lupus verrucosus and 1 lupus patient who had been very toxic at the end of the first course of treatment and had a raised blood-urea level and diminished kidney function at the beginning of the second course. The kidney function was also greatly diminished for all the controls. In 18 of the lupus patients and 3 of the controls the kidney function slightly improved after the patients had been off tablets for four weeks. For the patients on calciferol by injection the kidney function was diminished in all cases except the patient with Bazin's disease and the psoriasis control, both of whom had been on treatment for only four months.

Radiography showed calcification of the iliac arteries in 2 cases of lupus vulgaris on calciferol tablets, both of whom had had hypercalcæmia. This disappeared shortly after the cessation of treatment.

Alkaline Phosphatase.—This increases when bone is being formed or rapidly destroyed and should be normal

in the healthy adult. According to the method of Armstrong and King the normal number of units is 10. This was estimated for patients on injections only. In 3 cases of lupus it was raised to 14, 18, and 25 units, and in the psoriasis control to 25 units at the start of treatment. These figures fell during treatment to 6, 4, 7, and 16 units. Thus the alkaline phosphatase of patients treated with injections of calciferol shows a tendency to become normal.

PROPYLENE-GLYCOL SOLUTION OF CALCIFEROL BY MOUTH

So far I have tried only 2 lupus patients on a propylene-glycol solution of calciferol by mouth. With the same number of units as given to the patients on tablets—i.e., 150,000 I.U. daily—the clinical results were remarkable, but at the end of seven weeks treatment had to be discontinued because of toxic symptoms and hypercalcæmia. One patient had extreme nausea, with serum-calcium 12·8 mg. per 100 ml., and the other had extreme nausea and palpitations, with serum-calcium 14·8 mg. per 100 ml.

ALCOHOLIC SOLUTION OF STEROGYL 15 BY MOUTH

'Sterogyl 15,' an alcoholic solution of calciferol, has been administered to 6 patients in the dosages used by Charpy, but without his special diet. In 2 cases the serum calcium was raised to 13 and 13·3 mg. per 100 ml., and in 1 case the blood urea rose to 56 mg. per 100 ml. Clinical cure was no more rapid than with injections or tablets.

POSTSCRIPT

Of the patients who were still not cured after two courses of calciferol in tablet form, during which they were repeatedly obliged to cease treatment on account of toxicity, 4 have, after another three months' rest, been on intramuscular injections of calciferol for three months.

Case 1, who could take only 3 tablets daily—i.e., 1,050,000 I.U. weekly—for six to eight weeks before becoming toxic, with a blood-calcium level of 14·6 mg. per 100 ml. and over, felt perfectly well on two injections weekly (1,200,000 I.U.), and his serum-calcium level did not exceed 12 mg. per 100 ml.

Case 2, who would take only 3 tablets daily for five to six weeks before becoming toxic, with a blood-calcium level of 13·7 mg. per 100 ml. and over, felt better than usual on two injections weekly, and her serum-calcium level never exceeded 11·3 mg. per 100 ml. She is now clinically cured.

Case 3, who could take only 3 tablets daily for eight weeks before she became toxic, with a blood-calcium level of 13·1 mg. per 100 ml. and over, has felt perfectly well on two injections weekly, and her blood-calcium level has not exceeded 12·2 mg. per 100 ml. On tablets she made no headway, but on injections her lupus is clearing.

Case 4, who could take only 3 tablets daily for six to eight weeks before becoming toxic, with a serum-calcium level of 12·6 mg. per 100 ml. and over, has felt perfectly well on two injections weekly, and his serum-calcium level has not exceeded 11·7 mg. per 100 ml.

SUMMARY

Calciferol by intramuscular injection is a better mode of treatment than calciferol in tablet form for the following reasons: (1) results are more rapid; (2) pigmentation is absent; (3) there are no toxic symptoms and therefore no unavoidable breaks in treatment; (4) there is little or no hypercalcæmia and therefore there is less chance of calcification in soft parts; (5) all patients do not get a diminished packed red-cell volume; and (6) the blood-urea level is raised in a smaller proportion of cases.

Examination of the blood gave no help in diagnosis, prognosis, progress, or cure.

Kidney function is impaired in all cases treated with calciferol, whether by injection or by mouth in tablet form, for a considerable time. For this reason courses of treatment should not last longer than four months without a rest period.

I wish to thank Dr. F. Glyn Hughes, senior dermatologist, Liverpool City Hospitals, for permission to publish the results of these investigations, and Dr. J. Carr Brundret, pathologist, Liverpool City Hospitals, for assistance in laboratory work.

PETHIDINE IN OBSTETRICS

REVIEW OF 153 CASES

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PETHIDINE hydrochloride, now included in the British Pharmacopœia, has an antispasmodic action and relieves pain rapidly without impairing consciousness or coördination. Its constitution and pharmacology have been described by Gallen and Prescott (1944).

Since its introduction in 1939 it has been used in labour both alone (Gilbert and Dixon 1943) and in combination with other analgesics, such as hyoscine (Cripps et al. 1944, Flatt 1946), scopolamine (Schumann 1944, Hingson 1945), and phenobarbitone (Carter 1945). Most workers agree that the use of pethidine, either by itself or in combination, is a definite step forward.

In February, 1947, pethidine hydrochloride was introduced to the County Maternity Home, Rugby, as a routine analgesic. A careful record was kept of its effect on mother and infant. The results in 153 successive cases are presented here.

My predecessor, Dr. J. L. Farmer, had introduced and used successfully as an analgesic a combination of heroin and 'Trilene.' It was felt that these drugs could be combined successfully with pethidine, and therefore the following method was adopted:

(1) Where necessary primiparæ received a preliminary dose of heroin gr. $^1/_4$, on admission. When the os was 3 or 4 fingers dilated, pethidine 100 mg. was given intramuscularly, followed by 100 mg. an hour later and 100 mg. 4-hourly up to a total 24-hour dosage of 400 mg.

(2) After the head was crowned and during its passage over the perineum trilene was self-administered.

(3) In multiparæ the preliminary heroin was rarely found necessary.

In our early days of its usage we got the impression that when pethidine was given too soon it tended to arrest labour.

In all our cases pethidine (Roche) was used. One injection was given in 41 (26·7%) cases; two injections in 77 (50·3%), 1 of which was a forceps delivery; three injections in 24 (15%) cases; four injections in 6 (3·9%) cases, 2 of which were forceps deliveries; and more than four injections in 5 (3·3%) cases, of which 4 were forceps deliveries.

EFFECT ON MOTHER

Toxic symptoms were rare; they consisted chiefly in vertigo and vomiting, and they were transient.

Of the 153 women 100 were primiparæ and 53 multiparæ.

In the primiparæ there were 7 forceps deliveries—5 for disproportion and 2 for fœtal distress. The average duration of labour from the time of the first pethidine injection was 4·02 hours. If we exclude the 7 forceps cases, the average duration of labour was 3·1 hours.

In the multiparæ there were no forceps deliveries. The average duration of labour from the time of the first pethidine injection was 2·3 hours. For the whole series the forceps-rate was about 4·5%.

In 1947 we had two cases of obstetric shock. The first was in a primipara who had had pethidine. It was felt then that the hypotension due to pethidine might have been aggravated by a sudden fall in intra-abdominal tension. However, about five weeks later we had another case in a multipara who had not had pethidine.

The analgesic effect was carefully observed both by the midwives and from the patients' own observations. In 39 (25·5%) the pains were relieved rapidly and in many cases completely, the patient became calm and coöperative, and cervical dilatation was rapid. In 69

(45·1%) the intensity of the pains was lessened considerably, the patient became coöperative, and cervical dilatation was rapid. In 31 (20·3%) the pains were made more bearable and the patient became coöperative. In 14 (9·1%), though the intensity of the pains was not diminished, in all but 6 cases apprehension was allayed and coöperation achieved.

EFFECT ON BABY

Some degree of asphyxia was seen in 23 babies, of whom 6 (3·9%) were slightly asphyxiated, 8 (5·2%) were in blue asphyxia, and 8 (5·2%) were in white asphyxia. In 6 cases the asphyxia was due to the cord being tight round the neck; in 5 cases to excess of mucus in the air passages, in 1 case to congenital heart disease (proved at necropsy), and in 1 case to prematurity (in a twin); leaving 10 (6·5%) cases in which there was no obvious cause of asphyxia. In these 10 cases 1 mother had had one injection (100 mg.), 4 had had two injections, 3 had had three injections, and 2 had had four injections of pethidine. We may conclude that the total dosage bears no direct relationship to asphyxia in the infant, even if we presuppose that pethidine may be a causal factor. Of the 10 infants 3 had slight asphyxia, 4 had blue asphyxia, and 3 had white asphyxia. All 23 infants except 1 recovered with simple routine treatment.

In 153 unselected deliveries in 1942, when the only "analgesic" in use was potassium bromide, the number of babies born with asphyxia was 13 (8·5%).

In the present series the number of stillbirths was 3 (1·9%). Of these, one was a macerated twin, one was syphilitic, and the third was a shoulder presentation which had undergone combined version.

CONCLUSIONS

Mother.—At least by intramuscular administration the toxic effects of pethidine are slight and infrequent and may be discounted. It is my impression that pethidine hastens dilatation and accelerates delivery. Apart from its analgesic properties, we were struck by the manner in which it allayed apprehension and helped to achieve the patient's coöperation. We have found that, combined with heroin and trilene, it is a most useful and helpful drug during labour.

Baby.—Comparison with the 153 cases in 1942 seems to show an increase in the incidence of asphyxia. This was not unduly high, however, and most of the babies responded quickly to simple treatment.

SUMMARY

The use of pethidine hydrochloride in combination with heroin and trilene is described in 153 successive deliveries. This combination was effective in 70·6% of cases.

Apart from being a potent analgesic, pethidine has a striking effect in allaying apprehension and achieving the patient's coöperation.

Though the incidence of fœtal asphyxia was somewhat higher than in a previous year, in which pethidine was not used, this is not a contra-indication to its use.

I am grateful to Dr. S. W. Savage, county medical officer of health, for permission to publish these findings. My sincere thanks are due to the matron, Mrs. M. Middleton, and to our keen and competent staff midwives, Nurses Foley, Mellon, Driscoll, Booden, and Robson, without whose cheerful coöperation and helpful criticism it would have been impossible to keep our records.

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New Inventions

SPLINTAGE OF THE HAND DURING OPERATION

EFFECTIVE fixation of the hand during operations on it is always difficult and often a source of irritation. Many surgeons have an assistant to hold the hand in the required position; some are content to try and control the limb with strips of gauze, towel clips, strapping, &c.; while others use a rigid metal or wooden splint. But such methods do not permit of ready adjustment during operations which are commonly long and tedious and likely to involve alterations in position. At their best they restrict the surgeon's field of operation and tend to block his view.

The splint described here overcomes these disadvantages and is extremely simple. It consists merely of a flat shape cut from a sheet of lead 12 in. by 14 in. and $^1/_{16}$ in. thick (fig. 1). The hand is laid on the splint, which is then accurately moulded round it. The fingers are fixed by bending the tips of the splint over them (fig. 2), or if necessary they can be held straight by making gutters

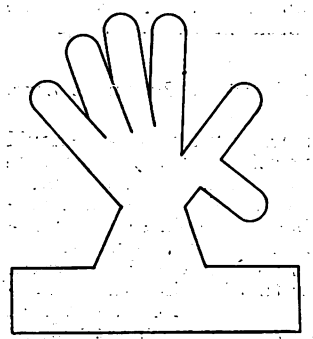

Fig. 1.—Outline of splint cut from sheet lead.

Fig. 2.—The splint applied.

of the metal tongues. The thumb is held by an additional piece at the side. The wrist is bent into the required position, and the side bars are folded obliquely round the forearm.

The following advantages are claimed for this form of leaden splint:

(1) It can be quickly and accurately moulded into any position. It may be applied equally well to the back or front of either hand and to a limb of any size. The hand and fingers are firmly held without the use of clips, straps, or retractors. It is particularly useful in operations on the side of the finger, since the other digits can be held effectively out of the way.

(2) Sheet lead of this thickness is sufficiently malleable to be easily bent by hand, and is soft enough not to damage the tissues by pressure or to tear the surgeon's gloves. At the same time it is sufficiently rigid to fix the hand in the position required. If further support is needed, the hand encased in the splint may be rested on a folded towel.

(3) The splint is easily sterilised by boiling and may be applied safely either directly to the hand or over a stockinette glove.

(4) It is quickly and cheaply made, is durable, and can be rapidly bent or hammered flat again after use.

(5) It releases an assistant and affords the surgeon a clearer field of operation.

My thanks are due to Mr. R. G. Pulvertaft, both because his work on the surgery of the hand stimulated me to develop this splint, and for his willingness to try it and later to adopt it as a regular part of his equipment.

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Reviews of Books

The Basis of Chemotherapy

T. S. WORK, B.SC., PH.D., a member of the research staff, National Institute for Medical Research, London; ELIZABETH WORK, B.A., PH.D., a member of the research staff, University College Hospital medical school, London. Edinburgh: Oliver & Boyd. 1948. Pp. 435. 26*s*.

THIS book is a solid contribution to what the authors describe as the "hybrid subject of chemotherapy, the boundaries of which stretch from organic chemistry through biochemistry and physical chemistry to bacteriology, pharmacology, and therapeutics." The historical introduction, which ranges from early Chinese herbal remedies to streptomycin, is followed by informative chapters on cell metabolism, essential metabolites, and enzyme inhibition. This fundamental aspect of chemotherapy, dealing with advanced chemical problems, will be of especial interest to doctors with inquiring minds. The chapters on drug antagonism and drug resistance bring together much scattered work on an aspect of chemotherapy which is partly chemical and partly biological. The book ends with a logical chapter on the relation of structure and activity of drugs, followed by an extensive and well-selected bibliography, in which justice is done to the numerous contributions of British workers. The book should appeal not only to those who work in any branch of chemotherapy, but also to the senior student who wishes to broaden his knowledge.

Osteo-arthritis of the Hip-joint

H. WARREN CROWE, D.M. London: Pulman & Sons. 1948. Pp. 70. 35*s*. 6*d*.

Dr. Warren Crowe says that "textbooks should summarise ideas which are generally accepted by members of the profession, and advocate methods of treatment which have the full support of specialists in that particular subject." His own book, he points out, is not a textbook but a monograph founded on personal experience of a large number of cases of osteo-arthritis of the hip-joint. He includes under this heading all forms of arthritis of the joint, at whatever age it occurs, and (if the usual classification is accepted) of varying ætiology. He gives a detailed account of the anatomy and pathology of the hip-joint, and discusses the diagnosis and the clinical examination of the patient. He attaches great importance to the differential white-cell count, sedimentation test, examination of the blood for hypo- or hyper-œstronæmia, and a test for liver dysfunction.

It is a difficult book to understand. Dr. Crowe holds the view that osteo-arthritis is caused by infection, and that basic or ætiological treatment is by the use of vaccines. However, he does point out that the presenting symptoms of pain and stiffness arise mainly from the synovial membrane and that the adductor spasm is closely associated with these inflammatory changes. Most people will agree with him that intra-articular injections and physical measures may relieve these symptoms, but the evidence he offers that infection causes osteo-arthritis, and that vaccine therapy will arrest the process of the disease, remains unconvincing.

Syphilis

HENRI MATHIAS. Paris: Maloine. 1947. Pp. 722. Fr. 600.

THIS is a long discursive book in which the author has much to say about the treatment of syphilis, little about diagnosis, something about the public-health aspects of the disease, and a great deal about his own very unorthodox ideas. His methods of treatment place great reliance on two drugs—arsphenamine and mercury—which are not now much used in this country, and his method of giving these is unusual. He is extremely critical of some of his colleagues who favour long-continued treatment with bismuth and have little confidence in the possibility of ultimate cure. Discussion of penicillin is limited to two pages, and it is clear that the drug is not highly esteemed. Dr. Mathias is quite prepared to use his methods of treatment for the prophylaxis of syphilis, a proceeding which some of his colleagues and most experts in this country consider to have considerable dangers. His views on congenital syphilis as a cause of a number of common skin conditions such as psoriasis and herpes zoster, and as a predisposing cause of conditions like chronic appendicitis and diabetes, are frankly heretical, and would require more than the forcible expression of his personal opinion for even limited acceptance. If this book is at all representative of Continental ideas about syphilis, then we have indeed diverged from the views of our near neighbours who in the past have contributed so much to the subject.

Chest Examination (3rd ed. London: J. & A. Churchill. 1948. Pp. 170. 12*s*. 6*d*.).—Dr. R. R. Trail's little volume attempts to correlate physical findings and radiographic appearances over the whole range of chest diseases. It is a provocative book, and both clinicians and radiologists may be tempted to criticise some of the arguments; but the final-year students and house-physicians for whom it is written will find it of great value. As Sir Walter Langdon-Brown wrote in his foreword to the first edition, it will give them "a grasp of the first principles involved, which will enable them to arrive at a correct opinion without imposing burdensome details on their memory."

The Clinical Apprentice (Bristol: J. Wright. 1948. Pp. 200. 15*s*.).—This little book is intended for the student beginning his medical clerking. Dr. John Apley and Dr. John M. Naish give simply and clearly the bedside teaching from which accurate diagnosis must be learnt, and on which the foundation of medical training is based. It cannot, of course, replace practical demonstration and instruction at the patient's bedside, but it does give simple reasons for clinical methods and sound principles of history-taking and examination. If one of the failings of the newly qualified is that he thinks he can run before he can walk, it will be remedied by such a book as this; and many failures in higher examinations are due to poor grounding in the fundamental principles given here.

Pharmacology (3rd ed. London: Oxford University Press. 1948. Pp. 504. 25*s*.).—This work by Prof. J. H. Gaddum, F.R.S., is widely recognised as a standard textbook on pharmacology for undergraduate students. Its directness of statement, informed by clear thought and spiced with occasional droll comment, compels attention. The rapid advance of the subject can be gauged by comparing the meagre legacy of synthetics—the coal-tar antipyretics and aspirin—left by the Victorians, with the wealth of new drugs devised during the present century. Many substances make their first appearance in this edition, including dimercaprol (BAL), the anti-histamine compounds, 'Paludrine,' streptomycin, and folic acid; but the design of the book goes far beyond that of the old materia medica or compendium of useful remedies which so often in the past has masqueraded as a textbook on pharmacology: the author builds up a concept of the background of experiment. The student will be grateful for the increased understanding this brings, not only at examination time but in future practice when appraising the probable worth of new drugs.

The Trial of Gozawa Sadaichi (War Crimes Trials, vol. III. London, Edinburgh: Wm. Hodge. 1948. Pp. 245. 18*s*.).—An English barrister, Mr. Colin Sleeman, was assigned to defend nine Japanese officers and N.C.O.s charged with maltreating (and in one case beheading) Indian soldiers who were prisoners-of-war. In editing the proceedings for publication he has, in a lengthy introduction, analysed and expounded the mentality of Japanese military witnesses. The trial has otherwise only slight medicolegal interest. To British eyes Orientals tend to look alike. There was difficulty in identifying the accused from photographs. In later cases, we learn, care was taken to provide two photographs of each man (one full-face and one in profile) hatless and clean-shaven. One of the accused was released during the trial; the rest were convicted and sentenced. The court rejected two points submitted by the defence—first that Japan had never signed the 1929 International Convention on the the Treatment of Prisoners of War, and secondly that the Japanese regarded their Indian captives as "auxiliaries" or collaborators. The evidence is sometimes tortuous and tedious, but the book shows the success of the attempt to make this, the first "war crimes" trial under British jurisdiction in the Far East, a model of fairness.

THE LANCET

LONDON: SATURDAY, DEC. 25, 1948

Christmas

"It is now Christmas, and not a cup of drink must pass without a Carol: the beasts, fish, and fowl come to a general execution, and the corn is ground to dust for the bakehouse and the pastry.—Now good cheer and welcome, and God be with you."—NICHOLAS BRETON, 1626.

The trend of the age is towards uniformity, in people, places, and times. The common man has common opinions; everywhere his towns and homes are losing their individuality; and the days of the week are treated alike. We no longer wear Sunday clothes, and we eat sausages and ice-cream throughout the year. Fruit is esteemed more highly for appearing out of season than for natural flavour. We seem, indeed, to seek a dead level at which we shall have everything at all times, and nothing therefore will be worth having. In all this we depart from the habits of our ancestors, whose life changed so much with the seasons and who were so conscious of variety within a basic rhythm. To the countryman, even today, the best weather is not good weather but seasonable weather: things should happen at their proper times. Likewise from dim antiquity there have been fasts and festivities proper to the times of year; and very long ago our forefathers decreed that mid-winter, soon after the shortest day, was the proper season for a festival of home—the time when families and friends should be gathered before a fire and shout defiance at winter and at fate. Like ourselves they had plenty of cares; but they were perhaps more fully aware of the need to prevent monotony by deliberate changes of mood—by feasts as well as fasts. Their festival at mid-winter was already a festival of hope long before it received its new name from the Christian church; but now the hope has a deeper significance through its association with the great idea of good will among men, as children of one father. In 2000 years this idea has lost none of its validity; and its strength, with our own, can be renewed at Christmas.

"In sum, it is a holy time", wrote NICHOLAS BRETON. "I hold it a memory of the Heaven's love and the world's peace, the mirth of the honest and the meeting of the friendly."

Smoke

DEATH from poisoned air has always had peculiarly terrifying associations. Yet over the centuries the thought and fact of atmospheric pollution has been presented so gradually and familiarly that it is hard to persuade the public that poisonous fumes are no less lethal when generated by industry, and no more genial when derived from the family hearth. Not long ago we commented [1] on the disaster at Donora in the United States, where 18 elderly patients died in one day, and 200 people came under treatment, from the effects of smoke and fog which had been kept at low levels by an accident of weather. It is true that the fog at Donora probably had a high concentration of exceptionally poisonous fumes from a zinc-smelting plant; but ordinary fog, such as we have lately experienced, is well enough laden with milder poisons; and every year, in cold foggy weather, many elderly people die before they need—just as surely as the Donora victims, if less spectacularly. If it is hard to assess the harm that atmospheric pollution does to health, it was no doubt equally hard, in the old days, to assess the harm done by defective sanitation. The results of cleansing the air might be little less remarkable than those of cleansing the water.

Bituminous coal, the common domestic and industrial fuel of Great Britain, throws into our atmosphere every year about 3 million tons of solid matter—as tar and oil particles, and soot—together with 5 million tons of sulphur dioxide and various other products of partial combustion, including methane and carbon monoxide. Mr. ARNOLD MARSH,[2] general secretary of the National Smoke Abatement Society,[3] has estimated the direct annual cost of smoke—in cleaning of buildings, repairs to masonry, laundry, replacement of plants in parks and open spaces, waste of fuel by imperfect combustion, extra lighting, and so on—at £100 million a year. The remedies are expensive, too, since they mean much new equipment, and giving up bituminous coal in favour of smokeless fuels, some of which are dearer to buy, though they may be more economical in the long run; but Mr. MARSH believes that the cost of the remedies could not approach the cost of smoke. Half the money nowadays wasted in ten years would suffice to convert all domestic grates to types which would produce virtually no smoke; and domestic grates are responsible for half the smoke in our atmosphere. It is good news, therefore, that the Ministry of Health has now forbidden local authorities to install outmoded grates and stoves in their new houses.[4] In future, grates must be chosen from among varieties approved by the Government as efficient—of which there are no fewer than 69, the simpler ones costing about £5. Even bituminous coal, if fully combusted, does not pollute the atmosphere; but it is unlikely that we shall ever be able to burn it completely in domestic appliances, and certainly we shall not be able to do so in open fires. The conscientious householder who does not wish, or cannot afford, to replace all his grates is therefore in a dilemma: his grates will not burn the natural smokeless coals, such as anthracite and Welsh steam coal, which incidentally are more expensive than ordinary coal; and though he may be prepared to use the low-temperature smokeless fuels, such as gas coke and 'Coalite,' he will probably not be able to buy them in sufficient quantity, though they will burn in most types of grate. He is thus apt to forget his conscience, buy a few logs to eke out his coal ration, and wish the legislators would begin by reducing the smoke from the factory next door. Alternatively he may rely on gas and electricity—regardless of the fact that the Simon Committee in 1946 reported that these were twice as expensive as

1. *Lancet*, Nov. 6, p. 738.

2. Smoke: the Problem of Coal and the Atmosphere. London, 1947.
3. Chandos House, Buckingham Gate, Westminster, S.W.1.
4. *Times*, Nov. 22.

solid fuel burnt in an efficient appliance. It is easy to sympathise with his feelings, especially as most people find a coal fire companionable, and some have beautiful ancient grates which they wish to keep.

Actually, much of the fuel saving of recent years has been achieved in industry; for there is some legal restriction over all forms of smoke except that from domestic chimneys. Much of this consists in inflicting fines after the nuisance has been caused, but some local Acts—such as the City of London (Various Powers) Act, and the Manchester Act, both passed in 1946, and a spate of others passed subsequently—aim at prevention. Thus the City of London Act gives the common council power to make by-laws requiring that in new buildings, and in buildings where the heating arrangements are being substantially altered, the new equipment should be chosen "to prevent or reduce to a minimum the emission of visible smoke." Presumably this refers to business houses rather than factories where furnaces are used; nevertheless the abatement of smoke by such regulations should be considerable. In many industries, Mr. MARSH notes, coal-fired kilns are being replaced by kilns using producer-gas, town gas, and electricity; and in many others better instruments for measuring fuel consumption, more efficient control of draught, and better stoking have made fuel waste and smoke production negligible. The National Smoke Abatement Society recommend modernisation of coal-burning plant, approval of new plant by a competent authority, better training for stokers, more research on pollution, and of course a greater use of smokeless fuel as this becomes available. Another policy they favour is the setting-up of smokeless zones, such as the one planned for Manchester, where the 1946 Act requires that "no smoke shall be emitted from any premises in the central area," and where the corporation may, if it thinks fit, "contribute the whole or part of the expense necessarily incurred by any person in making premises smokeless." (Unfortunately little active progress seems to have been made yet, except in Salford, which is taking the lead.) Clearly such smokeless zones could begin as scattered centres, and be extended until whole cities were included; and the plan is flexible, and allows for minor infringements such as the production of smoke when a cold boiler is being lighted up.

Most of the Simon report's thirty-five practical recommendations still need trying. Meanwhile we live under a cloud. One of the weaknesses of our position is that we can do little as individuals; but this situation was paralleled in the 19th century when the pioneers of public health were fighting our battles for clean water. The National Smoke Abatement Society are doing much to create an informed public opinion. Already before the war they were printing pamphlets to guide householders who wished to install better appliances, and they will always give advice to those who ask it. Also the Solid Smokeless Fuels Federation [5] publish a brochure showing types of grate and recommending appropriate smokeless fuels. The trouble is that most of us have underdeveloped consciences about smoke. But the periods of fog we have already experienced this winter may paradoxically have lightened our darkness.

5. 1, Grosvenor Place, London, S.W.1.

The Cause of Diabetes

THOUGH nearly thirty years have passed since insulin was discovered by BANTING and BEST, the cause of diabetes mellitus remains unknown. But interest is very far from flagging, as is shown by the Banting memorial lecture by Prof. F. G. YOUNG which we published last week and by the discussion he opened at the Royal Society of Medicine on Dec. 14. In this discussion he pointed out that as "diabetes mellitus" may comprise more than one condition, and as there are several ways of inducing it experimentally, there are possibly many related problems to be solved rather than a single one. The idea that it exists in more than one form was also brought out by Dr. H. HARRIS in speaking on the genetic aspect. A series of 1241 diabetics, he said, was divided into two groups, according to whether they developed the disease before or after thirty years of age, and it was found that the former, but not the latter, had a significantly higher rate of cousin marriages in the parents; which suggests hereditary differences between cases of late and early onset.

Experimentally there are five main methods of producing diabetes, at least four of which involve direct or indirect interference with the pancreas. These five methods are: (1) pancreatectomy, complete or partial; (2) the administration of alloxan, which brings about rapid necrosis in the β cells of the pancreatic islets; (3) the administration of anterior-pituitary extracts, which may lead to a persisting diabetes associated with lesions in the islets; (4) the administration of excessive doses of glucose, which in a partially depancreatised cat (or even in a normal one) may produce persisting diabetes, again also associated with lesions in the islets [1]; and (5) the administration of certain adrenal cortical steroids, which can cause glycosuria in animals. We must also mention the glycosuria that may follow the administration of large doses of adrenocorticotropin to the rat [2] or to man,[3] which is presumably mediated by the hypersecretion of adrenal cortical steroids. Professor YOUNG distinguishes between "idiohypophyseal" diabetes, which exists during a period of daily injections of diabetogenic anterior-pituitary extract, and "metahypophyseal" diabetes, which persists after such treatment has ceased. The latter is associated with structural changes in the islets of Langerhans, which have been clearly elucidated by Mr. K. C. RICHARDSON, and perhaps it can exist clinically in the absence of any sign of pituitary hyperfunction.

Professor YOUNG has found that after taking a high-carbohydrate diet dogs are less sensitive to the diabetogenic action of anterior-pituitary extract than they are after taking a diet containing a high proportion of meat protein. He has also shown that in the dog with metahypophyseal diabetes ketonuria is much greater when the diet consists largely of lean meat than when it contains a high proportion of fat. Relevant to these observations are those of TEJNING,[4] who estimated the volume of the islets of Langerhans in the pancreases of rats given

1. Dohan, F. C., Lukens, F. D. W. *Endocrinology*, 1948, **42**, 244.
2. Ingle, D. J., Li, C. H., Evans, H. M. *Ibid*, 1946, **39**, 32.
3. McAlphine, H. T., Venning, E. H., Johnson, L., Schenker, V., Hoffman, M. M., Browne, J. S. L. *Proc. Ass. Study int. Secretions* (U.S.A.), 1948.
4. Tejning, S. *Acta med. scand.* 1947, **128**, suppl. 198.

different diets for about nine months, and found that a diet rich in protein, and also one with a high proportion of fat, caused diminution in islet volume, which was slightly raised, on the other hand, in the animals receiving a high-carbohydrate diet. In such experiments the comparative calorie intakes of the animals on the different diets may be of commanding importance; and Prof. H. P. HIMSWORTH in the R.S.M. discussion did well to recall the dramatic fall in diabetic mortality in this country which followed the imposition of food-rationing during the 1914–18 war, and again during the late war. Mortality rose again after the first world war but not after the second, when rationing was (as we are all well aware) continued; and there is a strong probability that the falls in mortality had something to do with the restriction in people's choice of food. Professor HIMSWORTH pointed out that the curve showing reduction in diabetic mortality and the curve showing reduction in the total fat content of the diet are remarkably parallel. (Surprisingly enough, the protein content of the diet of the nation as a whole has tended to rise during the past few years, though it may well be that the meat protein component has fallen.) He was cautious in his conclusions, but his data supported the view that rationing has reduced the incidence, as well as the mortality, of diabetes.

Dr. R. D. LAWRENCE reviewed the work done since the dramatic report in 1943, by SHAW DUNN and his colleagues,[5] that alloxan causes necrosis of the β cells of the pancreatic islets and consequent diabetes. As yet, he said, there is no substantial evidence that diabetogenic doses of alloxan are ever produced metabolically in the animal body; indeed it is unlikely that alloxan diabetes occurs naturally. But the value of so simple a tool for the experimental induction of diabetes has been immense, and it is greatly to be regretted that Professor SHAW DUNN lived so short a time after his important discovery. So far alloxan has unfortunately proved of little value in the treatment of hyperinsulinism in human beings, though investigations continue.

Developing his suggestion that there are hereditary differences between diabetes appearing early and late in life, Dr. HARRIS discussed observations that fit the assumption that the milder cases of late onset are heterozygotes for the abnormal gene, while the severe cases of early onset are homozygotes. This assumption would account for many of the facts already known about familial distribution and population frequencies; but, as Dr. HARRIS said, much more work is needed to test it. He has found that in some families (mostly those with the disease in milder form) diabetes picks out mainly the females and in other families mainly the males, and this happens more often than it would if it were simply a random process. He also raised the question of how diabetes is maintained in the general population despite the fact that juvenile diabetics are liable to die before they have completed the reproductive phase of their life. One would expect that in each succeeding generation the genes determining the juvenile type of disease would be less and less represented. But the later the disease develops, the less likely is it to diminish effective fertility; and Dr. HARRIS mentioned an interesting observation that the proportion of women who bear a child or children may actually be higher among "elderly" diabetics than among non-diabetics of the same age-group. There is no unequivocal evidence for a greater fertility among diabetic or potentially diabetic women, as compared with non-diabetics, but the suggestion deserves further study.

No adequate and simple conclusion about the cause of diabetes can be drawn from the mass of data that is still accumulating. But the picture as a whole is becoming less rather than more confused. Careful analysis of hereditary factors in human diabetes has already produced some simplifying hypotheses, while the fact that the pancreatic islets are affected by so many, apparently different, methods of inducing diabetes is in itself encouraging. Dr. and Mrs. CORI, whose share in the Nobel prize for medicine in 1947 was so well deserved, have initiated researches concerning the in-vitro influence of hormones on the enzyme hexokinase which are of fundamental significance; and it is perhaps not too much to hope that such investigations will one day reveal that diabetogenic agents interfere at relatively few points with the normal processes of carbohydrate metabolism. That genetic, hormonal, and dietetic factors may all, directly or indirectly, affect carbohydrate metabolism by influencing a single enzyme system—or at least only a few such systems—is an attractive possibility revealed by the research of the last few years.

5. Dunn, J. S., Sheehan, H. L., McLetchie, N. G. B. *Lancet*, 1943, i, 484. Dunn, J. S., McLetchie, N. G. B. *Ibid*, ii, 384.

Osteopathy

"ABOUT things on which the public thinks long," said SAMUEL JOHNSON, "it commonly attains to think right." And we have to accept the fact that public opinion has come to lean on osteopaths for several types of treatment; that kings, nobles, and the common people patronise them; and that the medical profession is widely blamed for its grudging reception of the new ideas. In 1934 a Bill was introduced into the House of Lords, "to place the practice of osteopathy, as a developing system of treatment of diseases by manipulative methods, under the control of a statutory board." One of its sponsors, Lord ELIBANK, argued that the Medical Acts were never intended to put obstacles in the path of new methods in the treatment of disease; osteopathy, he said, was a new line of thought, and an Act was required to protect the public from the malpractice of persons "unqualified" in osteopathy. Lord MOYNIHAN, on the other hand, denounced osteopathy as a spurious science, "the derision of all competent and experienced minds," and feared that if it were encouraged other cults would soon be clamouring at the gates of Parliament. In this he was supported by Lord DAWSON OF PENN, who felt that the honourable path for the osteopath seeking recognition was the arduous one—to qualify first, in order to obtain the privileges of the doctor, and then to turn to his particular love, as the homœopath has done for generations past.

The Bill, after its second reading, was referred to a select committee, which subsequently advised that it be rescinded. During its discussion the fact emerged that in the United Kingdom at that time there were only about 170 men and women "qualified" in osteopathy, though some 2000–3000 were engaged

in its practice. Their craft and art was not limited, as commonly supposed, to the skeletomuscular system: they claimed as their field "all diseases of any description," and the Bill proposed to give them the right to sign birth and death certificates, administer anæsthetics, and perform minor operations. But their methods were almost unknown on the Continent of Europe, and in this country the only existing establishments for the training and examination of osteopaths were of negligible importance and "in thoroughly dishonest hands." The select committee accordingly recommended that the establishment of a register of qualified osteopaths by Act of Parliament should be deferred until the sphere of osteopathy had been defined, and until a reputable system of education in its principles and practice had been developed in one or more well-equipped and properly conducted institutions in Great Britain.

This advice did not fall on deaf ears, and in 1946 the first step was taken—the constitution of the "Faculty of Osteopaths" was drawn up, and the "London College of Osteopathy" was established. The object of the college was to teach the theory and practice of osteopathy to "qualified medical men," and it was housed in the same building as the "British Osteopathic Association Clinic," from which it was to draw its clinical material. The new college can be regarded as a creditable attempt to organise and evaluate osteopathic ideas, and to curb the opportunist or the quack, and to this extent the enterprise appears commendable. But there remains a danger that the functions of such a college may come to be extended in such a way as to realise the claims of non-medical osteopaths who seek to practise medicine without the elaborate training required for medical diagnosis. This week we publish a report from two surgeons, Mr. SOL. COHEN and Mr. BATCHELOR who have visited the college on our behalf. We share their opinion that osteopaths who undertake the full care of patients must first obtain a medical qualification, but we also agree with them that doctors who practise osteopathy should be given every chance of proving, in orthopædic departments, the value of their methods.

Better Late than Never

FROM October onwards the president of the Royal Medical Benevolent Fund has been saying that the time has come for contributions to its Christmas gifts. Unfortunately many of us find it impossible to think of any kind of present until, at earliest, Christmas Eve; by which time it may seem a little late to answer his appeal. The fact remains that the R.M.B.F. needs all the help it can get, both now and later; and outside their own circle our readers will find no better object for generosity than the relief of doctors and their dependants who have met one or other of the many kinds of misfortune that lie in wait for us all. Besides making grants, for support and for education, the fund has lately opened, for some of its older women beneficiaries, a house where they can live without hardship or loneliness. With support there will be others. Meanwhile a small present of money is going out again this Christmas to homes where it will mean a lot, both in comfort and in encouragement. Contributions and subscriptions should be sent to the R.M.B.F., 1, Balliol House, Manor Fields, London, S.W.15.

Annotations

DODGEMS

"Mr. Williams, meet Miss Jones. You are going to kill her in exactly twenty minutes' time."

In the Central Office of Information film *Worth the Risk?* Miss Jones is the young lady who steps off the curb and just keeps on walking—"they always stop." Mr. Williams is the man in a hurry who is going to get his brakes fixed tomorrow. This documentary—which is being shown in 3300 cinemas up and down the country—explains with ironic coolness that, though we are all careful drivers and good pedestrians, somebody in Great Britain gets injured in a road accident every $3^1/_2$ minutes. In the United States the casualty-rate is one death every $15^1/_2$ minutes, and one injury every 26 seconds. Such hazards to life and safety would hardly be tolerated on railways or air-lines: the public would rightly demand an inquiry. But our own failings bear less hardly on us than those of official bodies. Our grandfathers thought that trains moved fast; and the railings and regulations with which they fenced our permanent ways must have saved countless lives. Road vehicles, of course, are not as heavy as trains, but they can move as fast, and they swerve. And they are driven by almost anybody.

Those who have in their time frequented circuses will recall the dodgem. Small cars are provided in which patrons steer themselves, or fail to steer themselves (for the steering gear is deliberately capricious) about a crowded floor. Crashes are inevitable—they are part of the fun—but they do no harm because the little cars are encircled by massive rubber bumpers. Here is the germ of an idea which Dr. Fletcher D. Woodward[1] has lately considered in some detail. Studying the types of road accident seen at the University Hospital of Virginia, he found that the predominating injuries were damage to the face and head received from the dashboard, windscreen, or back of the rear seat; crushing injuries to the chest caused by the steering-wheel; injuries to the hip, pelvis, patella, or femur exposed to impact by protective rotation of the body; damage to the elbow projecting comfortably from the window; and associated injuries to the abdominal viscera, lungs, and brain. Many of these, he thinks, could be prevented. The National Safety Council in America has done good work in reducing the mortality-rate; but this is still enormous, and he thinks it would be more profitable to shift attention, anyhow for the moment, to the machine itself. During the war, many aeronautic safety devices were developed by the engineer and the doctor in collaboration, among them such things as safer parachute harness, better placing and design of escape hatches, instruments, and control handles, better oxygen and pressure equipment, safer clothing, standardisation of cockpits, and air-sea rescue equipment. The same approach to cars should be rewarding.

Speed might well be considered first, for in American statistics it is a factor in 2 out of 5 fatal accidents; and in 20% of all accidents in which speed was a factor the car was travelling at more than fifty miles an hour. He proposes the use of governors on all cars limiting the top speed to fifty-five miles, but not interfering with acceleration at lower speeds. A survey taken by the American Automobile Association shows that this would be more generally acceptable than might be supposed. Of 4102 people asked whether they would favour the universal fitting of governors, 4 replied Yes for every 3 who said No. The speedometer, he considers, should be at the top of the instrument panel directly opposite the driver, and should show, besides miles per hour, the stopping distance in feet under average driving conditions.

1. *J. Amer. med. Ass.* 1948, 138, 627.

This and other instruments should be illumined with red light, for night driving, to maintain the driver's dark adaptation. In the absence of a governor, a flashing red light or an auditory signal might be included to indicate fifty-five miles per hour. A frame and body of welded "unit construction" would be helpful, and should include crash struts, he suggests, like those in aircraft. Windows and windscreen should be made of plastic, not glass, and so should headlight lenses. Both windscreen and rear window should be placed nearer the vertical than has been the fashion lately, since the driver can see better through a vertical pane, especially in rain, sleet, or snow. Efficient windscreen-wipers and defrosting equipment should be supplied for both the windscreen and the rear window, and the range of outlook for the driver should be as wide as possible. Dr. Woodward proposes a windscreen offering a range of 360°, and this principle is embodied in a design for a safe car, by Mr. Stewart Rouse,[2] which accompanies the article: here the windscreen forms a wide bow, and the front supporting column of the roof has been moved back to a point just beside the wheel, and is as slender as its purpose allows. The rear supporting column is placed well behind the driving seat, so that the driver has a broad pane at his side and a wide sweep of vision ahead. Doors should conform to a standard pattern; and windows—which should all be large enough for a man to get through—should have sills high enough to discourage passengers and driver from using them as arm-rests. All cars should have door-latches having a safety lock, to prevent children from getting the doors open while the car is running.

Bumpers offer great scope for improvement. Mr. Rouse's design follows the dodgem principle: rubber bumpers, coloured to match the paint-work, encircle the whole car. The front bumper, Dr. Woodward suggests, should be mounted, like the landing gear of aircraft, on "oleo shock-absorbers"; and tyres should be designed to give the maximum degree of traction with the best antiskid qualities—points on which judgment should be passed by some disinterested agency. Blow-out-proof tubes should be used at the expense of some riding comfort, if need be.

Glare is probably responsible for more night accidents than any other single cause. A glare-proof rear-view mirror would save the driver much discomfort, and so would a polarised windscreen to minimise glare from the road surface. If headlight lenses were oppositely polarised, the sudden intermittent call on the driver's powers of light and dark adaptation would be abolished, and with it one of the greatest risks of night-driving. It is in the moment of blindness after the glare that the motorist kills the invisible child or rides down the cyclist who depends on a muddy reflector. Cars themselves should be made more visible by the use of reflectors at the corners of the fenders and the top, by dual tail lights, and by a large "stop" light. Luminous paint could be used on the outside margins of trailers, and perhaps also of lorries and buses; and luminous paint might also be tried for strip-marking on highways.

Inside the car there should be no shiny reflecting surfaces just under the driver's eye: the dashboard should be a dull black, and chromium trimmings should be reserved for other regions. The steering-column could be built to move forward under a force of about 100 foot-pounds, a device which would do much to save drivers from injuries to the chest; while sponge crash-pads on the dash and the back of the front seats would prevent many head injuries. Projecting handles, knobs, and buttons should be eliminated; and safety belts—which are standard equipment in aircraft—might be among the most effective single factors in preventing damage to motorists.

These are evidently only a selection of devices which have occurred to Dr. Woodward; and any driver will be able to add to the list if he sits and thinks about it. We could, if we would, now build cars capable of withstanding collisions, and even of leaving the road at high speed and overturning without injuring the occupants; moreover, drivers of cars fitted with the safety devices outlined by Dr. Woodward would be less liable to have accidents. These important suggestions deserve to be studied seriously, for there are limits to the results which can be achieved by appealing to the skill and discretion of the public in using the roads. It is hardly justifiable to place all our faith on what he calls "attempts to bludgeon 'old Adam' into safer driving practices"; we must try to make the machines safer too.

2. Reproduced from *Popular Science Monthly*, April, 1947, in an article by Devon Francis.

SURFACE-ACTIVE COMPOUNDS IN THE CHEMOTHERAPY OF TUBERCULOSIS

IN the U.S.A. Dubos [1] has shown that certain surface-active water-soluble compounds stimulate the growth-rate of the tubercle bacillus. He used a phospholipid, which is a naturally occurring surface-active substance, and also Tween 80, a commercially available wetting agent. The stimulating action is inherent in the hydrophobic end of the Tween-80 molecule, which is an oleate; the remaining portion of the molecule is a water-solubilising complex which consists of a sorbitan nucleus attached to three polyethylene glycol chains. In the presence of the tubercle organism the surface-active Tween-80 molecule concentrates at the water-bacterium interface, with the hydrophobic portion of the molecule directed towards, or possibly entering, the bacterium. Between the surface of the tubercle bacillus and the medium in which it is suspended there forms an interface, one side of which is aqueous and the other lipid; at this interface the surface-active molecules concentrate. Tween 80 probably acts by concentrating a known metabolite (the oleate) where it is most readily available to the bacterium—namely, at the periphery of the cell or possibly within it. It also stimulates bacterial growth by dispersing the clumped bacteria. Eiseman, [2] in search of a method for enhancing the effect of known tuberculostatic drugs, has modified the Dubos principle. Instead of concentrating an essential metabolite at the surface of the bacillus he employs a tuberculostatic drug at the hydrophobic end of the surface-active molecule, thereby increasing the effective concentration of the drug at or beneath the cell boundary. The surface-active molecules, instead of being spread evenly throughout the solution, would be expected to concentrate at the periphery of the organism. Several compounds were prepared by combining tuberculostatic drugs, such as 4,4'-diaminodiphenyl sulphone and its derivatives, with synthetic surface-active compounds such as carbowax and polymers of ethylene and ethylene oxide. Thirteen compounds were tested, and with some of them a thousandfold increase in tuberculostatic effect was obtained by coupling with surface-active substances.

It is not known whether this new approach to the chemotherapy of tuberculosis has any practical value. Only in-vitro tests have been done, and it is not certain whether rendering tuberculostatic drugs surface-active increases their activity in vivo, nor whether their toxicity is altered in any way. If in-vitro testing shows enhanced tuberculostatic activity, it might be worth while to convert the more potent drugs used in the treatment of tuberculosis, such as streptomycin and *p*-aminobenzoic acid, into surface-active compounds in the hope that their activity will be increased.

1. Dubos, R. *Proc. Soc. exp. Biol., N.Y.* 1945, **58**, 361; *J. exp. Med.* 1946, **83**, 409.
2. Eiseman, B. *J. exp. Med.* 1948, **88**, 189.

UNIVERSITY AWARDS

STATE scholarships were offered in this country for the first time in 1920. The number was small—200 each year—and there was an overriding limit of £80 for maintenance, while the test of hardship was stringent. The scheme did little or nothing to help parents in the middle and lower-middle income ranges. Even so it was killed two years later on the ground that the country could not afford the money. Since the end of the late war we have done better. The number of State scholarships has been increased from 360 in 1945 to 800 in 1948. In addition, 100 technical State scholarships are now offered annually to students who have completed satisfactorily a course for the Ordinary National Certificate or Diploma. This has increased the opportunities for students who leave school at fifteen and continue their training by full-time or part-time courses. A further 20 State scholarships are offered to students over twenty-five.

A big attempt has also been made to increase the value of these awards, and to reduce the sacrifices which parents make—and we suspect always will make—for their children. In 1946 the limit of £100 on maintenance grants was removed, and it was decided that the "full standard figures of maintenance" should be payable by the Ministry of Education. It was also decided to supplement open scholarships and exhibitions awarded by universities up to the amount paid to State scholars. These reforms have meant that State scholarships are no longer used to supplement open awards, and that local education authorities are no longer called upon to supplement open and State scholarships: their awards can now be devoted to helping other children of good intellectual quality. Most local authorities have responded by increasing both the number and amount of their awards, which have risen from around 1500 in 1945 to 4000 in 1948.

Taken together, these improvements make an impressive total. But, as many parents know, opportunity is still limited and there are still anomalies and injustices. With these in mind, the Minister of Education appointed last April a Working Party to consider changes in the present system. Many of the recommendations in their report[1] are thoroughly sensible. They suggest, for instance, that in future no boy or girl should be compelled to promise, in exchange for a university education, to teach in a grant-aided school. They also do well in recommending that scholars should no longer be stopped from going to the university of their choice merely because that particular university's quota of scholarships has been filled.

The Working Party are also concerned to increase still further the number of awards and to improve their value. They propose that the number of State scholarships should be raised from 800 to 2000 and of local-authority scholarships from 4000 to 7000. This is ambitious; in the view of some who are in a good position to judge, too ambitious:

> "Quality," says Mr. W. W. Grave, PH.D., registrar of Cambridge University, in a dissenting note to the report, "must not be sacrificed to quantity. . . . If the university authorities are unable to recommend for awards as many candidates as the report contemplates, it is to be hoped that there will be no feeling that they are placing unjustifiable obstacles in the way of deserving pupils. It is notorious that once standards are lowered, they are very difficult indeed to restore."

Whatever figure is fixed, it appears certain that there will be a considerable further expansion. It becomes all the more important then to ensure that the awards, once made, are generous. At present, the income scale for assessing the value of awards to resident students starts at £600 and proceeds to a ceiling of £1500. A parent with an income above this figure must meet the whole of a State scholar's expenses, and a parent's contribution rises steeply in the upper reaches of the scale. True, in calculating the parent's contribution, an allowance of £50 is made for each dependent child (other than the student), and extra allowances may be made in respect of a child's education—up to £60 for school fees and £100 for expenses of university education or professional training. But these allowances are too small, and a student who has won a State scholarship on his merits, but happens to be one of a large family, may have to forego a university education because the strain on his parents would be insupportable. The Working Party wisely recommend that the allowances should in effect be doubled, and that the student's maintenance should include allowances for books, instruments, clothing, midday meals, travelling, subscriptions, and pocket-money, as well as a contribution towards his keep during term-time and expenses during vacations. These improvements show an awareness of the difficulties which beset many parents today.[2]

The report also deals with the problem of those who are not eligible for any award because the income exceeds £1500. This ceiling introduces anomalies, for parents with three or four children and an income of £1550 get nothing although they are heavy taxpayers—while those with one or two children and only £100 a year less are helped. The Working Party propose that the ceiling should be raised to at least £2000; that the increased length of the scale should be used to make the change in parental contribution more gradual, and that all students who qualify for a highly competitive award such as a State scholarship should derive some financial benefit. Thus it is suggested that £30 a year should be given without regard to the parent's means. This concession would be welcome, though it seems inadequate. More important would be a recognition that a parent's position above or below the income ceiling should be ascertained *after* allowances have been made for his other responsibilities.

1. Report of the Working Party on University Awards. H.M. Stationery Office. 1948. Pp. 26. 9*d*.

MEDICINES UNDER THE ACT

WHAT is a medicine? Perturbed by the liberal answer of some practitioners, the Minister of Health is to refer this question to the standing medical and pharmaceutical advisory committees of the Central Health Services Council. Meanwhile executive councils are asked to be guided by two lists composed some years ago by an expert advisory committee in relation to National Health Insurance. One list is of substances which were considered never to be drugs, and the other of substances (including a number of "tonic" preparations) which might sometimes be deemed drugs or medicines. Neither list has any statutory force. Composed in 1929, they are not exhaustive. Of alcoholic liquors only brandy, champagne, and sherry are named as never being drugs, "whereas in the Minister's view all alcoholic liquors should be similarly classed and should not be ordered on E.C.10" (the National Health Service prescription form). Moreover, "while it is the practitioner's duty to prescribe for a patient on his list whatever drug or medicine is necessary for proper treatment, he is not, of course, authorised to prescribe toilet requisites or foods or foodlike substances."

Executive councils are empowered by regulations to recover from the practitioner the cost of substances prescribed by him under the Act which they deem not to be drugs or medicines; and if the doctor wants to challenge the decision he may ask for it to be referred to the local medical committee, with the possibility of appeal to referees. Given good sense on each side, such disputes will be rare. The substances likely to cause real difficulty are those in the broad borderland between drugs and food; it is here that the up-to-date ruling promised by the Minister is most urgently needed.

2. See *Manchester Guardian*, Nov. 26 and Dec. 3.

Special Articles

OSTEOPATHY

A VISIT TO THE LONDON COLLEGE

J. S. BATCHELOR F.R.C.S. SOL M. COHEN F.R.C.S.

IN July, 1946, THE LANCET published an advertisement from the London College of Osteopathy inviting applications from registered medical practitioners to attend a nine-month course in osteopathy. Tucker (1946) expressed the view that such publication was tantamount to sympathy and encouragement, and advised the medical profession to dissociate itself entirely from osteopathy. The dean of the college then invited THE LANCET to examine its work, and we later visited it as the Editor's representatives.

VISIT TO LONDON COLLEGE OF OSTEOPATHY

It may be said at the outset that we were impressed by the integrity of our hosts. We came not as armed critics but as friendly listeners, determined to decide whether or not the college was a "threat to public security." Admittedly, we were inclined to agree with Tucker that the organisers, while paying lip service to the law, might be out to gain their own ends. At once, however, we were shown the manifesto of the faculty, which clearly states that "ordinary medical training" is to be the sine-qua-non of any specialisation in their particular branch. The teachers appeared to be reasonable, rational people, with no extravagant enthusiasm, and they were ready to admit some of the defects of osteopathic doctrine, particularly as regards the speculative pathology of some of the lesions. Though much of the training in manipulative methods had still to be taught by non-medical osteopaths, anatomy and physiology lectures were being given by lecturers from some of the leading medical schools in London. The non-medical teachers were on the examining board, but the dean had no objection to the introduction, at a later date, of external examiners. The clinical material was limited to about 500 cases a year, but he was hopeful of being able to expand this.

We took the opportunity of independent discussions with the "student" doctors—some six of them—and inquired why they had entered this particular field. All showed a conviction that this was a neglected part of medical studies. We are all aware of the "unconventional" type—those with a bias and a grudge and a desire to flaunt recognised medical authority. We are also aware of the temptation to reap the monetary rewards said to be associated with this type of practice. But such thoughts may be dismissed as doing less than justice to men who seemed sincere and earnest.

We were given a demonstration on four patients:

The first was a middle-aged man suffering from backache and sciatica; he had had several previous attacks, and he had been under treatment for six weeks. Apparently he had hobbled into the clinic on crutches, and during this time had shown remarkable improvement. The demonstrating surgeon attributed the lesion to a displacement of the sacrum on the ilium; he determined this mostly from the relative position of the posterior superior spines of the sacrum. He then performed a series of manipulations, designed to correct this displacement.

The second was a lady with headaches, said to be migrainous, and a stiff, painful neck; she had had previous manipulations. The examiner—a non-medical osteopath—included an examination of the abdomen, and was not impressive in his reference to being able to feel a "sandy" bowel, indicating a need for colon lavage. He claimed that he could distinguish that the "rib heads" were tied down, and the first part of his treatment consisted in traction on the ribs via the scapula, in an unusual "embracing" method. He claimed that there was some displacement of the neck vertebræ, which it was difficult for us to appreciate. The neck was then manipulated, in what seemed most able fashion.

The third was a young man with a painful neck, and a history of injury in an armoured vehicle during the war. Recently there had been a return of the painful stiff neck. The manipulator—an experienced American osteopath—after a brief examination indicated that there was a primary osteopathic lesion, with secondary local effects. His plan of treatment was to reduce the primary joint lesion first, and the secondary lesions later. His manipulations were of some purpose, for he repeated them some six or eight times, until he was satisfied that the "displacement" had been corrected.

The fourth was a middle-aged woman, with classical low backache. Again a subluxation of the sacrum on the ilium was diagnosed, and manipulation undertaken to correct it.

THE OSTEOPATHIC LESION

The osteopathic lesion is defined as "essentially an unbalance of a joint, not amounting to a dislocation"; the word lesion encompasses all tissues—the overstretched ligament, the taut connective tissue, and the contracted muscle. It is contended that this lesion may influence all the blood and lymph vessels, and also the nerves, with their cell origins and connexions. The effects may thus be both local and remote.

Such lesions are found chiefly in the joints of the pelvis, spinal column, and ribs, and involvement of intervertebral discs is considered important. Osteopaths emphasise the osteopathic lesion as a constant ætiological factor in functional or organic conditions, but do not deny the existence of other ætiological factors, such as infection and chemical and metabolic disturbances. They argue that while orthopædic surgeons are ready to admit and accept the lesion as an isolated affliction of the joint or tissue, they have failed to appreciate its significance as a cause or predisposing factor in disease. By failing to preach the latter concept, the orthopæd has deprived the community of a valuable additional method of dealing with ill health.

The occasional existence of an "unbalanced joint" as a clinical entity cannot be denied. It is appreciated and accepted by the orthopædic surgeon. As Marlin (1934) put it, "there may not necessarily be any joint displacement, but a state of fixation or torsion of the bones on their long axis," and manipulative reduction may be required, "because no provision is made in the human mechanism for overcoming such defect." Reference to the simple finger hinge joint best illustrates this; the flexor and extensor muscles here act in one plane, and are unable to correct by active effort any lateral flexion or rotation brought about by violence. Nor could such voluntary action reduce any active joint subluxation, for this necessitates first separating the joint surfaces by traction, for which there is no voluntary mechanism.

Where osteopathy seemed to us to fail was in its wholesale claims for the presence of such mechanical disorders. At our visit we felt that the cases were approached with the conviction that such an osteopathic lesion was obviously present (but these were, of course, selected cases). The examiners too readily convinced themselves of the existence of fine variations in the relations of anatomical bony points—variations not always clear to us, and not greater than was to be expected as within normal limits. It might be argued that, not having received "osteopathic" training, we could not readily detect fine variations; but as surgeons of twenty years' standing, we believed that this should have been within our compass. X-ray films, which are used as an aid in excluding disease, do not show the osteopathic lesion; but we accepted the possibility that minor rotations—no displacement but a fixation—could not be demonstrated radiographically.

The osteopath has also magnified the extent of the lesion by allusions to "bones out of joint," which may be but a pandering to the "baby language" suitable for the lay patient, just as we talk of "nerves" to explain

the anxiety state. But to tell the patient that a bone has been replaced, when nothing of the sort has been done, is dishonest; particularly if the purpose is to discredit and disrupt the medical attendants' efforts. Our hosts certainly indulged in no such language.

The belief that such a lesion can by itself be a cause of disease seemed to us completely without foundation, and the medical profession can hardly be expected to yield to hypotheses based on "I believe, because I believe." It is true, as Kellgren and Lewis have shown (Lewis 1942), that there may be reflex referred visceral manifestations from somatic foci, and the subject is now being intensely studied. But resultant disease has never been demonstrated, and we cannot accept the idea that osteopathic adjustment will influence say pneumonia, tic douloureux, angina pectoris, or gall-bladder disease—to name but a few of the osteopaths' claims.

Some of the medical profession, recognising that the human will is a capricious thing, believe that osteopathy caters mostly for the "psychological" factor, which in turn may influence physiological processes. This view may sometimes be justified; but on the whole we felt that, judging from our hosts, it was prejudiced. And that brings us to the oft-repeated taunt of many a layman that doctors are prejudiced against osteopaths. We may quote the words of the late Lord Passmore in answer: "if you meet what you call an unprejudiced person, that means simply he has the same prejudices as yourself."

MANIPULATIVE METHODS

The osteopath has undoubtedly given much thought and attention to technique, and has a kitbag of technical tricks. The manipulations were beautifully performed, with skill and gentleness, and without pain; there was a light, easy, confident grasp, with ability to reassure the patient and gain his assistance in relaxation.

They have not attempted to shroud their methods in mystery; orthopædists have been welcomed and given full assistance and opportunities. In the '30s there was in fact a great revival of interest in these methods, and books on the subject were published by orthopædic surgeons. In more recent years orthopædic interest seems to have waned, and experience indicates that such general lack of interest is not to be discounted, for it is often due to unsatisfactory or indifferent results. One reason may be that the standard of management of the fracture and the soft-tissue injury is now far higher than it was; early ambulation and movements have been adopted, and the rôle of patient and masseuse reversed (a LANCET annotation summed it up well as "active patient, passive masseuse"). In consequence the stiff shoulder and other joint fixation disabilities no longer come to need manipulation or wander off to the osteopath for this.

Be that as it may, it has to be admitted that the osteopath has made a definite contribution to this aspect of treatment. His manipulative methods are not readily acquired from the textbook, and can only be truly appreciated by visual demonstration. These methods did not seem to us to be beyond the scope of the medical practitioner, and certainly the orthopædic surgeon can, and does, perform such manipulations with skill and proficiency. That there is a knack is true; as Marlin put it, "to turn the key in a difficult recalcitrant lock, is not a matter of force." As in golf, a certain measure of timing and velocity of motion are required for strength and direction. It was not clear to us why multiple repeated manipulations, as practised by the osteopath, should be more effective; but Marlin has aptly compared the repetition to the gentle tapping of the old lock, so as to get the key to turn. It may be mentioned here that the cracking of joints on manipulation, to which the patient attaches so much importance, can be demonstrated on normal joints. The osteopaths at our visit attached no significance to it, and tried indeed to avoid it.

We also found it difficult to understand why repeated manipulations should be more effective in reducing a subluxation, and we felt that much of the success of the osteopathic technique might be due to the breaking down of adhesions and the softening of fixed joints and soft tissues.

In our opinion craftsmanship in manipulative therapy is not to be regarded as a major achievement: such therapy is only a minor weapon in the medical armamentarium. What is far more important is for the osteopath, if he can, to explain in scientific language the pathology of the osteopathic lesion—which remains somewhat vague and obscure.

Moreover, "the correct use of manipulation in the first instance depends on diagnosis" (Mennell 1948). If osteopathy can cure early rheumatoid arthritis, then of course it is essential to be certain that this is the condition from which the patient is suffering; if lumbar manipulation can cure constipation, so too can several similar physical methods; if nervy people declare themselves able to relax and sleep after manipulative treatment, so can a number after a hot bath. Accounts of successful cases here and there are not always in themselves impressive, "for who will shoot all day without some times hitting the mark?" (Cicero).

THE FUTURE

To label osteopathy as refined quackery—which some medical men do not hesitate to do—is an unworthy insult; the osteopaths' premises may be false, but they are sincere men who feel that they have a mission to perform. They may perhaps be described as sentimentalists who, as Oscar Wilde remarked, see an absurd value in the worth of an idea. We have to remember that such vanities are not their sole prerogative, and medical vanities are by no means unknown if you look about.

Much of the osteopath's reputation with the public in this country is, we believe, reflected glory from a few skilled "bone-setters" or "manipulators" of the past—household names—who lived in the days when the management of bone and soft-tissue injuries was of poorer quality. It is not that the medical profession were ignorant of the possibilities of manipulation, but we were by no means insensible to its dangers. These bone-setters never preached or believed in osteopathy in its present wide, full meaning; but the public, ever craving for the miraculous or the unorthodox in medicine, has been unable to differentiate between their claims, and has thrust the mantle of honour on a similar resounding name.

In our view—and we do not claim to an extensive study of the subject—there is a limited field for this type of work, but it needs to be winnowed in the testing-ground, indeed battle-field, of the large modern hospital. Their claims seem to us extravagant; and it is right that doctors should only slowly weigh the scruples and reasons of any idea—that they continue to be chilled, unemotional people. Osteopaths, on the other hand, must fill themselves with the spirit of medicine, and be prepared to expose every cranny of their mind.

In no circumstances could the profession yield one step in its opposition to the non-medical osteopath. But we feel that medically qualified osteopaths should now be given opportunity to work and prove their case in orthopædic departments. They will find it an exhilarating, if somewhat trying, process, grinding their wits on the whetstones of others. Time will soon tell what ideas are "fit to be written but on air, or on the stream that swiftly flows."

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THE KING'S FUND

NEW WORK AND OPPORTUNITIES

In the course of his address when presiding over the general council of King Edward's Hospital Fund for London on Dec. 14 the Duke of Gloucester spoke on various aspects of the Fund's work:

Old People.—There are many people in hospitals, mostly over sixty years of age, who need not stay there but who do need some degree of nursing care and medical supervision. It is all but impossible to secure admission for these people to any other institution, but they are taking up beds which ought to be filled by the acute sick. The work of some of the religious orders, and of such voluntary bodies as Mrs. Hill's homes in Highgate, deserves every encouragement, and if other voluntary bodies will come into the field and run such homes the distribution committee will be glad to help them with substantial grants.

Convalescent Homes.—There are some 4000 beds in convalescent homes not included in the National Health Service, many of which need both advice and monetary help. The management committee are going to recommend that we should not only give £30,000 for ordinary grants next year, but also set aside a sum of £50,000 for special purposes.

Training for Ward Sisters.—We have this year undertaken to establish a staff college for ward sisters—i.e., a residential centre where would-be ward sisters can spend a term of some fifteen weeks. . . . The courses are to be directed to making the path of young sisters easier by instructing them in administration generally, in personnel management, and in teaching. These courses should greatly increase their efficiency and enable them to discharge their many duties more easily and smoothly with a saving of time and with less mental strain. We particularly want to stimulate and encourage sisters to take an active part in the practical teaching of their student nurses and to exercise a closer supervision over their work in the wards. We believe that if this can be done it will also check some of the wastage during training, because it will help to do away with the disappointment and frustration so many nurses feel when they are left to carry on as best they can without supervision and advice.

Hospital Catering.—We plan to establish at St. Pancras Hospital, now part of University College Hospital, a training centre for hospital catering. Since 1943 the Fund has been deeply interested in hospital catering and has, I think, been instrumental in effecting improvements. The old régime of one cooked meal a day is now a thing of the past. But the whole movement is held up, and is indeed in danger of slipping backwards, for lack of properly trained caterers and other personnel. We intend to have at St. Pancras a model kitchen, and room for various subsidiary and educational activities. And we intend, too, to continue to offer the advisory services on catering which have been a real help to so many hospitals.

Sir Edward Peacock said that the ordinary income for the year amounted to £257,000, and legacies received totalled £93,000. With the sum of £425,000 from the Nuffield Trust for the Special Areas, the total receipts amounted to £775,000, against £487,000 in the previous year. The year had been transitional, and disbursements totalled £166,000; but the Fund was already committed to further expenditure in various directions.

Sir Harold Wernher indicated that the Fund's activities will in future be conducted to a large extent on divisional lines. Each division will operate under a budget approved by the management committee. Thus, a division of hospital facilities has been created of which Captain J. E. Stone is director; a nursing division will be established, directed by Miss Muriel Edwards; and further divisions can be constituted as circumstances require.

As a result of these changes, the office of honorary secretary will disappear, and a warm tribute was paid by the Duke of Gloucester to the work done by the honorary secretaries since the establishment of the Fund, and particularly to the three now retiring, Sir Harold Wernher, Sir Ernest Pooley, and Sir Hugh Lett, F.R.C.S. Sir Ernest Pooley will succeed the late Lord Donoughmore as chairman of the management committee, which will be enlarged and will include Sir Wilson Jameson, F.R.C.P., chief medical officer of the Ministry of Health. Sir Archibald Gray, F.R.C.P., will become chairman of the distribution committee, and Sir Henry Tidy, F.R.C.P., will remain chairman of the convalescent homes committee. The chairmen of the four Metropolitan regional hospital boards—Mr. Fred Messer, Mr. J. W. Bowen, Mr. K. I. Julian, and Mr. F. H. Elliott—have been appointed to the council of the Fund.

CENTRAL HEALTH SERVICES COUNCIL

On the recommendation of the Central Health Services Council, which held its third meeting last week, the Minister of Health has decided to set up the following nine standing advisory committees:

Medical	Maternity and midwifery
Dental	Tuberculosis
Pharmaceutical	Mental health
Ophthalmic	Cancer and radiotherapy
Nursing	

These committees are to "advise the Minister and the Central Council upon such matters relating to the services with which the committees are concerned as they think fit and upon any questions referred to them by the Minister or Central Council relating to those services."

The Minister proposes that the medical, dental, pharmaceutical, and ophthalmic committees shall be professional in character, while the other committees will include lay members and will review the whole scope of the services in their particular field. It is hoped that all the committees will be constituted very shortly and that they will be able to start work in the New Year.

The Central Health Services Council has decided to set up committees of the council itself:

On *health centres*, "to consider and make recommendations on the lines along which health centres should be developed under section 21 of the National Health Service Act, 1946,"

on *hospital administration*, "to consider the administration and organisation of the hospital services under the National Health Service Act, 1946, and to make recommendations."

Both will include coöpted members. Pending the appointment of secretaries to the individual committees, communications should be sent to the secretary of the Central Health Services Council, Ministry of Health, Whitehall, London, S.W.1.

HALF A CENTURY IN TUBERCULOSIS

Societies whose titles contain the words "for the Prevention of" must look forward, like Azrael, to a millennium when their work will be done and they can acquiesce in their own extinction. The National Association for the Prevention of Tuberculosis has a better chance than most of fulfilling this honourable death wish, for much progress has been made during the first fifty years of its strenuous and successful life. It was founded in 1898, by King Edward VII, then Prince of Wales; and his successors as president have been King George V, King Edward VIII, the Duke of Kent, and the Duchess of Kent. At the time of its founding there were 36 million people in England, and some 70,000 died that year of tuberculosis. Today the population has risen to 48 million and the tuberculosis deaths are expected to be less than 27,000—still far too many, but only 0·6 per 1000 instead of 2·0. This has meant a saving of 1½ million lives in the fifty years, and N.A.P.T. has played its part in the reduction. It was active for ten years before the first tuberculosis clinic opened in England, and its job was to preach the value of open-air treatment and the preventive approach. In 1912 sanatorium treatment was made the legal right of every insured person, and in 1920 treatment and aftercare became the legal responsibility of the local health authorities. Throughout the years that led to these advances, and since, N.A.P.T. has encouraged and stimulated. It has seen the county tuberculosis schemes and the insurance committees come and go; and now the fiftieth anniversary number of the *N.A.P.T. Bulletin* can state the paradox that, under the National Health Act, voluntary work in tuberculosis has become statutory. What will become of this disease in the next fifty years? Even if the hope of effective antibiotics recedes, the association foresees great changes. If tuberculosis in the temperate zone ceases to be a major problem it will be free to give more attention to those regions of Asia and Africa which so greatly need it.

In England Now

A Running Commentary by Peripatetic Correspondents

My chief memory of early childhood is of waking up on Christmas morning and diving for the stocking at the foot of the bed. The first thing was to feel it over quickly, starting at the toe. Yes, there they were, the two round balls denoting an apple and an orange. Thus reassured I would palpate the rest at greater leisure. Of course it was never quite the same after the incautious entry of my father, stocking in hand, one Christmas Eve. But luckily nothing seems to shake my own children's belief in Father Christmas. Indeed it has been greatly strengthened by our new nanny, who encourages a brisk, if one-sided, correspondence with him. (At other seasons she promotes an equally lively correspondence with the fairies in our garden. She has even picked an answer out of the gooseberry bushes.)

Choosing presents is a ticklish job. For the two girls it is easy: we get what we think they should like, and then persuade them that these are what they thought of asking Father Christmas for. With my three-year-old son it is different. This year we got him a large engine, but when we got to work on him all he would say was "bus." No persuasion, and no tactful deferment of the topic, has moved him. In honeyed tones I came back to it when his mouth was full of a pudding he thinks rather well of; but he took time enough off to look up and spit "bus" at me. We even wrote "engine" in his personal letter to Santa Claus; but the boy didn't take the hint as he's more or less illiterate. So he's going to have an engine *and* a bus.

When it comes to presents between my missus and myself it is easier. You just think of the thing you yourself want most, and then give it with some casual word such as "I know you've always denied yourself this, dear." I happen to know that this year I am to receive a pressure cooker.

Just one more letter illustrating the perils of translation. This one comes from a former syce who sought re-engagement with the Artillery.

Sir,—Your humble petitioner is a poor man in agricultural behaviour and much depends on season for staff of life. Therefore he throws himself upon his families bended knees and begs of merciful commiseration. Your humble petitioner was too ill last rains and was taking vernacular medicines which made great excavations in coffers of your humble servant. That poor humble servant has large family of seven livers, two male and five females, last of whom is milking his parental mother and another birth coming through grace of God to second wife of bosom. Therefore he prays that if there is place ever so small in the backside of the honourable battery, this humble slave be allowed to creep in, for which benevolence your humble servant will as in duty bound ever pray for your long life and prosperity.

Walking back to my home one night I was attracted to a small crowd gathered round the railings surrounding a church. The cause of the trouble was a small boy who, playing within, had pushed his head out through the bars and was now unable to withdraw same. A well-meaning bespectacled gentleman was unsuccessfully applying pressure, but this was not at all appreciated by the subject, and a disreputable old woman was making unintelligible although obviously protesting noises. The man next tried manual rotation to disentangle the ears but this also proved ineffectual and only caused the old woman to cry "Ugh! Ugh! Arrh! Um! Arr! Hoch!" still more. Thereupon the man, emulating Samson at Gaza, wrenched laterally at the unyielding railings while pushing against the head with his stomach. At this point, as I turned my gaze once more on the weird female who had become more vocal and incoherent than ever, and the doctor in me was insisting that I must step in and do something, I was relieved to observe the approach of a policeman, for in the presence of the law my conscience allows me to maintain my anonymity in the face of street incidents and such.

Even the old lady and the small boy himself were silenced as the policeman broke through the circle. He advanced to the railings and, securing a foothold, jerked himself over, when he immediately lifted the child by the legs, rotated the shoulders into the vertical position, and simply thrust the body through the gap after the head. As the tear-begrimed urchin picked up his cap and scuttled off home the old lady's face was a picture; it expressed not relief or pleasure but unconcealed triumph. Though she could not make it clear in words, her face plainly indicated that she was saying "I told you so," and what fools we all were in ignoring her advice. I returned to my flat feeling I had received a valuable tutorial in obstetrics.

I keep these directions, taken from a New Zealand women's magazine, by me to browse on from time to time.

Here is your breathing exercise. It isn't necessary to stand before an open window to do it, but stand against a wall opposite an open window. Throw the shoulders back. Now cough breathily and press either hand on to the bottom of your lungs—you'll feel them coming to a point—make certain that they are emptied and the entire lung what is technically called collapsed, when it will seem to hang inside your ribs.

Then start to breathe in. Keep the shoulders back and down, but do not let them rise. Stiffen the muscle between the lower end of your lungs—the diaphragm. This will hold the lungs out like bags. Fill lungs from the bottom end, and when the top is full, empty them from the bottom end, still keeping the diaphragm stiff, so that they stay held out like bags. It is not easy to do. It is even very exhausting. But you will hear the blood sing in your ears, showing how circulation has buzzed up.

Breathe like this at least ten times.

"Ten times?" If I kept my lungs held out like bags even once I am afraid it would be a hymn tune that the blood would sing in my ears, and a funeral hymn at that.

"Spiv!" he cried, as my friend and I stopped at the crossroads on this lovely winter Saturday afternoon. I looked to see to whom the young man referred and alas! it was myself. My handsome friend probably had something to do with it, for our eleven years of hard-working companionship, during which we have journeyed 15,000 miles together every year, have hardly marked my faithful Bentley. But I doubt whether this young "sportsman," off on his weekend pleasures, would have thought himself a spiv if he had done my week's work.

On Monday I spent part of the day at a ministerial committee in London, but managed to get back nearly 200 miles in time for what should have been an after-dinner medical staff committee meeting. Two hours later, after coffee and sandwiches, I started work with my dictaphone, and I tumbled into bed well after midnight. On Tuesday from 9 o'clock I had ward rounds, then after 20 minutes for lunch there were outpatients until 5, followed by a hospital subcommittee for an hour and a half and the tail end of a staff conference for another hour. Three-quarters of an hour for dinner brought me to another medical staff committee followed by more writing and bed at 1 o'clock. On Wednesday I operated from 9 until 1.30, was fortunate in getting three-quarters of an hour for lunch, saw patients until 6, wrote letters until 7.30, and after dinner did o her work till midnight. On Thursday morning I operated until 12.45 and then had a fruitless interview with an income-tax inspector who has decided to charge me tax on the expenses paid out of my own pocket for a purely professional journey abroad. I had 15 minutes for lunch and the rest of the day was like Wednesday. On Friday I operated from 9 until 11.30 and did administrative chores until 12, when I started for the regional headquarters 80 miles away. After a four-hour committee I returned home for dinner at 8.30, and then motored 40 miles to the hospital in which I worked today. This

afternoon, when accosted, I was on my way to treat a doctor's ailing wife, and now at 6 o'clock I am back home at my desk to which I must bind myself until midnight if I am to satisfy my publishers who are clamouring for "copy." Tomorrow I shall be lazy and start work at 10, but before lunch I must see problem cases in the hospital and must visit another centre 16 miles away. The afternoon may be my own but the evening won't be.

"Spiv"—one who exists on other people's efforts? Well, perhaps I am. At two N.H.S. committees that I attended this week the minutes and relative documents occupied 155 sheets, mostly foolscap, of which no less than 44 were mimeographed on one side of the paper only. It's enough to give you a pain in the neck. Neck? Why, that's it. My neck *is* stiff and I suppose the exotic scarf I was wearing seemed as revealing to that young man as a notice saying SPIV on the windscreen.

> "Every woman by whom or on whose behalf a claim for maternity benefit is made shall furnish evidence that she has been, or that it is to be expected that she will be, confined by means of a certificate given in accordance with the rules set out in Part II of the said Schedule . . ."
> —*Statutory Instruments*, 1948, no. 1175, para. 2.

If this new method of midwifery is included in *The New Gynæcology*, to be issued by the Stationery Office, it would be wise to order your copy now. It sounds like a jolly easy way of earning your £4 14*s*. 6*d*.

Putting my house in order, to receive a locum the other day, I fell to musing on my own locum days. There was that ghastly early one, when I could scarcely drive a car. I arrived late at night, and the kindly doctor promised me a lesson before he went off to his camp in the morning. But at 5 A.M. a confinement call came from a distant village. He drove me there, muttering instructions; when we arrived it proved to be a primip., half full, dilating too slowly for him to stay and too fast for me to leave.

So he promised to have the car left ready for me and departed with a rather apprehensive blessing. After a long long period of inertia, the patient delivered herself at 2 P.M. Triumphant and exhausted, I emerged into the waiting car and pushed the starter button. Nothing happened for ten minutes, except that all the village boys gathered round; then I remembered to switch the engine on. After a perilous journey I got back for a shave and a meal, and then thought I'd better practise reversing in a nearby lane. I was doing fine when there was a bump and the car ceased to move. I'd reversed into a ditch, in which the back wheels were revolving freely; it took a crane to haul me out. After that my driving improved; the doctor's wife used to come out with me, and I could never understand why she clutched my arm every time we went round a corner.

Another memorable locum was in a heavenly village, for a queer bloke. Before departing he warned me against fraternising with his wealthier patients. He hadn't been gone two hours when the local squire's daughter dislocated her shoulder. I was lucky to get it back easily, and as her parents were disproportionately grateful I had a royal time with them. They were dears; both had been married before, and as they sat at each end of the table he would begin "My first wife used to say . . .", to which she would counter "Now *my* first . . ." in the most amicable fashion. In this practice, not 80 miles from London, I met an old coachman who still wore his long hair in a plait, neatly coiled round the top of his head.

Then there was that leisurely locum in the Middle Temple, where I cooked for myself and lived largely on boiled eggs and Bel Paese Cheese, and learned to love the grey old buildings, the plane trees, and the pigeons. And that suburb, where, on a first view of its drab streets and ugly houses, I swore I'd never live for gold untold. Well, I've been here 16 years now; either it wasn't as bad as I thought or my exquisite sensibility has been blunted. Perhaps a little of each.

This is the tale of DOCTOR GRIST,
Who trained as a Psychiatrist.
A meek and harmless man, he had
No urge to Cure the Almost Mad,
No flair for Certifying Earls
Or Tête-à-têtes with Nervous Girls:
Being quiet, cleanly and observant
He yearned to be a Civil Servant.
One day he spotted in the Press
A notice: "Motor Licenses
Require at Once, Psychiatrist,
(Grade A) With D.P.M.—Assist
Urgent Research—No Private Ties.
All Canvassing Disqualifies."
So ran the notice in the L****T
And DOCTOR GRIST resolved to chance it.

You've doubtless noted with a grin
A Bentley labelled B.I.N.
Or FUN inscribed upon a hearse,
And looked in vain for Something Worse.
Our subject, when he took the plunge,
Found that his Task was to Expunge
From Lists of Motor Registrations
The More Indecent Combinations.
He had a room in Birdcage Walk,
A table and a large blue chalk,
And day by day he scanned the list
For Dirty Words which had been Missed.
"We must be careful" said his Chief—
"The Unconscious Mind is Past Belief.
A motorist might well repine
To be inscribed BUM 99—
To stop such things from getting through,
We need a well-trained man like you."

He had not been at work a week
Before the colour left his cheek.
A fortnight saw him growing thinner—
He had no Appetite for Dinner.
Being a Conscientious Man
In every list he had to scan
He toiled and laboured to divine
Where Censorship should Draw the Line.
And Day by Day the Menace grew—
"Oh, what if I should Let One Through?
The simplest labourer would agree
We must dispense with * * *,
Now HOG and CAD are not obscene,
And yet—you gather what I mean?
The Thing's Impossible to Define:
Have Other People minds like mine?"
As week by week his weight declined
He wrestled with the Unconscious Mind:
He shunned companions, got no sleep—
The letters, like unruly sheep
Ran through his head in groups of three.
He said "What will Become of Me?"
He found he could no longer meet
The eyes of urchins in the street
And even Trivial Phrases bore
Meanings they Never Had Before.
He formed the idea that Men in Black
Were Chalking Things upon his Back,
Was ambushed out of Garden Gates
By Jesuit Priests on Roller Skates:
And when his Chief informed him: "You
Will note that as from '52
The letters will increase to FOUR,"
He bit a large piece from the door.

They fetched a new psychiatrist
Who soon obtained for DOCTOR GRIST
A plain van, marked appropriately
Before and after, M.A.D.

Moral

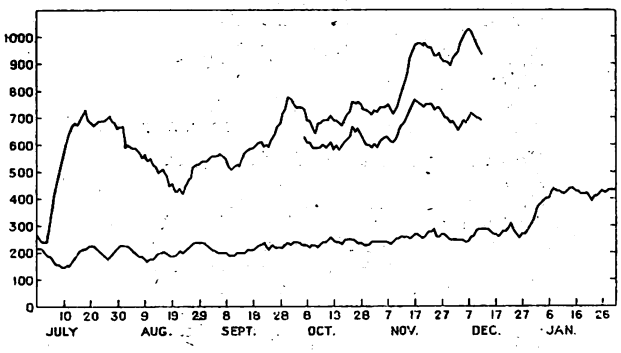
Learn from our hero's fate to shun
The Censorship of Harmless Fun.
Avoid the Habits of the Prude,
Don't live to hunt for What is Lewd
By Mrs. Grundy or by Freud,
Or you will End Up Paranoid.
But, if you're a psychiatrist,
Enjoy the Cracks the Censor Missed.

Letters to the Editor

NO ROOM AT THE HOSPITAL

SIR,—Having read last week's leading article, I think you may be interested in the accompanying chart of the work of the Emergency Bed Service.

The graph is made by plotting daily the total number of cases for the preceding seven days. (This is done



in order to smooth out the great variations which occur from day to day.) The top line shows the number of applications received for all cases other than infectious diseases. The middle line shows the actual admissions of such cases. The bottom line shows all applications (again excluding infectious diseases) in 1947. It will be observed that not only is the top line rising more steeply than in 1947, but that the applications are about three times as numerous. While the applications are still rising, the admissions remain at about 700. By the time just over 100 cases have been admitted on any day the hospitals can take no more. If, therefore, the applications rise steeply after Christmas, as is to be expected from the trend of the graph last January, a very serious situation will arise.

The use of the Emergency Bed Service by doctors is purely optional; there is nothing to prevent a direct approach to the hospitals. In this respect the service was unaffected by the appointed day. Why then did the number of applications increase so greatly on July 5? There can be no definite and simple answer to this question, but it seems probable that many hospitals decided that after the appointed day they would treat their nurses fairly and stop overcrowding. It is difficult to quarrel with this attitude, but the net result is a reduction in the number of patients who can be admitted to hospital and in consequence a reduction in our power to assist doctors. The cases now refused admission are mainly those which are, or might become, chronic, and which need urgent admission owing to an exacerbation of their condition; but already difficulties have arisen in other directions, notably babies requiring medical treatment. It must be borne in mind that not all the patients whom the service failed to admit should have been admitted. About 10% of all applications are unsuitable for admission, either because they can be sent to outpatient departments or nursed at home, or because they belong to categories which the service does not deal with—e.g., mental.

The task of the Emergency Bed Service is to admit patients to such beds as are available: it cannot create vacant beds. In consequence, however hard we try, our power to assist doctors is limited by circumstances over which we have no control. The service does its utmost to find beds for urgent cases, and will continue to do so; but doctors will greatly help if they will, whenever possible, make use of all the domiciliary services provided by the local health authorities or voluntary bodies, so that the patient may stay at home instead of going into hospital.

Emergency Bed Service, 10, Old Jewry, London, E.C.2. R. E. PEERS Secretary.

SIR,—Your thoughtful leader on this urgent subject made me wonder whether there was any remedy for the immediate danger other than those you mention: I doubt if there is. Jeremiads on the shortage of beds and of nurses are of little avail—it will not be possible to build large hospital extensions for many years, and, as was shown in a recent debate in the House of Lords, never has the number of nurses available been so large.

There is, however, a long-term policy which could, if energetically carried out, go a long way towards preventing a recurrence of the present difficulty, especially for elderly patients. Pioneer work carried out at a small number of large hospitals has shown that 45% or more of the so-called chronically sick, the majority of whom are elderly, can be so remedied as to be able either to return to their own home or to be admitted into a communal home: by energetic treatment one large hospital has been able during the past twelve years to reduce the number of beds required for its chronic sick from 700 to something over 200. If this enlightened policy were to spread over the whole country a large proportion of the present shortage of beds would disappear.

The provision of communal homes for elderly persons who are unable to return to their own homes, but who no longer need costly hospital treatment, is an urgent necessity: until they exist, in large numbers, in association with the general hospitals, the general freeing of hospital beds cannot occur. But this provision is now the duty of the local authority under the National Assistance Act, and the presence of a dangerous administrative gap between the regional hospital boards and the local authorities is already making itself felt: as you have pointed out, Sir, the margin between health and ill health in the elderly is narrow. The establishment of statutory committees comprising members of the boards, local authorities, and voluntary bodies would enable homes to be set up in close association with the hospitals, and this would lead to a great number of beds being freed for the sick, both young and old.

London, S.W.3. AMULREE.

THE UNIVERSITIES AND THE HEALTH SERVICE

SIR,—The payment of consultants for hospital work, and the disappearance of much of the competitive gamble of private consultant practice, combine to endanger the future usefulness of academic clinical posts.

It is well to remember that whole-time chairs and lectureships in the clinical field were rarities twenty-five years ago. Such posts were created in the hope of encouraging those who wished to escape from the hectic scramble of consultant work to devote time, thought, and experiment to clinical problems. Whatever hopes for the future progress of medicine the creation of such posts may have raised or indeed fulfilled, the prospects now are gloomy. Recruitment to junior posts is at the moment easy for the universities, which have a vast pool of "medical under-employed" to draw upon. The price they have to pay is low. This position will soon change. Hitherto the tendency has been to appoint from a plethora of candidates those with the most distinguished record of original research. This policy has caused a gulf to open between the academic and the vocational sides of medicine which I venture to suggest will grow wider and will not, as long as academic clinical departments are responsible for undergraduate teaching, be good for the growth of medicine in this country. The first two dangers are, therefore, both a quantitative and a qualitative failure of recruitment to clinical university posts.

The third danger, mentioned by Prof. Dible, in his article of Nov. 27, was some months ago thrown into dramatic relief by a B.B.C. broadcast in the "Professional Portrait" series. This danger is that professors will be swamped by administrative work.

The fourth danger is imminent. Because of the low salaries junior academic appointments will come to be looked upon as stepping-stones to consultant posts, which today have many financial attractions, and the possibility of just as much leisure for thought and research as is now given to the clinician or pathologist employed by a university. If this fear is justified by events, professors will have to cope with a stream of ever-changing juniors. This cannot be good for the morale of any department.

There seem to be two alternatives for the future. The first is to abandon the present system of whole-time university clinical appointments, and to revert,

for the purposes of undergraduate teaching to the old type of university chair, with, in parallel, an independent department of clinical research, which would be fed from the teaching hospital but lie outside its main structure, except in the sphere of postgraduate education. The second alternative is to set our present house in order by the following measures:

1. Let the regional interests of the universities be cared for by a medical administrator instructed by the faculty, and let academic workers be discouraged from committee work concerned with regional responsibilities.

2. Allow the clinical work of university staffs to be concentrated at one or other end of the week, so that whole days may be set aside for research. This is very important since those engaged in clinical work never know the freedom of vacations in which to pursue their own studies.

3. Raise the salaries of academic hospital workers by allowing them to enter into contracts with their hospital boards for such clinical sessions as they normally hold. Such a provision would tend to attract and keep the best, thus maintaining continuity in clinical departments.

Among the many controversial issues already raised in this letter I expect that those under (3) above are liable to most criticism. Why should the clinicians be paid more than other university workers? The arguments in favour of such a course should be appraised from two angles. First, would they be paid more? Workers in other faculties often have sources of income beyond their official salaries, for in practice no objection is raised to university employees offering advice or services to firms and Government departments and to their being paid for such services. Broadcasting and writing bring income to the more senior members of other faculties, and a widespread coaching system helps the junior members. Time for such extramural activity is provided by the long vacations, free from the burden of teaching and such routine work as is the daily responsibility of clinicians. Secondly, the clinician employed by a university who does, if anything, more teaching in a year than workers in other faculties, is surely entitled to payment for work done on behalf of the National Health Service. Since he must do clinical work to maintain his proficiency as teacher and research-worker, such duties cannot be considered as contrary to the interests of the university which employs him. The principle of payment for work done has been completely accepted in the National Health Service Act; so there should be no difficulty from that quarter.

I am well aware that many of these controversial questions must now be under consideration by those responsible for policy; but I hope, Sir, that you will agree that the expression of every point of view is desirable.

Department of Medicine, Bristol University. J. NAISH.

A NEW TYPE OF READING-LENS

SIR,—It is well known that many people of advanced age experience difficulty in reading small print, even when equipped with reading-glasses otherwise suited to the refraction of their eyes, as has happened to me on becoming old.

On consulting eye specialists to fill this want I was told that reading-glasses which could remedy this were not obtainable. About $1^1/_2$ years ago I tried to get over this difficulty for myself by fixing a lens ($6^1/_2$ dioptres), connected with a head-band, about 30 cm. from the eye. Since then Messrs. Simonsen and Weel, of Copenhagen, have constructed for me a satisfactory reading-lens, which they describe as follows:

> "Reading-lens mounted on a specially constructed support (fine wire stand) which is fixed to a head-band. It differs in particular from other reading lenses or magnifying glasses in that this model can be fixed on the forehead a suitable distance from the eyes, leaving both hands free during reading."

An additional advantage is that it is unnecessary to remove the band from the head if one is moving around or looking for something else in the room. Further, the lens is fixed so far from mouth and nose that it cannot become dimmed by breathing. With this lens it is possible to read for many hours at a stretch without getting tired. I also believe it may save old people from having frequently to change their reading-glasses for others of increased strength, but one should consult an eye specialist when adopting this model.

I want to improve the device by having the lens shaped wider and oval. The one I have is circular, 6 cm. in diameter. To obtain a wider field of vision it would have been better to make the lens 8 cm. wide and, in view of the weight, to reduce its height. I also recommend the use of a more powerful lens. I believe one of 8–10 dioptres would be best. The firm over here has ordered such a lens from a factory in England but has been told that for the present delivery is impossible, owing to lack of manpower. It is hoped that this will be remedied.

This type of lens will be useful not only to people who have difficulty in reading but also to people who handle small delicate objects (botanists, zoologists, watchmakers, &c.), since it will leave their hands free for working.

Kongens Lyngby, Denmark. JOHAN LEMCHE.

PATHOGENESIS OF THE ACUTE EXANTHEMS

SIR,—Dr. Fenner's article of Dec. 11 records an admirable piece of work and an important addition to our factual knowledge. His conclusions with regard to the allergic nature of exanthematous skin eruptions, however, betray a confusion too dangerous to go uncontradicted.

Whether we adhere to von Pirquet's original and cautious definition of allergy as a state of altered reactivity (*veränderte Reaktionsfähigkeit*) or accept Rich's more circumscribed concept of an intracellular antigen-antibody reaction, the evidence brought forward by Fenner serves in no way to weaken the case for the allergic nature of the exanthematous rash.

On the 7th day after inoculation Fenner noticed the first clinical change at the primary site, which he describes as œdema. On the other hand, in the skin remote from the point of inoculation, a maculopapular rash appeared 3 days after the first appearance in it of the virus. This different behaviour both in time-relation and in the nature of the lesion means that either the skin or the virus must have changed in their reactivity. Since the latter possibility is easily excluded (by transmission) the explanation is apparently an altered reactivity of the skin.

He found virus in the blood-stream on the 4th day, but in the skin not until the 6th day after inoculation. This also argues an alteration in the reactivity of the skin, enabling it to fix circulating virus.

Fenner obtained evidence of skin sensitisation to the virus on and after the 7th day. He has demonstrated the presence of large amounts of virus in the skin. And yet he concludes that the eruption on the 9th day—i.e., in a sensitised organ and in the presence of the sensitising agent—is not an allergic phenomenon. Perhaps the presence of virus in the skin lesions accounts for this confusion, Dr. Fenner having apparently transferred the concepts of bacterial allergy into the field of virus diseases without making the adjustments necessitated by the differences which separate most viruses from most bacteria.

It may be taken as axiomatic that antigen must be present for the initiation of acquired antibody formation. Many bacteria liberate diffusible substances which act as antigens; so both circulating and fixed antibodies can be formed in tissues remote from the invading

bacterium. Viruses do not liberate diffusible antigens but are themselves antigens, and their actual presence in the tissue is therefore a conditio sine qua non of antibody formation. To see in their presence in any lesion an argument against the allergic nature of that lesion is to ignore this fundamental fact. Even in bacterial diseases the presence of the causal organism in a lesion is in itself no criterion for or against the allergic nature of that lesion (e.g., leprosy). We can however postulate that in virus infection an allergic state cannot arise without the actual presence of the virus in the tissue concerned. The factual findings of Fenner are in accordance with this view.

It is significant that in Fenner's chart the curve for antibody titre shows in its ascending limb a close correspondence in time with the curve for the virus content of the skin. The interpretation of this would seem to be that in exanthemata the skin is a most important organ of immunity. The presence of virus in it induces the formation of antibody both free and fixed, so a state of rising immunity and allergy coexist. The latter enables the skin to filter off circulating virus and to fix it. The allergic reaction destroys the skin, which is shed and replaced by fresh epidermis. This is an example of an allergic reaction which, although detrimental to the affected organ, is of value to the organism as a whole. Coexistence of allergy and immunity is of course a well-known phenomenon, especially in tuberculosis.

This concept of the skin as the most active organ of defence in exanthemata and of the eruption as the allergic stage in this defence action is in agreement with the experience of physicians of all ages who have seen in a florid rash a good prognosticon, and have looked with anxiety upon cases in which the typical eruption was tardy to appear. Conversely we may see in the purpuric forms of the exanthemata conditions in which the skin fails to get beyond the allergic state, with a correspondingly grave prognosis.

Dr. Fenner says that "the symptoms and signs develop only when multiplication of the virus has almost reached a maximum." Possibly it would be more correct to say that the multiplication of the virus is halted soon after signs and symptoms appear because these signs and symptoms are the allergic expression of developing immunity. The idea that the lesions of infective diseases are simply due to the multiplication of the infecting organism is as moribund as the unfortunates to whom it applies. It is our reaction to the presence of the organism, not their presence itself, which is responsible for the signs and symptoms. Fenner has demonstrated that the skin lesions of mousepox contain virus; he has not demonstrated the nature of the reactions responsible for these lesions.

Usher Institute, University of Edinburgh. ERICH GEIRINGER.

INDEPENDENCE IN RESEARCH

SIR,—In his letter of Dec. 11 Dr. Waddington disagrees with my criticism of the Russian scientist, Lysenko. My objection was chiefly to the political control exercised by the Kremlin on scientific research in Soviet Russia. It is curious how closely Russia has copied the Nazi model. Early in the Hitler régime very similar activities to those of Moscow became apparent. I append some authentic statements bearing this out:

The leader of the Reich doctors, at a congress in Nuremberg in 1935, declared: "If we intend to establish a new medical science today the basis of this science can never be pure science but only our National Socialist philosophy of living." In 1934: "It is the task of our National Socialist welfare doctors to help enlighten the whole nation so that it learns to think racially, sociologically and politically." And again: "There is no room among the panel doctors for politically unreliable elements."

"The new medical curriculum comes into force on April 1, 1939. It introduces a curtailment of the medical course by nearly two years."

In an address at Heidelberg University in 1938, a professor said: "There is no such thing as international science; there is only German science, and German science can be created only by Germans."

It so happens that a report has been published (*Listener*, Dec. 9) of four broadcasts in a recent symposium on Lysenko's activities. Three of the four scientists (all fellows of the Royal Society) taking part expressed the most devastating condemnation of Lysenko as a scientist. The fourth speaker, Prof. J. B. S. Haldane, is a professed Communist. His defence of Lysenko is clearly an embarrassment to him, and his contribution might well be characterised as damning with faint praise.

House of Commons. E. GRAHAM-LITTLE.

CONTRACEPTION IN GERMANY

SIR,—Legally the present position in Germany is as Dr. Sandler outlined it on Dec. 4, but in practice there is little doubt that efforts by the German public-health authorities to establish birth-control and marriage-guidance clinics would receive sympathetic consideration from the authorities.

This organisation, set up as the result of the International Congress on Population and World Resources in Relation to the Family—which was attended by a German delegation—is maintaining contact with German doctors who are anxious to resume family planning work, and it is hoped that clinics will be opened before very long as part of the fight against illegal abortion and the sale of inferior contraceptives, so prevalent in Germany today.

Family Planning Association, 69, Eccleston Square, London, S.W.1 HELEN DONINGTON International Secretary.

Parliament

QUESTION TIME

Cost of N.H.S.

Colonel M. STODDART-SCOTT asked the Minister what moneys have been paid out of public funds since July 5, 1948, in respect of hospital services, general medical services, pharmaceutical services, general dental services, and ophthalmic services; and approximately what proportions these sums represent of the total liability incurred.—Mr. BEVAN replied: The total amounts paid out of public funds since July 5, 1948, and up to Nov. 30, 1948, are as follow:

	£
Hospital services	58,000,000
General medical services	7,982,994
Pharmaceutical services	5,438,709
General dental services	5,541,658
Ophthalmic services	4,047,568

The total liability incurred in that period cannot be stated.

Sir HUGH LUCAS-TOOTH asked the Minister what sums had been paid out of public funds in respect of hospital services under the National Health scheme.—Mr. BEVAN replied: Up to Nov. 30 a total of £58,000,000 had been paid by my department in respect of hospital services in England and Wales since July 5 last. Sir H. LUCAS-TOOTH: Will the Minister say how that compares with the estimate and whether it represents the total liability, or whether further sums have to be paid in respect of liability already incurred?—Mr. BEVAN: No, Sir, because it is not possible at the moment to carve up the estimates. Very many of these demands are still being examined.

Doctors' Pay

Sir ERNEST GRAHAM-LITTLE asked the Minister if he was aware that under the present statutory limitations a medical practitioner's income could not exceed £3600 per annum gross, whereas that of a dental practitioner could reach £4800 per annum gross; and if, in view of the fact that the period of professional training for the qualifying diploma in medicine was 57 months, while the period of training for the dental qualifying diploma was 48 months, he would review the position, which was causing dissatisfaction amongst medical practitioners.—Mr. BEVAN replied: I cannot accept many of the implications in this question, but I am about to review the present scale of dental fees in consultation with the profession.

Sir WAVELL WAKEFIELD asked the Minister if he was now in a position to state the amount of capitation fee doctors are receiving from their patients.—Mr. BEVAN replied: There is a fund of 18*s.* multiplied by 95% of the civil population. From this an agreed deduction is made for mileage payments, making the distributable fund about 17*s.* 5*d.* multiplied by 95% of the civil population. The actual payment per person on a doctor's list in any particular Executive Council's area varies with the proportion of the population who are on the lists of that area. I shall not be able to say until after the end of the financial year what was the actual rate payable in each executive council's area. Sir. W. WAKEFIELD: Is the Minister aware that doctors were expecting that the capitation fee would be 18*s.* without deductions, and that in certain areas as much as 2*s.* or 2*s.* 6*d.* may be deducted from the 18*s.*? Could he put that right?—Mr. BEVAN: The representatives of the British Medical Association never expected that the capitation rate would not be less than 18*s.*; they knew that there would be certain agreed deductions from it. Sir W. WAKEFIELD: Whatever the Minister may say, the fact remains that the majority of doctors throughout the country are suffering under this misapprehension.

Colonel STODDART-SCOTT: Was not the amount of money available for the doctors agreed to when it was thought that 18,000 practitioners would come into the scheme? Now that 19,000 have come into the scheme, should not a larger amount of money be available?—Mr. BEVAN: The information of the hon. and gallant Member is incorrect. The doctors are quite adequately represented at the moment, and discussions are taking place between my Ministry and the representatives of the medical profession. Perhaps hon. Members would await the result of those discussions before organising a single pressure lobby.

Prescriptions for Private Patients

Sir W. WAKEFIELD asked the Minister if he would indicate the administrative difficulties which prevent the disallowing of prescriptions prescribed at the public expense but not conforming to required conditions by doctors in the State service, for private patients, while similar prescriptions by the same doctors for State patients can be disallowed.—Mr. BEVAN replied: A doctor in the service, who prescribes for patients treated under the service, substances which are afterwards found not to be drugs or not to be necessary for the proper treatment of the patient, is subject to the disciplinary procedure provided in the regulations. The regulations do not, however, apply to private patients, for whom there is no prescribing at the public expense. Sir W. WAKEFIELD: Is it not clear, therefore, that what the Minister is now doing is to deprive private patients of the right to go to doctors, even though they be in the State service, by disallowing them the right to have pharmaceutical services?—Mr. BEVAN: I am not prepared to allow public money to be spent on any form of activity where we shall not have the power to correct abuses.

Medical Partnerships

Mr. V. J. COLLINS asked the Minister whether he proposed to accept the recommendations of the Legal Committee on Medical Partnerships.—Mr. BEVAN: Yes, Sir, and so far as legislation is required proposals will be made in the forthcoming Bill to amend the National Health Service Act. Mr. COLLINS: Can the Minister give any indication when he hopes to introduce the amending legislation?—Mr. BEVAN: I cannot at the moment, but I hope there will not be very much delay.

Regional Hospital Boards Estimates

Colonel STODDART-SCOTT asked the Minister what estimates he had received from regional hospital boards for the financial year 1949–50; and the total of these estimates. Mr. BEVAN: All regional hospital boards have submitted estimates for the financial year 1949–50. The total gross expenditure shown in the estimates as received is £157,680,000, of which £10,236,000 represents capital expenditure. Income is given as £9,021,000.

Repair of Dentures

Lieut.-Colonel MARCUS LIPTON asked the Minister whether he would authorise the direct use by the public, under the National Health Service; of the facilities afforded by denture repair undertakings.—Mr. BEVAN replied: No. The National Health Service Act provides that dental services under the Act shall be given by registered dental practitioners.

Prescriptions

Mr. M. L. ASTOR asked the Minister what information he had concerning the abuse of medical prescriptions under the National Health Service.—Mr. BEVAN replied: There are a number of individual cases. Disciplinary procedure is there to deal with them and I want it firmly and promptly used. But I am not aware of any general abuse.

Hospital Staff Committees

Mr. E. A. HARDY asked the Minister how many joint consultative staffs committees have been appointed by the hospital management committees under the control of the Manchester and Liverpool Regional Hospital Boards.—Mr. BEVAN replied: Three: one in the Liverpool regional hospital board area and two in the Manchester area.

Registration of Births

Mr. E. FLETCHER asked the Minister what instructions he proposed to issue as to the entries to be made in registering births resulting from human artificial insemination A.I.D.—Mr. BEVAN replied: No fresh instructions are necessary. Registrars already have instructions to ask every birth informant for the name of the child's father; if the informant cannot give this information the columns of the birth entry containing particulars of the father are to be left blank. Mr. WILSON HARRIS: Has that any bearing on the question of the legitimacy of the child?—Mr. BEVAN: None as far as I understand.

Physiotherapy in the Home

Sir ERNEST GRAHAM-LITTLE asked the Minister of Health whether he was aware that there was no provision for radiotherapeutic treatment under the new health services for insured persons who were bedridden at home and could not go to hospital; and whether he would remedy this omission.—Mr. BEVAN replied: I am advised that the limited physiotherapy facilities and staff at present available can be used to most advantage at hospitals and clinics. Regional hospital boards are, however, authorised to arrange exceptionally for home treatment.

Board Meetings of Teaching Hospitals

Mr. SOMERVILLE HASTINGS asked the Minister whether, in view of the increasing public interest in the health services, he would consider the admission of the press to the meetings of the boards of governors of teaching hospitals.—Mr. BEVAN replied: While I hope that boards of governors will take every opportunity of keeping the closest contact with public opinion, the admission of the press to their meetings is a matter for their own decision.

Agene in Flour

Mr. J. A. BOYD-CARPENTER asked the Minister of Food whether nitrogen trichloride was still being used in the manufacture of wheat flour.—Mr. JOHN STRACHEY replied: Yes, Sir. A scientific committee including Sir Edward Mellanby and Sir Wilson Jameson are reviewing its use and I shall of course be guided by their conclusions. Mr. BOYD-CARPENTER: Can the Minister say how long the deliberations of this committee have taken? Is he aware that there is increasing evidence from America of the dangerous nature of this drug?—Mr. STRACHEY: I cannot give the date when this committee will be in a position to report. As I understand it, the most recent work on this question was done by Sir Edward Mellanby in this country.

Industrial Diseases

Mr. J. F. F. PLATTS-MILLS asked the Minister of National Insurance whether he had considered the evidence given before the Departmental Committee on Industrial Diseases by the Trades-Union Congress, Mr. O. H. Parsons, solicitor, Prof. J. M. Mackintosh, F.R.C.P., and Dr. Donald Hunter, F.R.C.P., recommending that benefit under the National Insurance (Industrial Injuries) Act, 1946, should be payable in respect of every disease which the applicant could show was caused by his work; and if he would accept and act upon this recommendation.—Mr. TOM STEELE replied: The committee held these suggestions to be outside their terms of reference and therefore made no recommendation on them. The suggestions, which are by no means new, raise wide issues which cannot be properly assessed until we have had a good deal more experience of the working of the new scheme.

Mr. PLATTS-MILLS asked the Minister whether he accepted the recommendation in paragraph 36 of the report of the Departmental Committee on Industrial Diseases which proposed that the time-limit for the operation of a presumption should bear closer relation to the nature of the particular disease than it did under the Workmen's Compensation Acts.—Mr. STEELE replied: The regulations already provide more favourable time-limits for presumptions than did the Workmen's Compensation Acts, and the Minister will be watching their operation to see whether, in the light of the recommendations mentioned, any modification is necessary.

Cost of Disability Pensions

Mr. E. A. A. SHACKLETON asked the Minister of Pensions what was the total amount paid by his department inclusive of all allowances to pensioners whose disabilities were assessed at 100% in the years ended March 31, 1939, and March 31, 1948, respectively; and what was the average weekly payment in each year per pensioner assessed at the 100% rate.—Mr. H. A. MARQUAND replied: For year ending March, 1939, a total of £3,372,400 and an average of £2 7*s*. 10*d*. per week. For year ending March, 1948, a total of £10,305,300 and an average of £3 17*s*. 3*d*. per week.

Status of Legitimacy

Mrs. LEAH MANNING asked the Attorney-General if he would introduce legislation to establish the status of legitimacy of all infants born in wedlock, where both parents were cohabiting at the time of conception.—Sir HARTLEY SHAWCROSS, the Attorney-General replied: There is a legal presumption that children born in wedlock are legitimate. Difficult questions have arisen in regard to the legitimacy of a child born during wedlock in a case in which cohabitation existed at the time of conception but did not take place after the marriage. Further difficult questions have arisen where a child is conceived either by means of artificial insemination or in spite of the fact that there has been no complete intercourse. Such cases are very exceptional, and my noble friend doubts whether special legislation is desirable, but the matter is being kept under review.

Public Health

Food-poisoning

A DISCUSSION on food-poisoning was held on Dec. 6 by the section of epidemiology and State medicine of the Royal Society of Medicine. Dr. E. T. Conybeare said that the increase in the number of food-poisoning outbreaks, which began about 1942, was due largely to increased consciousness of the importance of even mild or missed cases in causing spread, and also to better laboratory facilities; but there was reason to believe that there had been an actual increase through greater use of prepared foods and storage of food in the home. It was uncertain whether further progress could be expected from fresh legislation, which would apply mostly to the control of large-scale food manufacture and catering. In relation to personal hygiene and to the smaller units engaged in food distribution, legal powers—such as those under the Food and Drugs Act, 1938—though useful, were less effective. It might well be that education in personal and domestic hygiene, as foreseen by Ballard sixty years ago, was the only real precaution.

Dr. V. D. Allison said that among the factors in the war-time increase of food-poisoning were the use of synthetic cream and of cooked meats, including sausages; shortages of hot water, soap, towels, and crockery (which too often was cracked); and the employment of insufficiently trained kitchen staffs. Contamination with staphylococci was a not uncommon cause of food-poisoning, characterised by a short incubation period (1–7 hours), and an acute onset with abdominal pain, nausea, vomiting, and often diarrhœa, lasting from 3 to 24 hours, followed by rapid recovery even from collapse symptoms. Recent surveys had shown that 50% of normal adults harboured such organisms in the nose, and in some 10–20% they were present on the skin of the hand. The accepted criterion of actual or potential pathogenicity among staphylococci was their ability to produce plasma coagulase. The organisms could be identified by serological and bacteriophage techniques, but these methods were not yet applicable to routine laboratory and epidemiological investigation. For proof of pathogenicity human volunteers and skilled observers were still necessary. When the organism had been destroyed by cooking or processing (leaving intact the toxin, which resisted boiling for even 30 minutes) the difficulties were great; the kitten test for enterotoxin was no longer accepted, and often the evidence was only circumstantial.

The Ministry of Health's memorandum (no. 221) on safeguards to be adopted in day-to-day administration of water undertakings has been revised, and is obtainable price 2*d*., from H.M. Stationery Office.

Obituary

FRANK BETT PARSONS

M.A., M.D. CAMB., F.R.C.P.

Dr. F. B. Parsons, physician to Addenbrooke's Hospital, Cambridge, and Papworth Village Settlement, died in London on Dec. 4 at the age of 46.

The son of Stephen Parsons, of Chatteris in Cambridgeshire, he was educated at Wellingborough and at Downing College, Cambridge, where he graduated as B.A. in 1923. After working at St. Bartholomew's Hospital he qualified in 1925, and held resident appointments at Barts and at the Maida Vale Hospital, and a clinical assistantship at the National Hospital, Queen Square. He then spent a year in a Guildford practice, before settling in Cambridge. To begin with he was in general practice, but he was also for several years anæsthetist to Addenbrooke's Hospital. He became a fellow of the Association of Anæsthetists, and many of his earlier writings dealt with his work in this specialty—particularly early developments in the use of bromethol.

After some years Parsons decided to restrict himself to consultant work, and he became a living testimony to the need to leave open the path between general and consultant practice. In 1937 he was appointed physician to Addenbrooke's Hospital, and in 1940 he was elected F.R.C.P. One of his special interests was medicolegal problems, and his advice was often sought by colleagues who found themselves on delicate ground. For many years he wrote little, but he showed many cases of great interest at clinical meetings of the Cambridge Medical Society and the Allbutt Club. At the time of his death he had lately been reappointed liaison officer between the University and Addenbrooke's.

"Frank Parsons was born in the heart of the fens and spent most of his life there or in Cambridge. Because of this," writes L. B. C., "he had an inside knowledge of the people among whom he worked. His ability as a physician, backed by his pleasant but shrewd personality, knowledge of local people, and, from personal experience, awareness of what the practitioner wanted, made his opinion widely sought. A big man, in demeanour he was grave and courteous, but a good joke would light up a delightful twinkle. His words tended to be few but were very much to the point, and he had a knack of explaining things in simple language to his patients and putting them at their ease. His whole bearing inspired confidence, and his patients knew that he had their interests at heart and would do all he could for them. Perhaps his most outstanding attribute was a shrewd and sturdy individualism. Jealous of the interests and confidence of his patients, he regarded with dislike and suspicion anything which might intrude on the relationship between patient and doctor. Bureaucracy he detested.

"As a patient he showed great courage. The day before he left Cambridge he discussed with me his symptoms and the results of investigations on himself dispassionately and with the greatest calm, although he had no illusions as to the odds against him. For twelve years he was my colleague at Addenbrooke's, and although we often disagreed I can never remember any friction between us. I came to rely on him in many ways and his support was always kindly and freely given. With many others, I shall miss him more than I can say."

In 1927 Dr. Parsons married Miss E. W. Sabberton, and they had a son and a daughter.

Diary of the Week

DEC. 26 TO JAN. 1

Tuesday, 28th

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

Thursday, 30th

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. Brian Russell: Affections of the Lips and Mucous Membranes.

Friday, 31st

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, W.9
5 P.M. Dr. H. E. Hobbs: Case demonstration.

Appointments

ARNOTT, STANLEY, C.B., C.B.E., D.S.O., M.D. Edin.: medical superintendent, Scottish Borders group of hospitals.
COLLINS, F. M., M.A., M.B., M.CHIR. Camb., F.R.C.S.: deputy chief M.O., Ministry of National Insurance.
GEE, A. C., M.R.C.S., D.P.H.: asst. county M.O., Suffolk, and M.O.H., Lowestoft.
LEWIS, J. B. S., M.A., M.D. Camb., D.P.M.: physician, Bethlem Royal Hospital.
RIGBY, J. P. V., M.A., B.M. Oxfd: chest physician, Deptford area, London.
WILLIAMS, H. G., M.R.C.S., D.P.M., D.P.H.: psychiatrist, London County Council.

Northamptonshire County Council:

District M.O.H. and asst. county M.O.H.:
AITCHISON, WILLIAM, M.C., M.B. Edin., D.P.H., D.T.M. & H.
BERMINGHAM, P. X., M.B. N.U.I., D.P.H.
LUCAS, ARTHUR, L.R.C.P.E., D.P.H.

Asst. county M.O.H.:
ROBINSON, MARGARET, M.D. Belf., D.P.H.

Births, Marriages, and Deaths

BIRTHS

BAGGLEY.—On Dec. 9, at Richmond, Surrey, the wife of Dr. Charles Baggley—a son.
BEADEL.—On Dec. 14, in London, the wife of Dr. Stebbing Beadel—a son.
HARVEY.—On Dec. 8, at Hove, the wife of Dr. N. W. A. Harvey—twin sons.
HOWELLS.—On Dec. 10, at Swansea, the wife of Dr. W. V. Howells—a daughter.
ILES.—On Dec. 8, the wife of Dr. J. D. H. Iles—a son.
MACKEITH.—On Dec. 13, in London, the wife of Dr. R. C. MacKeith—a daughter.
MILLER.—On Dec. 11, at Cressage, Salop, the wife of Dr. H. C. Miller—a son.
TAYLOR.—On Dec. 12, in London, the wife of Dr. J. H. Taylor—a daughter.

MARRIAGES

STOWERS—ALABASTER.—On Dec. 10, at Haslemere, Surrey, John M. Stowers, M.R.C.P., to Mary Alabaster, M.B.

DEATHS

ALFORD.—On Nov. 11, at Weston-super-Mare, Herbert Thomas Marmaduke Alford, M.R.C.S., aged 75.
BURGES.—On Dec. 13, at Stoke Bishop, Bristol, Richard Burges, M.R.C.S.
COLE.—On Dec. 9, at Seaford, Sussex, George Cole, M.R.C.S.
DICKSON.—On Dec. 11, Jack Edgar Dickson, M.B. Lond., D.P.H.
GREEN.—On Dec. 13, at Lakenheath, Suffolk, Hugh Frederick Green, M.B. Edin., aged 80.
JONES.—On Dec. 15, William James Bennett Jones, M.D. Edin.
MILSOME.—On Dec. 9, at Chertsey, Surrey, Harry Blunt Milsome, M.A., M.B. Camb., aged 78.
OLIPHANT.—On Dec. 11, at Bothenhampton, Bridport, Dorset, Frank Binfield Oliphant, M.B. Edin., aged 77.
PHILLIPS.—On Dec. 14, at Port Talbot, Evan William Monger Hubert Phillips, M.A., D.M., CH.M. Oxfd, F.R.C.S.E.
ROBERTSON.—On Dec. 14, at Oxford, William John Robertson, M.R.C.S., aged 85.
SMALLEY.—On Dec. 11, at Kingsbridge, Devon, James Smalley, M.B. Manc., D.T.M.

Notes and News

EYES IN THE JUNGLE

THE distinction between curable and incurable blindness disappears when the remedy is out of reach. Patients in out-of-the-way parts of the world often carry this great affliction to their graves, when in luckier situations they would be quickly cured or never allowed to lose their sight at all. A hospital to treat eyes in such a backward region does rewarding work, and such is the Santal Mission Hospital of the Free Church of Scotland, at Bamdah, some 200 miles north-west of Calcutta. Actually there are now three hospitals—at Bamdah, Tisri, and Pachamba. The story of this hardy and active enterprise has been told by Dr. R. M. Macphail,[1] whose father, Dr. J. M. Macphail, took a case of surgical instruments to India when he joined the mission in 1889, and persuaded the unwilling jungle people to let him use them for their relief. The hospital he founded at Bamdah treated 8000 patients in 1947, and 6895 of these were operated on, 2900 of them for cataract. The first patient had to be paid about 7*s.* 6*d.* before he would consent to the operation. The doctor travelled round his district with "a good supply of drugs and gospels"; and was kept busy teaching, preaching, and dispensing medicines. He did not confine himself to eye surgery; but as he got to know the people and gained their confidence he realised that none of his patients were more to be pitied than the blind: they could not earn a living in a community of manual workers, but were useless and miserable. When a blind man from one of the villages came home seeing from the mission, the problem of persuading patients to accept treatment was over; they came of their own accord. Bamdah lies on a pilgrim route, and thousands pass the hospital doors in cold weather; they too carried news of the hospital to their homes. Once there was a maharajah's elephant to treat for pink-eye. When a patient asked what treatment it was getting, old Dr. Macphail replied "The same as yourself." This made a deep impression on the people: poor as they were, they were being treated as well as a maharajah's elephant, and the prestige of the hospital rose afresh.

The surgical work has increased enormously since those early days. In 1895, eye operations numbered 49 and all operations 99; in 1947 the comparable figures were 5980 and 6895. Eyes take the lead, but the hospital also has a thriving surgical practice in hæmorrhoids, and in general operations of all kinds. Its credit is high with the people partly because it is homely; they are not asked to come into unfamiliar bleak surroundings. Their families camp in the compound, and when extra wards are needed the patients' friends put up a few turf wigwams. Patients sit round the walls of the operating-room, waiting their turn and consenting to have their eyes prepared and their caste-marks washed off by the Christian Santal orderlies, outcasts though they are. The work done is so good that a steady flow of skilled ophthalmologists visit the hospital to increase their experience, and help with the pressure of work during the cataract season. Dr. R. M. Macphail's account of his, and his father's, hospital is good reading. Like most people who are getting something done he does not waste words; but the ones he uses are lively and revealing.

DANGEROUS DRUGS REGULATIONS

THE Dangerous Drugs Regulations, 1948 (S.I. 1948, no. 2653), which come into force on Jan. 1, make some minor changes in the Dangerous Drugs Regulations, 1937, in order to bring these regulations into line with other legislation, and also to resolve certain doubts felt by the public during the past eleven years.

Under regulations 2 and 7 authority to dispense dangerous drugs in institutions is restricted to doctors, qualified pharmacists, and—if neither of these are employed—matrons or acting matrons. Persons having certain other qualifications who are now employed as dispensers will be qualified to continue in such employment.

Regulation 4 makes it the duty of every authorised person to take proper care of any dangerous drugs in his possession. The requirement that an authorised seller of poisons shall keep his stocks under lock and key is extended to all authorised persons. Under the Dangerous Drugs Act, 1920, as amended by the Dangerous Drugs and Poisons (Amend-

1. Whereas They Were Blind. The Church of Scotland Foreign Mission Committee, 121, George Street, Edinburgh, 2. Pp. 35. 1*s.*

ment) Act, 1923, the burden of proving "any licence, authority, or other matter of exception or defence" lies on the person seeking to avail himself thereof. "There would thus seem to be no need," says the Home Office, "for the prosecution to prove, or even allege, negligence when dangerous drugs are found otherwise than in a locked case, box, or other suitable receptacle." The Home Secretary has been advised that a cupboard in a room can be regarded as a suitable receptacle, but that the room of a house, or a motor-car, cannot.

In regulation 9 two new drugs—'Amidone' and pethidine—are added to those in respect of which a separate register or part of a register must be kept. All entries must in future be so made that the completed record shows each purchase or supply in its proper sequence.

Regulation 10 specifies the preparations of opium which practising midwives may obtain on their own authority; no proprietary preparations containing morphine are included.

COTSWOLDS CALLING

IN a period of urbanisation without parallel in English history Mr. Robertson Scott has devoted his time and journalistic talent to keeping alive the love of the countryside and the culture of man's whole personality. He could not have done this without possessing an attractive personality of his own which has brought him many friends, including 4 prime ministers. This book is a selection of articles and illustrations from the *Countryman* which he founded and edited for a score of years. The 60,000 subscribers may know already, in instalments, how Mr. Henry Wallace grows strawberries from seed, what Mr. Hugh Walpole does in his top room, and what happened to the duck that couldn't read; but the novice can now enjoy them all, at one sitting, for half a guinea (Odhams Press, pp. 352, of which 32 are illustrations).

CATHOLIC MEDICAL MISSIONARIES

IN 1936, a few months after missionary sisters of the Catholic Church were first permitted to engage in maternity and child-welfare work and in the practice of medicine, Miss Mary Martin sailed with two companions to Nigeria to become foundress of the Medical Missionaries of Mary. What has been achieved by the new order is set out in *The First Decade*.[1] In 1940 they took over Our Lady of Lourdes Hospital at Drogheda which has become their nursing training centre. At first it had 12 beds, now it has 75. They also have a house of studies near Dublin from which students attend University College. Since 1942 the sisters have been in charge of the mission hospital at Anua in Calabar, and last year Afikpu General Hospital was opened in Ogoja Province, where there are three leper settlements. The order has also two missions in Tanganyika. At present 29 sisters are working on the missions, of whom 4 are doctors.

VENEZUELAN TROPICAL ARCHIVES

THE Institute of Tropical Medicine in Venezuela began to publish last January *Archivos Venezolanos de Patología Tropical y Parasitología Médica*. In the first number pride of place is given to proof that *Trypanosoma rangeli*, discovered by Tejera [2] in 1920, can parasitise man. This trypanosome is a parasite of *Rhodnius prolixus*, a reduviid bug which is the vector of *T. cruzi*, the cause of Chagas's disease in man. Many of these bugs have the double infection, but until 1947 all attempts to isolate *T. rangeli* from the blood of a patient with Chagas's disease failed, though Dias and Torrealba [3] found in 1942 both trypanosomes in a previously uninfected bug which had fed on a patient with the disease. Two questions then arose: (1) is this disease due to a double infection? and (2) can *T. rangeli* alone cause it? In 1947 C. Pifano et al. [4] communicated to the Venezuelan National Academy of Medicine the fact that they had isolated *T. rangeli* from a case of Chagas's disease without being able to isolate *T. cruzi*, hitherto regarded as the sole cause of Chagas's disease. These workers admit, however, that this case may have been due to *T. cruzi* which they were unable to isolate, and the questions therefore remain unanswered until further work is done.

Other articles in the first number of this new periodical describe the lesions caused by *Schistosoma mansoni*; experiments on unisexual infections by *S. mansoni*; the distribution and characters of *Anopheles albimanus*, the chief vector of malaria in Venezuela; marsupials and primates concerned in sylvatic yellow fever; the treatment of bilharziasis with antimony compounds; sprue; and synthetic antimalarial drugs. The type and illustrations are good.

1. Obtainable from the Medical Missionaries of Mary, Our Lady of Lourdes, Drogheda, co. Louth.
2. Tejera, E. *Bull. Soc. Path. exot.* 1920, **13**, 527.
3. Dias, E., Torrealba, J. F. *Mem. Inst. Osw. Cruz*, 1943, **39**, 265.
4. Pifano, C. F., Mayer, M., Medina, R., Henrique, B. P. *Arch. venezol. Pat. trop.* 1948, **1**, 1.

Faculty of Radiologists

At a recent examination for the fellowship the following were successful:

E. P. Allen, J. H. Middlemiss (radiodiagnosis); G. W. Boden, W. M. Court Brown, O. B. Millar (radiotherapy).

British Legion Village

Dr. F. Temple Clive, physician-superintendent to Preston Hall Hospital, has been appointed acting hon. medical director of the British Legion Village. Dr. F. R. G. Heaf, who has resigned from the directorship, has been coöpted as a member of the council of management.

Services Hygiene Group

The second annual dinner of this group of the Society of Medical Officers of Health will be held in the Quadrant Restaurant, Regent Street, on Friday, Jan. 28 at 7.30 P.M. All past and present hygiene officers are invited to attend. Further information may be had from Dr. G. M. Frizelle, the hon. secretary, London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.

Ophthalmological Society of the United Kingdom

The annual congress of the society will be held at 1, Wimpole Street, London, W.1, on March 31 and April 1 and 2. The subject for discussion will be Corneal Grafting, and the opening speakers will be Dr. R. Townley Paton (New York), Prof. A. Franceschetti (Geneva), Prof. G. P. Sourdille (Nantes), and Mr. J. W. Tudor Thomas (Cardiff). Further particulars may be had from the hon. secretaries, 45, Lincoln's Inn Fields, W.C.2.

Congress of Obstetrics and Gynæcology

The twelfth British Congress of Obstetrics and Gynæcology will be held at Friends House, Euston Road, London, N.W.1, on July 6, 7, and 8 under the presidency of Sir Eardley Holland. The subjects for discussion are to include: Modern Cæsarean Section (opening speaker, Mr. C. McIntosh Marshall, Liverpool); Essential Hypertension in Pregnancy (Prof. G. W. Pickering and Prof. F. J. Browne, London); Modern Concepts in Diagnosis, Treatment, and Prognosis of Carcinoma of the Uterus (Dr. J. E. Ayre, Montreal, Prof. G. Strachan, Cardiff, Mr. A. Glucksmann, Cambridge, and Dr. Joe Meigs, Boston); Maternal Mortality (Sir William Gilliatt, London). Further information may be had from Dr. A. J. Wrigley, hon. secretary, 58, Queen Anne Street, W.1.

Ella Sachs Plotz Foundation

During the 25th year of this foundation for the advancement of scientific investigation, 26 applications for grants were received, of which 15 came from the United States, and the remainder from seven different countries in Europe and Asia. Altogether 15 grants were made during the year. Grants are made to researches in medicine and surgery. They may be used for the purchase of apparatus and supplies for special investigations, and for the payment of unusual expenses incident to such investigations, including technical assistance, but not for providing apparatus or materials which are ordinarily a part of laboratory equipment. Stipends for the support of investigators will be granted only under exceptional circumstances. Usually grants will not exceed $500, but in special instances they may be up to $1000. Applications for the year 1949–50 should be sent before April 15 to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston 14, Mass., U.S.A.

A report of the International Congress on Physical Education, Recreation, and Rehabilitation, held in London last July, has been published, and is obtainable, price 2*s.* 6*d.*, from the congress offices, 6, Bedford Square, London, W.C.1.

A new transparent elastic bandage for the rheumatic is composed of "an elastomer produced by reacting methyl salicylate with a mixture of polymerised thermoplastic synthetic resins, modified waxes and esters." At normal body temperature the bandage is claimed to release methyl salicylate at the rate of 3·5 mg per sq. in. per hour. This product is to be marketed under the name 'Polyestol' by Messrs. Polyestol Ltd., 45, Warwick Court, High Holborn, London, W.C.1.

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REFERENCES AND ABBREVIATIONS

Institutions and Corporations with the right to the prefix Royal will be found under that prefix, with the exception of Medical Societies, which are separately indexed under Societies. All Universities are indexed under the word Universities. (*A*) = *Annotation*, (*C*) = *Correspondence*, (*LA*) = *Leading Article*, (*ML*) = *Medicine and the Law*, (*NI*) = *New Invention*, (*O*) = *Obituary*, (*P*) = *Parliament, and* (*R*) = *Review.*

A Concordance of page numbers and dates of issue will be found on opposite page

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